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CONTENTS

Session 2: Keynote Lectures
AN OVERVIEW OF ADVANCED TECHNIQUES IN RT:
IMRT, IGRT, RADIOSURGERY

IAEA-CN-170/001
Overview of advanced techniques in radiation therapy................................................................. 3
J. Van Dyk

IAEA-CN-170/002
Technical innovations in radiation oncology: A clinician’s perspective....................................... 5
L.B. Marks

IAEA-CN-170/003
Advanced radiotherapy with small and IMRT beams: Limitations of current dosimetry.............. 7
P. Andreo

Session 3a:
ADVANCES IN CHEMO-RT FOR CERVICAL AND HEAD & NECK CANCER

IAEA-CN-170/004
Are we justified for concomitant chemo-radiation in advanced stage cancer cervix?............... 13
S.K. Shrivastava, U. Mahantshetty, H.B. Tongaonkar, S. Gupta, R. Engineer,
R.A. Ker kar, A. Maheshwari, K. Dinshaw

IAEA-CN-170/006
Advances in chemo-RT for cervical and head & neck cancer .................................................... 15
R. Ferrigno

IAEA-CN-170/007
Contraindications to cisplatin-based chemotherapy in the treatment of cervical cancer
in Sub-Saharan Africa .................................................................................................................. 17
O. McArdle, J.B. Kigula-Mugambe

Session 3b: COMMISSIONING AND IMPLEMENTING
A QUALITY ASSURANCE PROGRAMME FOR NEW TECHNOLOGIES

IAEA-CN-170/008
Commissioning and implementing a quality assurance programme for new technologies......... 21
J. Van Dyk

IAEA-CN-170/009
Introduction of RapidArc™: An example of commissioning and implementing
a QA programme for a new technology ...................................................................................... 23
W.P.M. Mayles

IAEA-CN-170/010
Image guidance in the radiotherapy treatment room: An opportunity to learn,
to improve practice and to generate evidence ................................................................. 25
T. Kron, C. Fox, F. Foroudi, J. Thomas, A. Thompson, R. Owen,
A. Herschtal, A. Haworth, K.H. Tai

IAEA-CN-170/011
Principles and practice of electronic brachytherapy ................................................................. 27
J.R. Hiatt, G.A. Cardarelli, D.E. Wazer, E.S. Sternick
Lunch Forum I: *Refresher Course on TRANSITION FROM 2-D TO 3-D CONFORMAL RADIOOTHERAPY AND IMRT*

**IAEA-CN-170/012**
The transition from 2-D to 3-D conformal radiotherapy – IAEA guidelines ........................................ 31
  - S. Vatiniskiy

**IAEA-CN-170/013**
Implementing 3-D conformal radiotherapy and intensity modulated radiotherapy in a clinical practice: Recommendations of IAEA-TECDOC-1588 ........................................ 33
  - M.S. Huq

**IAEA-CN-170/014**
From 2-D to 3-D conformal radiation therapy (3-D CRT) and IMRT:
The AC Camargo Hospital experience ................................................................. 35
  - P.E. Novaes

**IAEA-CN-170/015**
Transition from 2-D to 3-D conformal radiotherapy in high grade gliomas:
Our experience in Cuba ...................................................................................... 38
  - I. Chon, D. Chi, J. Alert, R. Alfonso, C. Roca

**Session 5a: Poster Session**
**POSTERS RELATED TO RADIATION ONCOLOGY AND RADIObIOLOGY**

**IAEA-CN-170/080P**
Volunteer outreach to radiation oncology facilities outside of North America by the American Society for Radiation Oncology .......................................................... 43
  - T.J. Wall

**IAEA-CN-170/081P**
Anesthesia in radiotherapy – 1048 procedures in children ........................................ 45

**IAEA-CN-170/082P**
A successful alternative to provide radiotherapy services in paediatric cancer care for low-income populations in Brazil ................................................................. 47

**IAEA-CN-170/083P**
Cervical carcinoma in women under 25 years old .................................................. 49
  - M. De Melo, P. Novaes, E. Alves, G. Teixeira, J. Salvajoli

**IAEA-CN-170/084P**
PTV coverage evaluation when comparing 3-D with 2-D techniques for breast treatment planning .............................................................. 51
  - D.E.E. Moura, W. Boccaletti

**IAEA-CN-170/085P**
Results and complications of high dose-rate brachytherapy associated with 2-D or 3-D external beam irradiation in prostate cancer ........................................ 53

**IAEA-CN-170/086P**
Intense modulated radiotherapy (IMRT) in paediatric patients:
When the indication is an advantage ......................................................................... 56
IAEA-CN-170/087P
Implementation of 3-D CRT and IMRT for prostate cancer: A three year experience
at the National Cancer Institute of Colombia................................................................. 58
R. Ospino, I. Vásquez, R. Cendales, H. Machado

IAEA-CN-170/088P
Recurrent glioma: Is re-irradiation a feasible option?.................................................. 59
P. Sminia, R. Mayer

IAEA-CN-170/089P
Design and evaluation of a national programme to increase the capacity for radiation oncology ..... 61
P.H. Vos

IAEA-CN-170/090P
Impact of $^{18}$F-FDG-PET/CT on staging and radiation treatment planning of patients
with primary locally advanced pelvic malignances ....................................................... 63
B. Paskeviciute, M. Weckesser, S. Könenmann

IAEA-CN-170/091P
Future of cobalt-60 in the treatment of cancer ............................................................ 64
B.N. Patil, K.V.S. Sastri, A.K. Kohli

IAEA-CN-170/092P
Intensity modulated radiotherapy for functional lung avoidance in radiotherapy
of non-small cell lung cancer: An update of a planning study.................................... 66
K. Lavrenkov, C. Singh, J.A. Christian, M. Partridge, E. Niotiskou,
G. Cook, J.L. Bedford, M. Brada

IAEA-CN-170/093P
CT-based planning for craniospinal irradiation............................................................ 68
I. Jaradat, L. Abu Arida, A.Al-Mousa

IAEA-CN-170/094P
Establishing plaque therapy for ocular tumours in Jordan........................................ 70
I. Jaradat, S. Ramahi, L. Mula Hussain

IAEA-CN-170/095P
Conformal forward radiation treatment planning using PET/CT and lymphatic
Atlas based target volume definition........................................................................... 72
S.M. Qatarneh, A. Nour, S. Al-Heet, A. Al-Mousa

IAEA-CN-170/096P
In-house low cost shield for pregnant radiotherapy patients...................................... 74
S. Wadi Ramahi, S. Heet, F. Waqqad, I. Rashdan, N. Al-Nassir

IAEA-CN-170/097P
Transition from 2-D to 3-D conformal radiotherapy of brain malignant gliomas............. 76
V. Kim, T. Antropova

IAEA-CN-170/098P
Tolerability of chemo-radiation in patients undergoing treatment for cervical cancer
in Sarawak, Malaysia ................................................................................................ 78
C.R.B. Devi, Tieng Swee Tang

IAEA-CN-170/099P
Development of specialist training programme in clinical oncology: The Malaysian experience....... 80
D.W.Y. Wong, G.C.C. Lim, F.N. Lau, N. Abdullah, I. Fuad, A.Z. Bustam

IAEA-CN-170/100P
Analysis of ethnic and regional disparities and appropriate intervention rate for the use
of radiotherapy in lung cancer in New Zealand ......................................................... 82
G. Stevens, W. Stevens, S. Purchuri, J. Kolbe, B. Cox
Effects of radiotherapy on cancer patients infected with HIV/AIDS in Nigeria

E. Oyekunle, M. Aweda

Experience and problems of managing a randomized clinical trial in a low income
and a low resource country, Pakistan: A success story

N. Begum

To compare treatment outcome with ring and Fletcher type applicators in
brachytherapy of carcinoma cervix

N.A. Laghari, K. Akhtar, Naseema, M. Nadeem

The role of brachytherapy in cancer cervix experience
at the Nuclear Medicine, Oncology and Radiotherapy Institute, Islamabad

H. Mahmood

Image-guided IMRT for prostate cancer: Influence of organ motion correction
associated with acute toxicity and quality of life

K.R.G. Britton, Y. Takai, K. Nemoto, Y. Ogawa, M. Mitsuya, R.S. Britton, S. Yamada

Definitive radiotherapy in young patients newly diagnosed with nasopharyngeal carcinoma

P. Kamnerdsupaphon, V. Lorvidhaya, I. Chitapanarux, E. Tharavichitkul, V. Sukthomya

Total lymphocyte count in HIV/AIDS patients with carcinoma during radiation therapy

P. Siraprapasiri, T. Siraprapasiri, Y. Kongthanarat

A randomized trial comparing between two fractionation schedules in the treatment
of metastatic bone pain

V. Sukthomya, K. Katanyoo, I. Chitapanarux, P. Kamnerdsupaphon, V. Lorvidhaya

Vaginal vault brachytherapy in low risk endometrial cancer

C. Nasr, L. Kochbati, D. Hentati, K. Mahjoubi, A. Abbassi, L. Salem, S. Abdessaied,
F. Ben Abd, M.Besbes, M. Maalej

Evolution from 2-D to 3-D: Crasniospinal irradiation

P.M. Sempere-Rincon

Retinoblastoma: Treatment of one eye. Comparative analysis of external radiotherapy techniques

E.C. Raslawski, L. Mairal

Experience in total body irradiation in one institution

E.C. Raslawski, C. Figueroa, M. Bonduel, M.L. Mairal

Adapting the linear accelerator room to perform electron intraoperative radiotherapy
for early breast cancer

C. Campos

Image guided high dose rate brachytherapy as salvage for recurrent prostate cancer
after definitive external beam radiotherapy

A.C.A. Pellizzon, R. Miziara, M. Miziara, C. Neviani, C. Soares, R.C. Fogaroli
IAEA-CN-170/115P
Collaboration with the IAEA to improve cancer care in Estonia .................................................. 106
  E. Gershkevitsch, M. Kuddu

IAEA-CN-170/116P
Robotic extracranial stereotactic radiotherapy in lung, liver and head and neck tumours:
The role of the CyberKnife® ......................................................................................................... 107
  E. Lartigau

IAEA-CN-170/117P
Train the trainers ................................................................................................................................. 109
  M. Coffey, G. Vandevelde, A. Osztavics, E. Rosenblatt

IAEA-CN-170/118P
Strategy of the system physicotechnical development of radiation oncology in Russia ............... 111
  V. Kostylev

IAEA-CN-170/119P
Implementing IMRT for head & neck – the steps of the process .................................................. 113
  M.C. Lopes, B.C. Ferreira, J. Mateus, M. Capela

IAEA-CN-170/120P
The dermatoradiotoxicity during radiotherapy ........................................................................... 115
  N.S. Karamyan, H.M. Galstyan, S.K. Karamyan

IAEA-CN-170/121P
Experience of transition from 2-D to 3-D radiation therapy in a centre of a developing country ... 117
  S. Afroz, A.M.M.S. Alam, A.F.M. Kamaluddin

IAEA-CN-170/122P
Establishing a quality assurance programme in radiosurgery .................................................... 119

IAEA-CN-170/123P
Efficacy evaluation of prophylactic low energy laser application in patients
  with chemotherapy and radiotherapy-induced oral mucositis .................................................... 121
  A. Gouvea de Lima, R.C. Villar, W. Nadalin, I. Snitcovsky

IAEA-CN-170/124P
Preliminary study of genes related to the concomitant chemoradiotherapy sensitivity
  in advanced uterine cervical squamous cell carcinomas ........................................................... 124
  An Jusheng, Huang Manni, Song Yongmei, Wu Lingying, Zhan Qinmin

IAEA-CN-170/125P
Concurrent chemo-radiotherapy versus radiotherapy with boost in locally advanced
  unresectable rectal cancers. A randomized phase II study ......................................................... 127

IAEA-CN-170/126P
Locally advanced inoperable carcinoma pancreas and gall bladder treatment with
  concurrent chemoradiation using tomotherapy based IMRT and IGRT: Case series ................. 130

IAEA-CN-170/127P
Role of the Board of Radiation & Isotope Technology (BRIT) in combating cancer in India ....... 132
  A.K. Kohli

IAEA-CN-170/128P
A Phase II randomized trial comparing IMRT with conventional radiation therapy
  in stage IIB carcinoma cervix: An audit ......................................................................................... 135
IAEA-CN-170/129P
Comparison of gross tumour volume and planning target volume with 3-D conformal radiotherapy planning versus 2-D ................................................................. 137
N. Gombodorj, L. Bold

IAEA-CN-170/130P
Adjuvant radiotherapy in ‘peculiar’ African breast cancer ................................................................. 140
D.A. Dawotola, V.I. Odigie, A.T. Ajekigbe, A. Adamua

IAEA-CN-170/131P
Radiation dose optimization and risk estimation to patients undergoing HDR brachytherapy with ring applicators................................................................. 141
E. Oyekunle, R. Obed

IAEA-CN-170/132P
Treatment outcome of 3-D conformal radiation therapy for localized prostate cancer: Preliminary experience................................................................................... 143
M. Mejia, A. Mejia, A. Alveo

IAEA-CN-170/133P
Hypofractionated external beam radiotherapy and interstitial HDR brachytherapy for intermediate and high risk prostate cancer ........................................ 145
A.C.A. Pellizzon, P.E.R.S. Novaes, J.V. Salvajoli, R.C. Fogaroli

IAEA-CN-170/134P
Treatment of malignant pheocromocitoma with high dose (800 mCi) of $^{131}$I MIBG in a young female. How to prevent and manage secondary side effects................................. 147
P. Orellana, G. Váldes, F. Barriga

IAEA-CN-170/135P
Angiogenesis of VEGF-A and MVD as the predictor of accelerated fractionation radiotherapy efficacy on nasopharyngeal carcinoma ......................................................... 149
S. Soetopo, B.H. Suryawati, L. Lasmingrum, B. Hidayat, F. Anwari, T.H. Fadjari, K. Lina

IAEA-CN-170/136P
Benchmark use of 3-D conformal planning dose-volume histograms to predict use of intensity modulated radiotherapy under resource constraints.............................. 152
G. Jones, N. Jones

IAEA-CN-170/137P
Development of indigenous HDR brachytherapy equipment: An effort towards affordable cancer treatment in India................................................................. 154
A.C. Dey, A.K. Kohli

IAEA-CN-170/138P
Dose-fractionation sensitivities of low/middle/high risk prostate cancer deduced from eight international primary institutional datasets ........................................ 156

Session 5b: Poster Session
POSTERS RELATED TO MEDICAL PHYSICS

IAEA-CN-170/140P
Establishing the efficacy of radiation oncology – standardizing the collection and validation of 3-D treatment planning data ................................................................. 161
M.A. Ebert, D.J. Joseph, A. Haworth, N.A. Spry, S. Bydder, R. Kearvell, B. Hooton

IAEA-CN-170/141P
Value of whole body bone SPECT for metastatic work-up in clinical oncology: A study with 120 patients ................................................................. 163
S. Afroz, S. Hossain, S. Reza
IAEA-CN-170/142P
Absorbed dose to water FeSo4-based standard for $^{192}$Ir HDR brachytherapy........................................... 165
  C.E. de Almeida, R. Ochoa, C. Austerlitz, M. Coelho, M. Gazineu, J.G. Peixoto,
  E.J. Pires, R.R. Allison, H. Mota, C. Sibata

IAEA-CN-170/143P
Contrast materials influence at computed tomography in 3-D radiotherapy planning
  for thorax tumours...................................................................................................................... 167
  J.R. Dias, H.L. Martins, K.W. Boccaletti, J.V. Salvajoli

IAEA-CN-170/144P
Integration and commissioning of the cobalt unit Terabalt 80 ASC
  into TPS Oncentra MasterPlan.............................................................. 169
  N. Gesheva-Atanasova, E. Dimitriou

IAEA-CN-170/145P
Radioisotopic therapy for neuroendocrine tumours with radiolabelled-somatostatin
  analogues in Chile..................................................................................................................... 171
  J. Canessa, T. Massardo, P. Arteaga, G. Cerda, J. Ilzauspe, P. Pineda, M. Cecilia Gil

IAEA-CN-170/146P
Dosimetric characterization of an aSi-based EPID for patient-specific IMRT QA .................. 173
  E. Larrinaga-Cortina, R. Alfonso-Laguardia, I. Silvestre-Patallo, F. Garcia-Yip

IAEA-CN-170/147P
Dosimetric verification of radiotherapy treatment planning systems in Hungary.................. 175
  C. Pesznyák, I. Polgár, P. Zaránd

IAEA-CN-170/148P
Output factors of small photon beams using GafChromic EBT film.................................... 177

IAEA-CN-170/149P
Commissioning of IMRT for small intracranial lesions................................................... 179
  J.M. Lárraga-Gutiérrez, O.A. García-Garduño, P. Ballesteros-Zebadúa,
  O. Galván de la Cruz, A. Celis Miguel

IAEA-CN-170/150P
Barriers to implementation of new technology in radiation oncology:
  The New Zealand experience..................................................................................... 181
  G. Stevens

IAEA-CN-170/151P
Cost implication of usage of cobalt teletherapy machine versus linear accelerator
  in a developing country............................................................................................................. 183
  D.A. Dawotola, V.I. Odigie, F. Ighinoba, A.R. Oyesegun, S.O. Ojebode, V. Sharma

IAEA-CN-170/152P
Pretreatment verification of dose calculation and delivery by means of measurements
  with PLEXITOM® phantom................................................................................................. 185
  P. Wolowiec, P. Kukołowicz, K. Lis

IAEA-CN-170/153P
TLD audits in non-reference conditions in radiotherapy centres in Poland........................ 187
  J. Rostkowska, M. Kania, W. Bulski, B. Gwiazdowska

IAEA-CN-170/154P
Quality assurance programme implementation for computerized treatment planning systems.... 189

IAEA-CN-170/155P
Implementation of linac quality control for IMRT technique.............................................. 191
  A. Chervyakov, E. Baranov, E. Kusnetsova, V. Khrunov
<table>
<thead>
<tr>
<th>Document Code</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAEA-CN-170/156P</td>
<td>Testing of treatment planning system in aspect of transitioning from 3-D to IMRT</td>
<td>M. Fominsteva, T. Bochkareva, D. Grischuk</td>
</tr>
<tr>
<td>IAEA-CN-170/157P</td>
<td>Practical aspects of radiochromic films implementation for clinical QA</td>
<td>M. Lavrova, V. Rebyakova, T. Tatarinov</td>
</tr>
<tr>
<td>IAEA-CN-170/158P</td>
<td>Transition of 2-D to 3-D craniospinal irradiation and resulting quality improvement: An IAEA/RCA RAS/6/048 project of Singapore</td>
<td>F.K.C. Chin, P. Salleh, V.K. Sethi</td>
</tr>
<tr>
<td>IAEA-CN-170/159P</td>
<td>Tissue equivalent absorption in combined wax and rubber layers using 1.25 MeV gamma ray</td>
<td>J. Jeyasugiththan, N. Jeyakumaran, N. Sivayogan, U. Sutharsini</td>
</tr>
<tr>
<td>IAEA-CN-170/160P</td>
<td>Doses to patients from photoneutrons emitted in a medical linear accelerator</td>
<td>M.K. Saeed, O. Moustafa, O.A. Yasin, C. Tuniz</td>
</tr>
<tr>
<td>IAEA-CN-170/161P</td>
<td>A method for testing the Linac jaw position of adjacent fields using the EPID</td>
<td>E. Nilsson, M. Berglund, A. Palm</td>
</tr>
<tr>
<td>IAEA-CN-170/162P</td>
<td>Superficial dose distribution in breast for tangential photon beams, clinical examples</td>
<td>R. Chakarova, A. Bäck, M. Gustafsson, A. Palm</td>
</tr>
<tr>
<td>IAEA-CN-170/163P</td>
<td>Use of an amorphous silicon electronic portal imaging device for fast and accurate MLC leaf position verification</td>
<td>C. Kakanaporn, S. Fuk-on, P. Iampongpaiboon</td>
</tr>
<tr>
<td>IAEA-CN-170/164P</td>
<td>Applications of statistical process control to radiotherapy quality control</td>
<td>T. Sanghangthum, T. Pawlicki, S. Suriyapee</td>
</tr>
<tr>
<td>IAEA-CN-170/165P</td>
<td>Comparison of dose distributions of Novalis Brainlab treatment planning system, Monte Carlo (BEAMnrc and DOSRZnrc) and in vivo dosimetric measurement methods</td>
<td>N. Kodaloglu</td>
</tr>
<tr>
<td>IAEA-CN-170/166P</td>
<td>Evaluation of radiation dose for stereotactic radiosurgery systems in Korea</td>
<td>Dong Han Lee, So Hei Seo, Dong Oh Sin, Mi Sok Kim, Chang Hoon Rhee</td>
</tr>
<tr>
<td>IAEA-CN-170/167P</td>
<td>Radionuclide study of sentinel lymph nodes in patients with breast cancer</td>
<td>O. Solodyanykova</td>
</tr>
<tr>
<td>IAEA-CN-170/168P</td>
<td>Analysis of dose uniformity in total body irradiation for paediatric patients</td>
<td>M.L. Matral, S. Paidon, D.B. Feld, E.C. Raslawski</td>
</tr>
<tr>
<td>IAEA-CN-170/169P</td>
<td>First steps in 3-D radiotherapy in Bolivia with cobalt-60</td>
<td>R. Delgado Aguirre</td>
</tr>
<tr>
<td>IAEA-CN-170/171P</td>
<td>Clinical usage of a novel verification system for intensity modulated radiation therapy</td>
<td>S. Heyden, M. Kretschmer, F. Wuerschmidt, L. Mueller</td>
</tr>
</tbody>
</table>
IAEA-CN-170/172P
Verification of LGP prediction in gamma knife in presence of inhomogeneities using PAGAT polymer gel dosimeter .......................................................... 221
M. Allahverdi, T. Allahverdi Pourfallah, N. Riahi Alam, M. Ay

IAEA-CN-170/173P
Production of a new type of low-cost high-density concrete for shielding megavoltage radiotherapy bunkers .................................................. 224
M.A. Mosleh-Shirazi, S.M.J. Mortazavi, M.R. Maheri

IAEA-CN-170/174P
CT-based intracavitary brachytherapy for gynaecologic tumours: First experience .................. 226
V. Bairac, D. Sorfoni, N. Samet, L. Gutu

IAEA-CN-170/175P
Results of practical implementation of film dosimetry for routine verification of IMRT plans .... 228
K. Chelmiński, W. Bulski, P. Kamiński, J. Rostkowska, M. Kania, A. Walewska,
M. Zalewska, I. Markiewicz, P. Grochowska

IAEA-CN-170/176P
What is an appropriate radiotherapy technology? A Pretoria Academic Hospital perspective .... 230
A. Janse van Rensburg

IAEA-CN-170/177P
A. Quarneri, A. De Rosa, C. Mara, A. Patiño Tec, B. Tasende

IAEA-CN-170/178P
Regulating emerging technologies .................................................................................. 233
C. Flannery

IAEA-CN-170/179P
Effectiveness of IVD as a tool for QA in radiotherapy .......................................................... 234
W. Nyakodzwe

IAEA-CN-170/180P
University based IMRT implementation in Chile .................................................................. 235
P.C. Besa, A. Viera, J. Delgado, P. Besa

IAEA-CN-170/181P
Pre-clinical commissioning of plans with an aperture based IMRT treatment planning system .......................................................... 237
M. Nápoles, Y. Yanes, Y. Ascenció, R. Alfonso, C. Calderón

IAEA-CN-170/182P
Building of a low cost calibrated density phantom to perform quality assurance
to comply with IAEA TRS-430 protocol ........................................................................... 238
C.A. Castellanos

IAEA-CN-170/184P
Elaboration and commissioning of a phantom for quality control in a linac based stereotactic radio surgery system ........................................ 241
A. Osorio, M.A. Ortega, E. Hernández, L. Ureta

IAEA-CN-170/185P
Absolute dose measurement as a verification tool for patient specific QA in IMRT ................ 243
T. Kataria Sethi, N. Janardhan, R. Nair

IAEA-CN-170/186P
Intensity modulated radiation therapy for craniospinal irradiation using helical tomotherapy:
Initial experience from planning to delivery ........................................................................ 245
R. Phurailatpam, B. Zade, T. Gupta, R. Jalali, Z. Master, R. Sarin, A. Manshi,
D. Deshpande, S. Shrivastava, K. Dinshaw

ix
IAEA-CN-170/187P
Dosimetric characteristics of 2-D ion chamber array matrix for IMRT dose verification .............. 247
S. Sathiyan, M. Ravikumar, S.S. Supe

IAEA-CN-170/188P
Inverse planning simulated annealing (IPSA) planning for 3-D image based HDR
brachytherapy in cervical cancers: A dosimetric study ................................................................. 249
S. Sharma, S.V. Jamema, U.M. Mahantshetty, R. Engineer, S.K. Shrivastava,
D.D. Deshpande, K.A. Dinshaw

IAEA-CN-170/189P
A new biologic radiopharmaceutical for targeted therapy of breast cancer:
177Lu labelling of Mab PR81 and quality control ................................................................. 251
M. Salouti, M.H. Babaei, H. Rajabi, M.J. Rasaei, F. Johari Daha, H. Forootan,
J. Mohammadnejad, A. Bitarafan, M. Shafiee

IAEA-CN-170/190P
4-D CT imaging technique for conformal forward planning in lung tumours .......................... 253
S. Wadi-Ramahi, J. Khader

IAEA-CN-170/191P
The role of deep inspiration breath hold with active breathing control and image-guided
radiation therapy for patients treated with lung cancers .......................................................... 256
K.R. Muralidhar, Madhusudhansresty, R. Lochan Shu, B. Kumar Raut, Poornima,
Subash, Mallikarjun, Anil, A.K. Raju, Vidya, G. Sudarshan, S. Mahadev, P. Narayana Murthy

IAEA-CN-170/192P
Implementation of IMRT techniques in treatment of head & neck tumours ............................ 258
E. Bolsesiková, M. Zemanová, M. Svantnerová, M. Sandorová, G. Králik, J. Svec

Session 6: Keynote Lectures
IMAGING IN RADIOTHERAPY PLANNING

IAEA-CN-170/016
PET/CT: Is there a role in RT planning? ...................................................................................... 261
C. Messa

IAEA-CN-170/017
New advances in CT: Dose reduction and functional imaging .................................................. 263
Ting-Yim Lee

IAEA-CN-170/018
Functional image-based adaptive IMRT: Dream or reality? ...................................................... 266
V. Grégoire

Session 8a: CURRENT TRENDS IN BRACHYTHERAPY

IAEA-CN-170/019
Current issues and trends in brachytherapy: A medical physics perspective ......................... 269
J.L.M. Venselaar, M.J. Rivard

IAEA-CN-170/020
Potential and limitations of image-guided brachytherapy in cervical cancer .......................... 272
R. Pötter

IAEA-CN-170/021
New directions in prostate brachytherapy .............................................................................. 273
M.J. Zelefsky

IAEA-CN-170/022
A prospective randomized study comparing three-fraction regimen of HDR
brachytherapy for cancer of uterian cervix stages IIB and IIIB ............................................. 275
W. Tigeneh
Session 8b: HOW TO SET UP A QA PROGRAMME

IAEA-CN-170/023
How to set up a QA programme ................................................................. 279
T. Knöös

IAEA-CN-170/024
Developing a quality assurance programme for cooperative group clinical trials ............... 282
G.S. Ibbott

IAEA-CN-170/025
How to set up a quality assurance programme .................................................. 284
K.Y. Cheung, K.H. Yu, A.T.C. Chan

IAEA-CN-170/026
Setting up a QA programme: ESTRO's recommendations ........................................ 286
P. Scalliet

Session 9: Keynote Lectures
TRAINING, EDUCATION AND STAFFING:
GETTING READY FOR NEW TECHNOLOGIES

IAEA-CN-170/027
Training and educating the medical specialist: The CanMEDS model.............................. 291
R.K. Chhem

IAEA-CN-170/028
“He who can does. He who cannot, teaches.” A blueprint for the partnership
between professional educators and medical education........................................ 292
T. Van Deven

IAEA-CN-170/029
Cultivating a capacity for phronetic action to address the needs of diverse learners .......... 294
K. Hibbert

IAEA-CN-170/030
Educating radiation therapists in developing countries............................................. 296
P.C. Engel-Hills

IAEA-CN-170/031
Training, education and staffing: Getting ready for new technologies ........................ 297
K. Inamura

IAEA-CN-170/032
IAEA support for education and training of staff in radiation oncology.......................... 299
A. Meghzifene, E. Salminen

Session 12: IMRT/IGRT/ADAPTED RT:
CLINICAL CHALLENGE AND EVIDENCE

IAEA-CN-170/033
Overview of IMRT in head and neck cancer.......................................................... 303
J. Bourhis

IAEA-CN-170/034
IMRT: Current state of the evidence ........................................................................ 304
B. Vikram

IAEA-CN-170/035
Prescribing, recording, and reporting – ICRU considerations and recommendations for IMRT .... 308
P.M. DeLuca, Jr., T. Rockwell Mackie, V. Grégoire
Session 13a: RADIOTHERAPY IN PAEDIATRIC ONCOLOGY

IAEA-CN-170/036
How to improve paediatric radiation oncology in Latin America .......................................................... 313
P.E. Novaes

IAEA-CN-170/037
Radiotherapy in paediatric oncology ........................................................................................................ 316
S.L. Wolden

IAEA-CN-170/038
Radiotherapy related sequelae in childhood cancers: The current status ................................................. 317
S. Laskar

IAEA-CN-170/039
The view of the AFRA designated centre on how to respond to the challenges
in paediatric radiation oncology in the region .......................................................................................... 319
M.M. El-Gantry

Session 13b: REDUCING LATE RADIATION TOXICITIES

IAEA-CN-170/040
Biological approach to reduce late radiation toxicities ............................................................................. 323
J. Overgaard

IAEA-CN-170/041
Biological weighing of absorbed doses in particle-beam therapy:
ICRU-IAEA recommendations on the isoeffect-dose concept ............................................................... 324

IAEA-CN-170/042
Relating three dimensional dose/volume data to clinical outcomes:
An overview of the QUANTEC effort ........................................................................................................ 327

IAEA-CN-170/043
Acute and late toxicity after fractionated total body irradiation as conditioning
for bone marrow transplantation ............................................................................................................. 329
L. Gocheva, K. Sergieva, B. Avramova, I. Koleva, V. Vasileva, B. Sultanov

Lunch Forum II: ALTERED FRACTIONATION IN CURE AND PALLIATION

IAEA-CN-170/044
The rationale and radiobiology of altered fractionation in cure and palliation ........................................ 333
M. Joiner

IAEA-CN-170/045
Altered fractionated RT: What is the magnitude of the benefit in head and neck carcinoma? .......... 335
J. Bourhis

IAEA-CN-170/046
Applications of hypofractionation in the curative treatment of cancer ..................................................... 336
K. Kiel
Session 2:

*Keynote Lectures*

AN OVERVIEW OF ADVANCED TECHNIQUES IN RT: IMRT, IGRT, RADIOSURGERY
Overview of advanced techniques in radiation therapy

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Modern radiation therapy continues to progress at an unprecedented rate. This rapid evolution is primarily related to the significant advances in the modern technology of radiation oncology [1]. These advances are strongly linked to the evolution of computer technology and the corresponding developments in imaging equipment both for diagnosis and therapy. New “buzz words” have evolved in the last decades, i.e. “three dimensional conformal radiation therapy” (3-D CRT), “four dimensional (4-D)” imaging and radiation treatment, “intensity modulated radiation therapy” (IMRT), “tomotherapy”, “treatment gating”, “breathing control”, “inverse treatment planning”, “dose-volume constraints”, “multileaf collimation”, “image segmentation”, “image-guided radiation therapy” (IGRT), and “adaptive radiation therapy” (ART). The goals of radiation therapy have always been to maximize the tumour control probability (TCP) and minimize the normal tissue complication probability (NTCP). This is done by minimizing the margin between the clinical target volume (CTV) and the planning target volume (PTV) resulting in a reduced treated volume, i.e. irradiating a smaller volume of normal tissue while irradiating the defined target volume in each treatment fraction [2]. The achievement of this goal is the key factor driving these technological developments.

IMRT uses non-uniform beam intensities within the radiation field resulting in dose distributions that conform more tightly around the tumour and includes the capability of providing concave isodose volumes. Thus, smaller margins can be used, and higher doses can be delivered to the tumour while at the same time reducing the volume of irradiated normal tissues. This dose escalation, however, also requires improved precision in patient set-up. Furthermore, there is an assumption that target volumes can be defined with great accuracy. Conventionally, anatomical imaging such as computerized tomography (CT) has provided a means of defining the gross tumour volume (GTV). In recent years target volume delineation has been enhanced with the use of biological or molecular imaging (e.g. PET, SPECT, MRI, functional CT). The use of image fusion has allowed the combination of anatomical and biological imaging to define target volumes.

In IMRT, treatment plans are designed using an inverse planning approach which requires the use of objective functions combined with the input of dose-volume constraints as well as factors defining the relative importance of specific tissues or organs. The latter are often specific to a particular inverse planning algorithm and class solutions are derived from personal experience. The use of IMRT continues to increase and is now available in various forms in many cancer centres in the developed world. A survey conducted of US radiation oncologists indicated that the proportion of respondents using IMRT had increased from 32% in 2002 to 73% in 2004 [3]. Reasons cited for using IMRT were normal tissue sparing (88%), dose escalation (85%), and economic competition (62%). The most common sites treated with IMRT in 2004 were genitourinary, head & neck, and central nervous system tumours, whereas only a small number of respondents (18%) used IMRT for lung cancer. This is likely due to the dosimetric concerns about the combination of dynamic dose delivery and patient breathing motion.

The increased use of IMRT has focused attention on the need to better account for inter- and intra-fraction spatial uncertainties in the dose delivery process. A further reduction of the treated
volume is achieved by the use of image guidance on daily treatment set-up, i.e. IGRT [4, 5]. The most recent implementations include the use of an ultrasound or CT imaging system in the treatment room or the generation of CT images directly on the radiation therapy machine with technologies such as helical tomotherapy or cone beam CT. Images from the latter two technologies can also be used for dose recalculation (i.e. ART). While IGRT is already in clinical use in various places, routine image-guided ART is still at an early stage of application.

Breathing motion adds to uncertainties in the volume that is irradiated and, in the past, this has been addressed by leaving an appropriate margin between the CTV and the PTV. Superior-inferior motion of lung tumours as large as 5 cm has been reported although it is recognized that the average superior-inferior diaphragmatic motion is about 1.5 cm [6]. With 4-D CT, the effects of breathing motion can be quantified. Breathing motion predominately affects the thoracic region although breathing effects have been observed in regions as distant as the pelvis. Various strategies exist to alleviate the effects of breathing during irradiation [6] including: a) incorporation of respiratory motion in the planning process, b) respiratory gated IMRT delivery, c) breath hold IMRT delivery, and d) tumour tracking IMRT delivery.

Another radiation therapy technology that has been used to minimize treated volumes is stereotactic radiosurgery (SRS) or stereotactic body radiation therapy (SBRT) [7]. Both techniques are relatively non-invasive means of administering high-dose radiotherapy to discrete tumours in cranial or extracranial locations. Both forms of treatment share the use of image guidance and related treatment delivery technology. Both methods are achieved with a “stereotactic” technique, implying that external fiducial reference markers serve to align the treatment machine so that an internal lesion is targeted accurately. However, notable differences in clinical applications exist between cranial and extracranial targets. High spatial accuracies are expected, and time constraints from planning to delivery are relatively short. Since SRS and SBRT use either single-fraction or hypofractionated regimens, there is little chance for adjustment once treatment has been initiated.

In summary, new and advanced techniques in radiation therapy have become available to reduce the treated volume to more closely align with the defined target. These technologies should provide the capability of improving the probability of tumour control and reducing treatment related morbidity.

REFERENCES

Recent advances in planning/delivery tools in radiation therapy (RT) hold promise to improve the therapeutic ratio. I herein present a clinician’s perspective on the role, limitations, and unexpected consequences of the introduction of new technologies into the radiation therapy clinic.

The irradiated volume, PTV (GTV + CTV + margin for motion and set-up uncertainties), reflects the known gross target (GTV), plus a series of uncertainties regarding microscopic spread (CTV), and set-up errors (PTV, including internal motion [ITV]). Many new technologies address one of these PTV components.

Three dimensional (3-D) imaging/planning facilitates the definition of the GTV. It allows us to use CT (or other 3-D imaging such as PET) based anatomic information when designing treatment beams. Detailed 3-D dosimetric and anatomic information can be readily displayed and enables the physician to better select “optimal” beam orientations and beam shapes. Care must be taken to review the RT fields actually on the patient, since some clinically meaningful information is not included in the imaging (drain sites, scars, palpable induration). Overall, 3-D/conformal planning has been one of the most important advances in clinical radiation oncology. The limitation of this approach relates to the occasional inability to visualize target tissues on CT imaging (e.g. some head & neck sites are not easily visualized on CT, and when the target is largely based on areas of possible microscopic disease such as post-operative breast or rectal cancer). However, even in these cases the imaging can help to define critical normal tissues to be spared.

But we need to be careful that we do not get too fancy. There are underlying limitations to the imaging and our knowledge of microscopic spread. If we make the fields too tight we may miss the target. Data from Israel [1] revealed a higher rate of local failure for orbital lymphoma for conformal vs traditional wide-field RT. The authors should be commended for reporting this finding.

Respiratory gating/breath hold can reduce the margin needed for this “internal” motion, and can be useful, for example, to reduce normal tissue exposure. However, treatment times are extended. Many patients with poor lung function are not able to tolerate breath hold, and the degree of motion in patients with extreme COPD (i.e. those where sparing lung may be most critical) is usually small. This limits the utility of this technology. I find breath hold most useful during radiosurgery for small lower lobe lung, or upper abdominal (e.g. liver, adrenal) lesions, and in cardiac sparing for left sided breast tangents.

On-board imaging (planner or cone beam) reduces the margin needed for set-up uncertainties. Cone beam requires that the gantry rotate about the patient (which may raise clearance issues), is time consuming, increases radiation exposure, and does not address intra-fraction motion.
Intensity modulated radiation therapy (IMRT) allows better conformity of the therapeutic high dose volume to the target tissues, is particularly helpful for concave targets (Reese IJROBP 73:585, 2009) and may provide “fancy compensation” to improve target dose homogeneity. However, the planning, delivery times, and costs are usually increased. The volume of normal tissue exposed to low-modest doses may be increased. IMRT redistributes (rather than eliminates) the normal tissue dose. Indeed, the integral dose to the surrounding normal tissues, and the average dose gradient around the target, is relatively constant with 3-D vs IMRT [3–5].

Technology is seductive. One needs to guard against over-reliance, and not to forget “simple” solutions (e.g. bubble wrap for skin folds, decubital position or belly boards for bowel sparing). DVHs discard spatial and anatomic information that may be critical in predicting normal tissue risks. Traditional quality assurance steps (e.g. checking the light field relative to the surface anatomy), and “intuition regarding the accuracy of a treatment plan or delivery” may be less applicable in the IMRT era [6].

REFERENCES

Advanced radiotherapy with small and IMRT beams: Limitations of current dosimetry

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Developments in radiotherapy techniques have increased substantially the use of small fields for stereotactic treatments, mostly with linear accelerators and larger uniform or non-uniform fields, which are composed of small fields such as for IMRT. Micro- mini- and standard multi-leaf collimators (MLCs) have become almost routine equipment on conventional accelerators (e.g. BrainLAB\(^1\)). At the same time there has been an increased use of treatment units specifically designed for stereotaxy (GammaKnife\(^2\), CyberKnife\(^3\)) or intensity modulated treatments (TomoTherapy\(^4\)).

These developments have gradually undermined clinical dosimetry, as the widely disseminated codes of practice for dosimetry, or dosimetry protocols, cannot be applied to the conditions under which these small or novel beams operate and no specific dosimetry recommendations have formally been developed. Users must then decide by themselves how to perform clinical dosimetry.

Dosimetry errors have become considerably larger than in conventional beams mostly due to two reasons. First, even if the reference conditions recommended by codes of practice cannot be established in some machines, or treatment modalities be traced to them, dosimetry protocols are applied as if standard reference conditions would be valid. Second, even if relative dosimetry of small fields and composite fields appears to be conceptually simple, dosimetry issues mostly linked to the type of detector utilized have contributed to the problem. Such dosimetry errors usually affect the entire number of patients being treated with a specific modality.

Among the reasons: there are machine-related specific issues, like some of the small or composite non-standard field radiotherapy systems cannot be calibrated using standard dosimetry protocols because they cannot create the field size specified in the protocols’ reference conditions, some deliver non-uniform dose (e.g. no field flattening filter), or they cannot be calibrated with the ion chambers recommended by the protocols. They are special machines not included in accepted national or international protocols and, instead, they are cross-calibrated often against a source (e.g. linac) that has been calibrated using an accepted protocol; the procedure provides traceability to national and international standards. There are also a number of issues related to the use of ionization chambers recommended for ‘conventional’ reference dosimetry. And finally there are major constraints related to the lack of commercial treatment planning systems that can calculate the dose accurately for

\(^1\) BrainLAB – m3\(^a\) High-Resolution Multileaf Collimator, BrainLAB AG, Feldkirchen, Germany.
\(^2\) Leksell GammaKnife\(^b\), Elekta Instrument AB, Stockholm, Sweden.
\(^3\) CyberKnife\(^c\) Robotic Radiosurgery System, Accuray Inc., Sunnyvale, CA, USA.
\(^4\) TomoTherapy\(^d\) Hi-Art\(^e\), TomoTherapy Inc., Madison, WI, USA.
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non-standard fields due to the difficulty to model the dose from small and composite fields analytically and even with Monte Carlo simulations. As a consequence, comparisons among different institutions have shown very large variations in basic steps, like machine output measurements for stereotactic treatments where differences of up to a factor of 2 (in dose determination) have been obtained, or failures of up to 30% in the number of institutions failing to perform a ‘correct’ head and neck IMRT treatment.

In order to develop standardized recommendations for dosimetry procedures and detectors, an international working party on Small and Novel Field Dosimetry has been established by the International Atomic Energy Agency (IAEA) in cooperation with the AAPM Therapy Physics Committee. Other similar groups have been organized at national levels which are linked to the international working party.

The presentation will outline why standard dosimetry methods do not apply to small and composite non-standard (novel) beams, emphasize why dosimetry errors have become considerably larger than in conventional beams, and overview the proposed methodology for the dosimetry of small single field and composite fields that will form the basis of new international recommendations schematized in Fig. 1.

The contribution of the other working party members (see authors in Ref. [1]) is gratefully acknowledged.

REFERENCE

FIG. 1. Schematic overview of the proposed formalism for the dosimetry of small static fields with reference to a machine-specific reference field [1], and of non-standard composite fields with reference to a plan-class specific reference [2]. Adapted from Ref. [1].
Session 3a:
ADVANCES IN CHEMO-RT FOR CERVICAL AND HEAD & NECK CANCER
Are we justified for concomitant chemo-radiation in advanced stage cancer cervix?


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The main stay of treatment has traditionally been radical radiation therapy and over decades the survival rates have achieved a plateau of 30–45% at five years. Over the last decade there have been studies on the use of chemo-radiotherapy in carcinoma cervix. Over 19 randomized trials have been published addressing the issue of chemo-radiotherapy. However, heterogeneous data, poor randomization, inadequate number of patients, sub-optimal radiotherapy, non-uniform use of chemotherapeutic drugs, its sequencing and poor documentation have not yet provided the evidence to substantially alter the practice. The Cochrane and Canadian meta-analyses have to a large extent tried to address the role of concomitant chemo-radiation, but carcinoma cervix stage III accounted for only 30–35%. Moreover, evaluation with optimal radiation schedules and comparison of late toxicities still remain unanswered. What is more important is that the cisplatin is relatively inexpensive and is available worldwide. This means that cisplatin-based chemo-radiation is affordable in the developing countries where carcinoma cervix still forms the major cancer. However, the role of chemo-radiation in carcinoma cervix stage IIIB in developing countries including India still remains unexplored. With an aim to evaluate the role and benefit of chemo-radiation in patients with cervical cancer we proposed this randomized study.

Patient and methods

Patients with histologically proven cervical cancer (squamous carcinoma only) FIGO IIIB after obtaining written informal consent are randomized to either the Standard arm of Radical Radiation Therapy alone or the study arm of concurrent chemo-radiation with cisplatin (40 mg/m2 weekly×5#). With an expected improvement in absolute survival by 10% for stages IIIB, α-error of 0.05, power of detection of 80% and 10% patients more to compensate for lost-to-follow-up and major violations, a total of 850 patients will be randomized with stratification for stages and brachytherapy treatment.

Results

In this ongoing randomized study, 627 patients were randomized till November 2008. Currently, we present an audit of 528 patients randomized till December 2007. Of 528 patients, 14 are under treatment and 514 have completed treatment. The treatment related grade III toxicities in the form of gastrointestinal (3% Vs 4%), genitourinary (2% Vs 3.5%), anemia (1% Vs 6.8%), neutropenia (1% Vs 5.2%) and thrombocytopenia (1% Vs 3.5%) were higher in chemo-radiation arm and required active support more often than radical radiation arm. With a median follow-up of 24 months till 2007, 48 patients in radiation alone while 37 patients in chemo-radiation arm had recurrences. The patterns of recurrences were comparable in both arms.
Conclusions

Concomitant chemo-radiation, although feasible, appears to be associated with higher incidence of grade III hematological and gastrointestinal toxicities. These toxicities need active support for completion of planned treatment. In this ongoing randomized study, completion of accrual, comparison of toxicities (acute and late) and outcome is essential to evaluate the exact role of concurrent chemo-radiation in advance cervical cancers. An interim analysis is ongoing to assess the toxicities and early outcome.
Advances in chemo-RT for cervical and head & neck cancer

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Nowadays, head and neck cancer (HNC) is the fifth most common neoplasm in the world with an estimated annual global incidence of more than 500,000 new cases (Parkin, et al., 2001). HNC is more frequent in the sixth, seventh and eighth decade of life and is diagnosed with locally advanced disease in approximately 60% of the cases (Chin, et al., 2006). Patients with this disease are at a considerable risk of mortality with a rate of more than 300,000 deaths per year (Parkin, et al., 2001).

The treatment of HNC patients should be decided through a multidisciplinary team. The current available treatment methods are surgery, radiotherapy, chemotherapy and novel targeted therapies. The decision is based on the primary site, clinical stage, tumour histology, patient’s age, and general medical conditions. Curability and quality of life are the main goals of HNC management decision.

In the last three decades, the main advances in the non-surgical treatment of cervical and HNC have been the combination of chemotherapy (CT) and conventional or altered fractionation radiotherapy (RT). Traditionally, patients with initial or advanced clinical stages had been treated with conventional fractionated radiotherapy only, with no differences in total dose. Curability with this strategy has been very limited for locally advanced tumours, with control rates lower than 20%.

Several studies have been testing the employment of some drugs concomitant with RT to achieve a better local control and to avoid the development of distant metastasis. For locally advanced and unresectable tumours, these studies have showed that the combination of RT with cisplatin (Jeremic, et al., 2000), with 5-FU (Lo, et al., 1976; Sanchiz, et al., 1990), with bleomycin (Fu, et al., 1987) or with mitomycin C (Dobrowsky, et al., 1998) significantly improved the loco-regional control and survival in comparison with radiotherapy alone. Due to the lower toxicity, cisplatin has become the most common used drug in combination with RT in the treatment of locally advanced and unresectable HNC, especially in carcinomas of nasopharynx, orofarynx and larynx (Al-Sarraf, 2002; Pfister, et al., 2000; Forastiere, et al., 2003). The most widely CT and RT scheme used in clinical practice today is based on three cycles of cisplatin every three weeks, with a dose of 100mg/m² concurrent with conventional fractionated RT (Aldestein, et al., 2003).

The combination of RT and CT has also been investigating in resectable tumours as an alternative to radical surgery in an attempt to preserve organ function without compromising curability (VA Laryngeal cancer group study., 1991; Jeremic, et al., 2000; Zorat, et al., 2004; Hitt, et al., 2005). These studies have used different timings of chemotherapy, different drug combinations and different RT fractionations, which have led to great difficulty in the interpretation of results and conclusions about the best RT and CT regimen. The EORTC randomized phase III trial for stage III and advanced resectable stage IV hypopharyngeal showed that neoadjuvant CT and RT had the same chance of local control compared with
radical resection and adjuvant RT (Lefebvre, et al., 1996). More recent studies have shown other interesting results: induction CT followed by concurrent RT with cisplatin-based CT might reduce distant metastasis rate (Licitra, et al. 2004); induction CT with taxanes added to cisplatin-fluorouracil regimen was more effective than the only cisplatin-fluorouracil regimens (Hitt, et al., 2005; St John, et al., 2006). However, it has not yet proven the superiority of induction CT followed by concomitant CT and RT over concomitant CT and RT or targeted therapy combined with RT (Posner; 2005).

Considering evidence based medicine about HNC treatment, an interesting search was recently published (Corvò, 2007). In this review, the author collected data from more than 100 phase III trials included in six meta-analyses about combination of CT and RT and/or altered fractionation in the management of locally advanced HNC. These data showed that the combination of CT and RT improved overall survival, especially if concomitant association is employed; neoadjuvant CT followed by RT alone is less effective than concomitant association; cisplatin is still the best drug in association with RT; polychemotherapy is not superior than mono-CT; and the association of CT and altered fractionation RT might boost the effect of CT and RT, but this benefit has still to be proven.

Recently, two important prospective and randomized trials (EORTC and RTOG) showed the benefit of post-operative combined CT and RT in the treatment of locally advanced tumours. Patients treated with combined modality had not only higher local control, but also better overall survival than those treated with adjuvant radiotherapy alone (Cooper et al., 2004; Bernier et al., 2004).

In the near future some ongoing trials will probably be able to show the best treatment regimen of chemotherapy combined with radiotherapy in order to decrease the toxicity and to identify which patients will have the real benefits of these treatments, based on molecular biology and target definition.

The main advance in the area of radiation therapy was the development of intensity modulated radiotherapy (IMRT). This technique has lots of potential benefits when employed in head and neck region due to the more conformal dose distribution and higher dose gradients between target volume and organ at risk, especially parotids, spine cord, normal mucosa, brain stem, cochlea and optic nerves, when compared with other techniques. Another advantage is the possibility to deliver different daily dose to the distinct targets which gives the possibility to perform simultaneous integrated boost. The delivery of higher daily dose to the primary tumour has not only a potential biological benefit but also represents an option of accelerated RT regimen. The GORTEC group is conducting a randomized phase III trial comparing conventional RT with IMRT in the treatment of HNC. In the future, this study will show a level 2 of evidence about the real benefits of IMRT in local control and toxicity.
Contraindications to cisplatin-based chemotherapy in the treatment of cervical cancer in Sub-Saharan Africa

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We conducted a prospective study to assess the eligibility of patients presenting with cervical cancer in the developing world (Mulago Hospital Radiotherapy Department, Kampala, Uganda) for chemotherapy.

Materials and methods

Patients with biopsy proven cervical cancer were eligible.

Workup included history, examination, pre-treatment Karnofsky performance score, evaluation under anesthesia to establish FIGO stage, complete blood count, renal and liver functions tests, HIV test and ultrasound of the abdomen and pelvis. Exclusion criteria: Stage 1A, Stage IV, HIV status positive, Karnofsky performance score <60, age >70 years, hydronephrosis, hemoglobin <8g/dL, white cell count <2,000/µL, creatinine >97 µmol/L.

Results

There were 314 patients included. After workup, 47 patients (15.1%) were eligible for combined modality treatment and 190 (60.5%) were not eligible. Eligibility could not be established in 77 cases (24.4%). Thirty-seven (37) or 11.6% of the group were HIV positive. HIV status was not established in 38.4% of cases.

The most frequently encountered exclusions were hydronephrosis and anemia. Application of a hemoglobin cut off point of 8 g/dL for cisplatin based chemotherapy resulted in the exclusion of 55 (17.4%) which increased to when a limit of 10g/dL was used, it increased to 21%. Hydronephrosis was diagnosed in 99 (31.4%). 56% had unilateral hydronephrosis while 44% had bilateral hydronephrosis.

Conclusion

Only 15.1% of our patients with cervical cancer would benefit from chemoradiotherapy with concomitant cisplatin, illustrating the difficulties of applying “standard” treatment to the developing world. The provision of accessible radiotherapy facilities and the introduction of national screening programmes should be the major priorities in the developing world setting.
Session 3b:
COMMISSIONING AND IMPLEMENTING
A QUALITY ASSURANCE PROGRAMME
FOR NEW TECHNOLOGIES
Commissioning and implementing a quality assurance programme for new technologies

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The unprecedented rate of progress in modern radiation therapy is primarily related to significant advances in the modern technology of radiation oncology [1]. Due to this rapid technological evolution, every cancer treatment facility is involved in the purchase of new treatment equipment, or in upgrading existing equipment with new and improved features. While the purchase and clinical implementation process varies from one institution to another, there are certain generic considerations that should be addressed either overtly or indirectly. These considerations include: (1) clinical needs assessment, (2) definition of specifications, selection and purchase process, (3) installation, (4) acceptance testing, (5) commissioning, (6) training, (7) clinical use, and (8) periodic quality control (QC) [2, 3]. Generally, medical physicists are involved in all of these activities with varying levels of responsibilities. For many technologies national or international committees or task groups have developed recommendations on acceptance testing, commissioning and QC. However, with new technologies, task groups may not yet have been convened, or may not yet have completed detailed documentation on how to commission or how to develop a standard set of QC procedures. A recent symposium entitled Quality Assurance of Radiation Therapy and the Challenges of Advanced Technologies [4] concluded that “the current process of developing consensus recommendations for prescriptive quality assurance (QA) tests remains valid for many of the devices and software systems used in modern radiotherapy (RT), although for some technologies, QA guidance is incomplete or out of date. The current approach to QA does not seem feasible for image-based planning, image-guided therapies, or computer-controlled therapy. In these areas, additional scientific investigation and innovative approaches are needed to manage risk and mitigate errors, including a better balance between mitigating the risk of catastrophic error and maintaining treatment quality, complimenting the current device-centered QA perspective by a more process-centered approach, and broadening community participation in QA guidance formulation and implementation.”

There are some fundamental considerations when contemplating the implementation of new radiation-related technologies in a clinical environment. Generally, this technology is complex and requires appropriate resources, appropriately qualified staff, as well as an infrastructure capable of handling this technology most efficaciously. The details of each of these aspects depend on the technology being considered, i.e. “What is its level of novelty?” (e.g. “Is this the 1st, 5th, or 100th installation of its kind?”); “Have commissioning and QC protocols been developed?”; “Does the institution have the resources and clinical backup to deal with increased downtime for the new technology compared to existing technologies?”; etc.

The general process for testing new technologies is to first perform a series of (phantom) tests for specific configurations to ensure that specified tolerances have been achieved. For example, with the implementation of intensity modulated radiation therapy (IMRT), additional tests, beyond the normal QC procedures for linear accelerators, have to be performed on the multileaf collimators (MLC) and their ability to provide rapidly changing beam configurations for either the segmented field or the dynamic MLC delivery approach. Once convinced that clinically relevant fluence...
maps are deliverable in a predictable and reproducible manner, further tests are performed using clinically relevant phantoms to assess the delivery of an entire technique. Once sufficient confidence is established with this process, some form of in vivo assessment (possibly with an anthropomorphic phantom or even in real patients) is developed to ensure that the total patient dose delivery per fraction is consistent with that predicted by the treatment plan. Publications on the implementation of IMRT first appeared around 1997; however, it was not until 2003 that a publication, sponsored and endorsed by American Association of Physicists in Medicine (AAPM), appeared, which was associated with the use of this new technology [5]. It was mostly a descriptive and guidance document on the implementation of IMRT with only one paragraph devoted to “QA of equipment and individual patient treatments”. Included in this paragraph is a statement: “It is important to emphasize that IMRT is a rapidly evolving modality and the QA program must also evolve to handle new issues that arise.” This was followed in 2004 by a joint article of the AAPM and the American Society for Therapeutic Radiology and Oncology (ASTRO) on implementing IMRT in clinical practice [6].

The problem is that new technologies are being produced at a historically high rate. Thus new commissioning and QA programmes have to be developed for image-guided radiation therapy (IGRT), for breathing controlled or gated treatments, for stereotactic body radiation therapy (SBRT), for tomotherapy, for proton or ion therapy, etc. The issue is that staff resources are not available to perform every possible check that would conventionally be checked. Thus new approaches are being discussed, such as failure modes and effects analysis (FMEA), so that QA activities are prioritized in such a way that there is a balance between being reasonably achievable and optimally beneficial to the patient [7]. This includes a systematic review of the possible errors over the course of a radiation treatment and the potential clinical impact of each so that appropriate priorities can be determined. However, this approach is still under development. Until the efficacy of the new paradigm is clarified, we will need to maintain the old, but perhaps inefficient, paradigm of QA, to ensure safe implementation of new technologies into clinical practice.

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Introduction of RapidArc™: An example of commissioning and implementing a QA programme for a new technology

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Volumetric modulated arc therapy (VMAT) is a new approach to the delivery of radiotherapy treatment with intensity modulation. While the linear accelerator gantry is rotating around the patient, gantry speed, dose rate and multi-leaf collimator positions are changed continuously in order to conform the dose to the specified target volume while minimizing the dose to normal tissues. In principle a complete 360° arc is delivered, but it is possible to reduce the angle, or to avoid particular parts of the arc where the dose to normal structures would be higher or where, as in the case of artificial hip joints, there is an increased dosimetric uncertainty. Both Elekta (VMAT) and Varian (RapidArc™) have provided this facility within the last year. There are evidently a number of differences between this method of beam delivery and conventional IMRT and there is little published literature on which to base quality assurance protocols, apart from an article by Ling, et al. [1]. Development of a QA programme must therefore rely on staff at individual centres performing risk assessment. This talk is based on implementation of the Varian RapidArc™ approach.

The first step in the process of introducing a new technique is to establish a multi-disciplinary team including doctors, physicists and radiation technologists. An important early decision is to choose a tumour site for which the team is confident in their understanding of the implications of different normal tissue doses. The team must also establish a programme of work that will lead to safe delivery of treatment. Factors to consider are:

- Requirements for the treatment machine to deliver volumetric arc therapy accurately and subsequent quality control procedures
- Planning system parameters that may need to be known more accurately
- Phantom measurements to verify achievable accuracy
- Requirements and methodology for ongoing quality assurance of patient treatment plans
- Patient set-up and verification.

In order to deliver a volumetric arc treatment accurately it is necessary to control:

- the dose rate
- gantry speed of rotation
- leaf speed and position.

Ling, et al. have developed a series of tests to enable each of these factors to be separately assessed and it is important that the linac can achieve satisfactory results in each respect. Our linac achieved good results without making any adjustments. Major deviations in these factors should be corrected, but in practice it is difficult to define the limits of acceptability as the accuracy of delivery of an individual patient treatment will depend on the degree of modulation required. However, if measurements of treatment dose distributions give poor results, these detailed tests will provide an indication of what needs to be corrected.
The principles of volumetric arc planning are not significantly different from those of inverse planned IMRT, but it is important to understand the factors that can affect the accuracy of dose delivery. As with conventional sliding window IMRT the dosimetric leaf gap can make a significant difference to dosimetric accuracy and it should be carefully measured and entered into the beam model. Achieving rapid changes of modulation may limit accuracy because of the limitations of leaf speed and it is therefore advisable to set leaf speed parameters conservatively in the optimizer. With fixed beam directions it is possible either to avoid irradiating through the couch or to ensure that the couch attenuation is minimized by appropriate positioning of the supporting couch bars. With arc therapy this is more difficult. We found that ignoring the effect of the couch gives errors in the dose to the isocentre of 2-3% using a couch with carbon fibre couch bars, and the couch therefore needs to be explicitly included in the patient model. Metal couch bars would have an even more significant effect.

Before the system is used clinically it is advisable to carry out plan comparisons with an IMRT technique with which the department is familiar. It is wiser to make incremental changes in techniques rather than moving from 2-D radiotherapy techniques straight to volumetric arc therapy. If it can be shown that the dose with the new technique is equally uniform in the target with a higher conformity index and with lower doses to normal tissues, it is easier to justify the introduction of the new technique even if the risk of error may be potentially higher. However, with any IMRT optimization, it is likely that some aspects will be improved and others will get worse. It has been reported that dose homogeneity in the target is harder to achieve with a single arc, but that organ at risk doses can be significantly reduced [2, 3]. A second arc may be useful to reduce the variability of dose within the target volume. It is therefore necessary to determine an appropriate balance of speed and plan quality. Once a satisfactory treatment plan has been developed measurements should be carried out in a phantom, ideally including measurements in a phantom of a similar shape to the anatomical site being treated. An important part of these measurements is to carry out a dummy run of the whole process in which the phantom is scanned and treated by the staff who would normally be involved in patient treatment.

Individual patient quality assurance is a particular challenge for modulated arc therapy. For IMRT treatments it is common practice to measure the fluence from individual beams using a planar diode array. Although such an array can be mounted on the head of the treatment machine it is not easy to calculate the expected fluence. Alternatively the portal imaging device can be used without the patient [4]. Three dimensional arrays, which measure the volumetric dose distribution, such as Delta4™, are particularly useful. In spite of the potential difficulties, our experience has been that RapidArc™ can be delivered as accurately and reliably as IMRT and that it offers worthwhile patient benefits.

REFERENCES


Image guidance in the radiotherapy treatment room: An opportunity to learn, to improve practice and to generate evidence

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One of the most significant recent advances in radiation oncology has been the introduction of high quality imaging equipment into the radiotherapy treatment room. A large variety of equipment is available ranging from ultrasound to electronic portal imaging (EPI), kilovoltage (kV) X-ray imaging and different types of volumetric CT scanning prior to treatment delivery. While it intuitively makes sense to verify the patient position prior to treatment there are many issues that need to be addressed to optimize the introduction of image guidance in respect to patient benefit and resource allocation. Questions include the choice of equipment, clinical indication depending on treatment scenario, training needs, imaging frequency, radiation dose and the most appropriate action to take after an image has been acquired. Over the last five years several pieces of image guidance equipment were installed at our institution. This was accompanied by an attempt to prospectively record information in a database for evaluation.

Aim

The present study aims to evaluate the database of set-up information on prostate cancer patients treated with image guidance at Peter MacCallum Cancer Centre to address the issues above.

Methods

Since January 2007, our institution has implanted three fiducial gold markers into all prostate cancer patients treated with radical radiotherapy. Treatment is delivered in 3-D conformal or intensity modulated radiation therapy (IMRT) using one of six Varian linear accelerators equipped with EPI and kV on-board imaging (OBI). From an orthogonal image set acquired immediately prior to treatment the set-up difference of the gland compared to treatment planning is determined and corrected for on-line. A second set of images is collected either during (EPI) or at the end of treatment (OBI) and image registration repeated. The difference between the prostate location on post- and pre-treatment images provides a minimum estimate for the movement of the prostate during the treatment (intra-fraction motion).
The radiotherapy information system (Impac™) is used to store the large amount of data related to treatment of this group. A set of queries written in Crystal Reports™ extracts information from Impac™ for set-up error, treatment times and incidence of toxicity. Institutionally developed software was used to write this information to an independent database for further analysis.

**Results**

The database was evaluated for a number of different outcomes that will be discussed. Examples for the type of information that can be obtained are:

1) *Comparison of kV and MV imaging*

One hundred forty-three (143) patients treated in a centre with two linacs, one with OBI and one with EPI only were compared. Set-up correction patterns varied strongly between OBI and EPI with the modal shift being 3 to 4 mm for OBI and 2 mm for EPI. This is at least partially a result of automatic set-up correction for all OBI patients while a threshold of 3 mm used for EPI resulted in a clear skew of distribution of set-up shifts. Mean time from first imaging to the end of treatment using OBI was 423 seconds and EPI 603 seconds. Systematic and random treatment errors were found to be smaller for OBI patients. A cost minimization analysis was carried out for a total of 5,151 image sets (kV imaging 68%). In a typical Australian department where staffing is the major contributor to expenses, the cost was less using OBI over a 8–10 year equipment lifetime.

2) *Study of intra-fraction motion*

The shift of fiducial marker position relative to isocentre was evaluated in a total of 2,706 image pairs 102 patients. This shift can be seen as a minimum estimate for intra-fraction motion and was evaluated for time intervals between 3 and 30 minutes between pre- and post-imaging. The mean three dimensional vector shift between images was 1.7 mm ranging from 0 to 13 mm. No significant increase of shift with time between images was found. Motion in anterior and posterior directions was found to be equally likely and no variation of motion with time of the day was found. There was a large variation in average shifts between patients (range 1 +/- 1 mm to 4 +/- 3 mm) with no apparent trends throughout the treatment course. Clearly, intra-fraction motion of the prostate gland appears to be a limiting factor when considering internal margins as defined by ICRU Report 62 for radiotherapy. Even in relatively short times there is a 5% probability that the prostate has moved more than 3.5 mm. Given the variation between patients, a uniform set of margins for all patients will not be satisfactory. Individualized margins would appear to be a more appropriate approach.

**Conclusion**

Image guidance offers an opportunity to improve the set-up of individual patients for radiotherapy. However, image guidance also yields information on patient groups, underlying systematic errors and performance of equipment. In order to gain the most benefit from the introduction of image guidance it is essential to record relevant data prospectively.
Principles and practice of electronic brachytherapy

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Electronic brachytherapy (EB) is a new technological advance for brachytherapy, during which a microminiature 50 kV X-ray source is employed to deliver the radiation. Only recently introduced as a commercially available system, the Axxent Electronic Brachytherapy System (Xoft, Inc., Sunnyvale, CA) has been relatively unstudied thus far in the clinical setting and is consequently unfamiliar to many medical physicists and radiation oncologists. Our institution was one of the early U.S. sites to treat patients with the Axxent system for breast cancer and the first in the world to offer EB for gynaecological cancer.

The EB modality has several advantages. Since the 50kVp X-rays are produced by an electronic source instead of a radioactive isotope, oversight by the U.S. Nuclear Regulatory Commission (NRC) is not mandated. Because of the relatively low energy of the device, treatments can be delivered in an unshielded room in contrast to the significant bunker shielding required for HDR, iridium-192 brachytherapy. The low exposure rate allows staff to remain near the treatment couch during dose delivery and an opportunity to provide comfort and encouragement while in close proximity to the patient. It also facilitates installation in satellite clinics, mobile service or rural locations that lack heavily shielded rooms. The high dose rate, low energy source closely approximates the therapeutic dose of iridium-192 at the prescription point. It generates however, a more targeted dose with very rapid dose fall-off, resulting in significantly less dose to healthy tissue beyond the prescription point.

System components consist of the controller, which includes a touch-screen monitor, USB port, pull-back arm (adjustable arm with a high voltage port for the source connection), barcode scanner, X-ray source cooling pump, a standard imaging well chamber, a standard imaging Max-4000 electrometer; and 50 kV miniature X-ray sources (Fig. 1). For exposure to air kerma strength conversions, the University of Wisconsin Accredited Dosimetry Calibration Laboratory has provided a calibration coefficient for the X-ray source.

The initial application of the system was for the treatment of breast cancer, adapting one of the most widely accepted techniques for accelerated partial breast irradiation (APBI). In this procedure, a saline-filled balloon with an attached after-loading catheter, through which the X-ray source travels, is inserted into the lumpectomy cavity. The balloon wall is impregnated with barium; thus the need for contrast inside of the balloon, as is required with other breast APBI intracavitary devices, is eliminated. The balloon applicator is equipped with drainage ports for extraction of air and seroma to create more conformal treatment geometries and is shown in Fig. 2a.

Gynaecologic applicators in the form of vaginal cylinders are also now available (Fig. 2b). The applicators are compatible with both CT and fluoroscopy and range in diameter from 2 cm to 3.5 cm. The endometrial applicator kit includes a specialized base plate and clamp assembly for fixation of the device within the patient.
We have developed a comprehensive quality assurance process for the commissioning of an EB system [1]. The commissioning tests include eight elements: a) well-chamber constancy, b) beam stability, c) source positional accuracy, d) output stability, e) timer linearity, f) dummy marker/source position coincidence, g) controller functionality and safety interlocks, and h) treatment planning data verification following the recommendations of the American Association of Physicists in Medicine (AAPM) Task Group 43 (TG43) [2, 3]. Together with TG43, our methodology provides a comprehensive EB system check for medical physicists commissioning such a device.

Although EB uses new technological approaches for the management of breast and gynaecologic cancers, the equipment is relatively easy to implement clinically. By virtue of its many advantages, it is likely that in the near future, EB will emerge as the brachytherapy modality of choice for an increasing number of institutions.

FIG. 1. Xoft Axxent Controller (a) and 50 kV X-ray source.

FIG. 2. a) Xoft Axxent intracavity breast applicator; b) gynaecological applicator.

REFERENCES


Lunch Forum I:
*Refresher Course on*
TRANSITION FROM 2-D TO 3-D CONFORMAL RADIOTHERAPY AND IMRT
The transition from 2-D to 3-D conformal radiotherapy – IAEA guidelines

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Recent developments both in diagnostic imaging and in the technology of radiation treatment delivery are enhancing greatly the practice of radiotherapy by strengthening its focus on treating patients with curative intent. Advances in computer technology have enabled the possibility of changing from simple two dimensional treatment planning and delivery (2-D radiotherapy) to a more sophisticated approach with three dimensional conformal radiotherapy (3-D CRT). Whereas 2-D radiotherapy can be applied with simple equipment, infrastructure and training, transfer to 3-D conformal treatment requires more resources in technology, equipment, staff and training. The transfer can significantly improve the precision, accuracy and efficacy of radiotherapy through the use of 3-D imaging of patient anatomy and advanced methodologies for treatment planning dose delivery and verification. However, the initial costs of creating facilities for 3-D treatment are higher and, substantially, more training of the staff is needed.

The need for the International Atomic Energy Agency (IAEA) to establish general guidelines for the transition from 2-D radiotherapy through 3-D CRT and further to IMRT, taking into account training, equipment, and other considerations, has been identified through its Member States’ interest in the safe and modern application of radiotherapy. At each stage in the process of improving the physical basis of radiotherapy, the technological and staffing milestones must be achieved in order that the changes in practice can be conducted safely. The IAEA has published a technical document, IAEA-TECDOC-1588, which provides guidelines and highlights milestones that need to be accomplished by radiotherapy centres as they plan to make a transition from 2-D to 3-D conformal treatment planning and delivery and then transition to IMRT. The necessary steps and the milestones for the transfer from 2-D to 3-D conformal radiotherapy, as described in this document, may serve as complementary recommendations to the recent IAEA publication entitled Setting up a Radiotherapy Programme: Clinical, Medical Physics and Safety Aspects. Both documents provide a comprehensive overview of the required radiotherapy infrastructure and processes for a broad spectrum of the radiotherapy services to support the interest of Member States in the safe and up to date application of radiation technology.

Starting a conformal radiotherapy programme requires considerable planning. There are significant differences between conventional 2-D radiation treatment planning and delivery and 3-D conformal radiation therapy. To establish 3-D CRT in an institution the following steps should be taken:

– define the scope of the programme,
– develop staffing needs for the programme,
– identify necessary space and equipment,
– develop a programme budget,
– purchase equipment and prepare space,
S. Vatnitskiy

– hire new staff,
– train all personnel to be involved with the programme,
– acceptance test new equipment,
– commission new equipment,
– develop necessary policies and procedures, and
– develop and implement a comprehensive QA programme.

A complete understanding of all these steps is necessary before one can successfully start a new programme in 3-D CRT. This presentation will describe the IAEA’s recommendations for transitioning from 2-D to 3-D CRT.

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Implementing 3-D conformal radiotherapy and intensity modulated radiotherapy in a clinical practice: Recommendations of IAEA-TECDOC-1588

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Recent technological advances in radiation oncology have had a profound impact on the radiation therapy for a variety of cancers. As newer technologies to plan and deliver three-dimensional conformal radiation therapy (3-D CRT) became available, this way of planning and delivering radiation therapy for many types of tumours with curative intent became the standard of practice in the developed countries. The rationale for transitioning to 3-D CRT as the preferred method of radiation treatment is that, with 3-D CRT, one can achieve conformity of high dose region to the target volume thus permitting the delivery of a radical dose of radiotherapy while limiting the dose to the normal tissue structures. Local control can therefore be improved by increasing the dose delivered to the tumour, without unacceptable toxicity.

In recent years a transition from 3-D CRT to a new paradigm of radiation therapy known as intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT) and/or image guided adaptive radiation therapy (IGART) has taken place in many developed countries. The reason for this transition is that IMRT allows for the delivery of highly conformal, even concave, dose distributions. Traditional radiation therapy techniques, including 3-D CRT with uniform radiation intensity and/or with simple beam fluence modifying devices like wedges, do not provide a method for sparing critical structures that push into and are partially or fully surrounded by a target or combination of targets. IMRT, on the other hand, uses all the tools of 3-D CRT and adds other novel features to further shape the dose distributions by modulating the intensity of each radiation field. It employs sophisticated radiation treatment planning systems with inverse planning capabilities and computer controlled radiation therapy treatment delivery systems equipped with a multileaf collimator. The treatment planning systems with inverse planning capabilities allows the user to optimize the in-field radiation fluence in order to achieve pre-determined constraints for doses to targets and allowable doses to normal tissues. Such planning and delivery systems have made possible the implementation of 3-D CRT with modulated radiation fluence. IMRT has the potential to achieve a much higher degree of target conformity and/or normal tissue sparing than most of the other treatment techniques, especially for target volumes and/or organs at risk with complex shapes and/or concave regions.

IMRT practice is continuing to develop and evolve with the addition of multi-modality and functional imaging, tumour control and normal tissue complication probability modeling, and image guidance. The dosimetric advantages of IMRT over 3-D conformal radiation therapy — in the conformity of the high dose regions to the target and avoidance of high doses to critical neighboring structures at the expense of higher tissue volumes receiving low doses and higher dose inhomogeneity within the targets — are well established. Therefore, the highly conformal dose distributions produced by IMRT offer a means of reducing the volume...
of normal tissue that is irradiated, potentially allowing for further dose escalation. Escalating
the dose, while preserving, or even decreasing, the toxicity rate offers significant potential to
improve the therapeutic ratio.

Whereas 3-D CRT and IMRT are widely used in the developed countries, the same is not
necessarily true for developing countries. Transition from conventional radiotherapy to 3-D
CRT and IMRT requires considerable knowledge and understanding of patient
immobilization, volumetric imaging, patient set-up and internal organ motion uncertainties,
three dimensional heterogeneous dose calculation, large-scale optimization, and dynamic
beam delivery of non-uniform beam fluences.

The International Atomic Energy Agency (IAEA) has published a technical document IAEA-
TECDOC-1588 in 2008, which provides guidelines and highlights milestones that need to be
accomplished by radiotherapy centres as they plan to make a transition from 2-D to 3-D
conformal treatment planning and delivery, and then transition to IMRT. These guidelines and
milestones facilitate the process and represent continuation of the work at the IAEA for
providing access to safer and better quality treatment for the steadily increasing number of
cancer patients in the Member States.

The goal of this presentation is to discuss the recommendations given in IAEA-TECDOC-
1588 for making a transition from 2-D to 3-D CRT and IMRT.
From 2-D to 3-D conformal radiation therapy (3-D CRT) and IMRT: The AC Camargo Hospital experience

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The AC Camargo Hospital is a reference oncology centre of Brazil and Latin America. Founded in 1953 by Professor Antonio Prudente, it is one of the most important cancer hospitals in São Paulo City, dedicated to assistance, learning and research. The Radiation Therapy Department is under permanent development of new technologies, adding science, modernity and humanization to the patient care.

Until the end of the last decade, external beam radiation therapy was administered with two dimensional (2-D) techniques, based on orthogonal X ray films from a conventional simulator and 2-D TPS planning system. Since 2001, an institutional programme of technology incorporation was starting, making possible a gradual substitution of 2-D for 3-D techniques with improved radiation therapy administration and clinical results.

The objective of this presentation is to show the steps to achieve this reality on a Brazilian Cancer Hospital. It can serve as a model for another Latin American institution.

To move from 2-D to 3-D CRT is a complex project that begins with a new concept: to change planning from bone landmarks to CT image. Radiation oncologists, physicists and technologists need to be trained and prepared to understand CT anatomy and the operational infrastructure adapted to transfer the image slices to a 3-D TBS under a DICOM language. The concepts of GTV, CTV, PTV and OAR must be incorporated in practical routine and the progressive familiarization with delineation rules and dose constraints are mandatory. Internet atlas is very useful in this setting. One of the great advantages of 3-D planning is the DVH generation. Knowledge of the dose received by normal tissues is possible only with 3-D planning. Under a clinical point of view this information is very important to define the treatment intent, increase the final dose (dose escalation) and improve the interaction between radio and chemotherapy, offering the possibility to adopt preventive and corrective actions. The possibility to know previously the dose received by normal tissues and organs around the target rescues the clinical face of radiotherapy, improving patient care. Patient localization for radiation delivery is made easier by changing from skin source distance to isocentre technique. Immobilization systems and lead block construction (mould room) need to be improved by providing training to technologists, new material utilization and routine incorporation. The change to multi-leaf collimator use makes easier the development of 3-D CRT and it represents a great jump on operational activity, reducing treatment time and improving patient localization for radiation therapy.

On the other hand, multi-leaf collimators need improvement in equipment maintenance and technical care. Physicists have a fundamental role on 3-D RTC introduction. Training about multiple fields arrangement, filters use, isodoses composition and presentation on TPS, DVH generation respecting the dose constraints and development of QA programme are essential to 3-D conformal radiotherapy. To share and achieve experience with more advanced
institutions by local training and expert visits are of great importance to improve a 3-D CRT project. People to be trained need to be chosen according their capacity to be a repeater pole, transferring the information to all staff members. International organizations and scientific societies have a very important part on this setting. The development of collaborative programmes between the AC Camargo Hospital and the IAEA on different levels were fundamental to the introduction of 3-D CRT to routine practice.

The transition from 2-D to 3-D radiation is slow and progressive. In our view it is interesting to start with low complexity cases and, with the experience gained, to go to more difficult situations.

3-D CRT started at the AC Camargo Hospital in 2002. In this year, 227 procedures were done, representing approximately 20% of all attended patients. We selected prostate, lung and CNS as the priority sites to begin. At this time we used a CADPLAN TPS and personalized lead blocks for conformal field design. With increased experience and system familiarization, more and more cases were selected for 3-D planning; multi-leaf collimators were incorporated in all linear accelerators; 3-D TPS was changed by a Varian System (Eclipse) and, in the last year, by an ARIA environment. During 2008, 3-D CRT represented about 50% of all radiation therapies, with 968 cases performed (mean: 95/month) on 2000 treated patients. Nowadays, 3-D CRT is the preferential technique to treat prostate, CNS, lung, upper abdominal, Hodgkin lymphomas, soft tissue sarcomas and paediatric tumours. Fig. 1 shows the 3-D CRT evolution from 2002 to 2008.

To move from 3-D CRT to IMRT was a necessary and natural process. The development of IMRT techniques began in 2005, after an accumulated experience of more than 1,000 cases in 3-D CRT. Again, all staff members, especialy the physicists, have fundamental participation in this programme. Under a radiation oncologist’s point of view, the target delineation process and OAR definition are the same for 3-D CRT but the priorities and constraints need to be defined under an inverse planning concept. Fields arrangement, photon fluence studies and QA programme to the machine are essential to guarantee optimized dose distribution. Immobilization devices need to be implemented.
IMRT experience is progressively increasing in AC Camargo Radiation Therapy Department. The clinical situations selected to start were prostate and head & neck tumours, prostate by the possibility to treat pelvic lymphonodes and to make dose escalation, H&N by the advances to spare the parotid glands, reducing xerostomy, and to have a better dose distribution on complex situations like nasopharynx, nasal cavity and paranasal sinus tumours. IMRT techniques are very useful for the re-irradiation of recurrent or second tumours on previous irradiated sites and to sculpture the dose on targets very close to normal structures. Fig. 2 shows the gradative increase in the number of IMRT treatments at AC Camargo Hospital.

In conclusion, the decision to move from 2-D to 3-D in radiation therapy needs a strategic plan definition. All staff members must stay involved in the project and participate actively. Changes may be gradual, according to the experience accumulated step by step. A rigorous QA programme is necessary with progressive technology implementation. To share experiences with more advanced institutions and develop a permanent project of continued education and actualization are fundamental to improve results and to offer the best patient care.

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Transition from 2-D to 3-D conformal radiotherapy in high grade gliomas: Our experience in Cuba

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The goal of three dimensional (3-D) conformal radiation is to increase the dose delivered to the tumour while minimizing dose to the surrounding normal brain. The aim of this study is to compare the effects of radiation dose escalation in adult patients treated with 3-D conformal radiation therapy (3-D CRT) versus 2-D standard radiotherapy (2-D RT) for supratentorial high grade gliomas, and the impact of 3-D CRT in the post operative radiotherapy like the treatment of choice for malignant gliomas.

From 2004 to 2007, a total of 43 patients with supratentorial high grade gliomas, histologic subtype of anaplastic astrocytoma (AA) (grade III) in 34% of patients and glioblastoma multiforme (GBM) (grade IV) in 66%, and 70 or higher Karnofsky performance score (KPS), age (18–65 years), and extent of surgical resection (it was gross total in 42% and subtotal in 58%), were included in this study.

There were two treatment arms. For Arm 1 of 22 patients, who received standard 60 Gy total dose: 2 Gy × 5 d/wk for six weeks, the treatment volume was the tumour and oedema with a 2–3 cm margin using local fields with 2-D conventional radiotherapy as a retrospective control.

For Arm 2 of 23 patients, high dose group, dose prescription was 66–70 Gy and fraction size 1.8 Gy with level 2 (the European Dynarad Consortium) of 3-D CRT enrolled prospectively. It required a full 3-D data set of CT images and the improved tumour visualization of MR images, on which the gross tumour volume (GTV), clinical target volume (CTV), planning target volume (PTV) and planning organ at risk volume (PRV) were defined following the concepts of ICRU 50 and 62, immobilization of patients with thermoplastic masks; computed tomography (CT) scanner for therapy CT scans for planning conformal radiotherapy (slices separation and thickness of 2 mm to 3 mm); 3-D ERGO radiation treatment planning system; evaluation of the dose plan and the biological effect using dose volume histograms (DVH), tumour control probability (TCP), normal tissue complication probability (NTCP); an electronic network system for data transfer — from imaging facilities to the radiotherapy treatment planning system (RTPS) and then to the delivery machine — was desirable and this should comply with DICOM-RT protocols; the verification of patient position, beam placement and dosimetry; the measurement of outcome.

A linear accelerator fitted with a multileaf collimator, but it is not fitted with an electronic portal imaging device (EPID) thus conventional port films can be used for the verification of patient set-up and beam portals. The median age was 54 years and the survival time was much better in patients who were younger than 55 years old, good performance state, anaplastic astrocytoma histology, total resection of tumour. Median survival (Kaplan-Meier method) was significantly better in patients who were treated with 3-D CRT, it was 16 months in
Arm 2 and nine months in Arm 1 ($p<0.0001$). The survival at one and two years was 51% and 28%, respectively, with high dose 3-D CRT at 28% and 16%, respectively, with 2-D RT. Acute toxicities were mild and no significant treatment toxicities were observed. There was no difference between the actuarial survivals of the two groups.

These results indicate that intensification of local radiotherapy with dose escalation is feasible for some patients with GBM or AA with good prognostic factors. High dose 3-D CRT was well tolerated in all patients and no severe side effects occurred. This possibility of escalating doses, thus increasing local control and potentially improving survival. Local control can therefore be improved by increasing the dose delivered to the tumour, without unacceptable toxicity. Evidence exists of a dose-response relationship in brain tumours.
Session 5a: 
*Poster Session*
POSTERS RELATED TO RADIATION ONCOLOGY 
AND RADIOBIOLOGY
Volunteer outreach to radiation oncology facilities outside of North America by the American Society for Radiation Oncology

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The American Society for Radiation Oncology (ASTRO) has, as a stated organizational objective, an interest in assisting its members who wish to volunteer support to radiation oncology in “low and middle income” nations around the world. ASTRO has a programme that matches donations of volunteer time, materials and expertise with the needs of colleagues outside of North America. This programme is administered through the International Relations Committee of ASTRO.

In February 2008, with substantial financial support from private donors, the ASTRO Board of Directors approved a new initiative to match ‘donor interest with recipient need’ through an on-line searchable database accessible to ASTRO members through the ASTRO website.

ASTRO is presently in the process of soliciting the needs of their colleagues outside North America. Interested members of the radiation oncology community are invited to complete a form indicating the type of assistance that would be of value to their radiation oncology programme.

Forms will be sent to selected facilities worldwide, and will be available at ICARO. The ASTRO International Committee has authorized Dr. Terry J. Wall, J.D., M.D. to attend the ICARO meeting in order to explain the programme and solicit participation.

Requests may be for such things as:

- formation of an ongoing, collaborative relationship with a U.S. academic programme or large private practice
- inviting ‘visiting professors’ in various fields
- soliciting donations of educational materials or therapy equipment or any other form of support that would be helpful to their radiation oncology practice.

Once needs are identified, a searchable database will be accessible by ASTRO members on the ASTRO website. Members will be able to search by nation of interest, or by the type of support that they wish to volunteer.

An ASTRO member who wishes to respond to the need will indicate their interest on the website, at which time that ‘item of need’ will be removed from the database. If the member has not been able to respond to the need within four months, the need will be restored to the database in hopes that another ASTRO volunteer will respond accordingly.

Interested parties may contact the ASTRO International Committee outreach volunteer: Dr. Terry J. Wall at 5011 Neosho Avenue, Shawnee Mission, Kansas, USA 66205-1431 or
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via email at windriver@pol.net, or the ASTRO staff liaison to the International Relations Committee, Janet Mitchell at janetm@astro.org.

This programme is entirely voluntary on behalf of ASTRO members. Unfortunately, ASTRO does not have funds for travel, shipping, salaries, repair or maintenance of donated equipment, etc, and is unable to provide support beyond attempting to match donated resources with those who could benefit from them.
Anesthesia in radiotherapy – 1048 procedures in children


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This is a retrospective analysis of anesthetic procedures for radiotherapy in children emphasizing the use of oxygen/sevoflurane in inducing and maintaining anesthesia with no need of peripheral or central intravenous access.

Fifty-three medical charts of children who were submitted to radiotherapy under general anesthesia (from January 2001 to July 2006) were analysed, for a total of 1048 anesthetic procedures. All the children were monitored with pulse oximetry, heart rate, capnography, one-lead electrocardiography, and given sevoflurane by inhalation. The airway was provided by guedel canulae and face mask or binasal canulae and, therefore, for planning and simulation process, intravenous access was provided. For daily treatment, however, no intravenous procedure was needed most of the time. We report the main types of tumours and the average age and anesthetic group of patients. The results were analysed in terms of treatment interruption, complications and time on the machine.

The studied group included children from eight months to six years of age, with the following physical condition: ASA II (45), III (7) and IV (1) and tumours of CNS (12), retinoblastomas (19), leukemia (6), rhabdomyosarcomas (5), Wilm’s tumours (5) and others (6).

The children were submitted to anesthesia on a daily basis. Forty-eight of them were given sevoflurane by inhalation and five were treated by a balanced anesthesia with sevoflurane and propofol. Jaw relaxation was complete and vital signs stable in all children.

The average treatment time was 15 minutes, increased by the application time and phase I recovery (10 minutes) in the treatment room. The post anesthetic recovery was completed on ward. The expended time of linear accelerator was 25–30 minutes to perform all the procedure.

Thirty-seven children were treated for >4 weeks and 16 children for <4 weeks. In 40 out of 53 cases (75.5 %) there were no interruptions in the course of treatment, in 11 cases (20.5%) there was an average interruption of two days, and two children stopped the treatment due to progression of the primary disease. Main reasons for the interruptions were leukopenia, vomiting pneumonia and diarrhea.

In most reports of the use of anesthesia in children treated with radiotherapy we find reports of general anesthesia using intravenous propofol [1]. With a central venous line it is proven to be a safe resulting in a low rate of complications, and is quickly removed and there is no tolerance development after continuous use. However, there are reports of a 15% risk of sepsis due to catheter infection [2].
Alternatively, inhalatory anesthesia with sevoflurane alone has proved to be safe with a low complication rate to maintain anesthesia in paediatric radiotherapy.

Inhalatory anesthesia with sevoflurane is ideal for radiation therapy in children. The loss of consciousness is fast, supplemental use of opioids or muscle relaxants is not necessary, and the venous access may be avoided, reducing the risks of catheter infection, without compromising safe treatment.

Furthermore, the procedure is well tolerated, indicated by high hemodynamic stability, a reduced rate of post operative restlessness, shivering, nausea and vomiting resulting in a low incidence of interruption during radiation treatment.

Our institutional experience confirms the safety of the use of inhalatory anesthesia for paediatric radiotherapy, with low rates of complications and short time of the occupation of the machine.

REFERENCES


A successful alternative to provide radiotherapy services in paediatric cancer care for low-income populations in Brazil


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Objective

To demonstrate that the optimization of a preexisting physical and technical structure of the radiotherapy sector of a private hospital had been able to extend its capacity of attendance to a great number of low-income patients, part of a restrained demand for public health services, and in a self-sustained economic perspective.

Materials and methods

According to projections from international organizations like the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO), only 20–25% of patients in developing countries that need radiotherapy can access it [1]. Some of the reasons given for this scenario are the shortage of both infrastructure (equipment) and staff training [2]. In paediatric cancer care, similar comments have been made with the purpose to either increase access to oncologic treatment or stimulate professional training [3, 4]. In Brazil, it is estimated that in 2008 9,890 new cases of cancer in children and adolescents will be diagnosed [5], but, although there are no precise data, existence of a global restrained demand for public health services suggests a similar situation in those projected by international organizations.

The Hospital Israelita Albert Einstein (HIAE) is a health-related philanthropic entity bestowed with a certification that allows exemption from some taxes, tied to the provision of services to the public health system by performing, for example, studies of technology evaluation and incorporation, human resources qualification and health researches related to issues of public interest.

Following these premises, the HIAE established in 2003 a partnership with local institutions that provide paediatric cancer care for the public health system (non-governmental or public institutions), creating a project of Radiotherapy in Tumours of Infancy and Adolescence (RATI). With this project, the radiotherapy sector of the HIAE granted whole access to its physical and technical structure by low-income children and young adults, but limited to a 96 patients/year (120 patients/year since 2008), due to pre-requisites of economic self-sustainability and adjustment to the legal requirements of the institution’s philanthropic certification.
Results

From September 2003 to July 2008, treatments of 426 patients from five institutions (three permanent and two temporary) were sponsored by the project. Mean age was 6.5 years (0–24 years) and treatments performed included conventional, 3-D conformal, stereotactic fractionated and intensity modulated RT, in addition to “total body” and “total skin” irradiation, brachytherapy. Since 2008 image-guide RT assisted treatments were included.

Mean estimated cost per treatment per patient was R$21,500.00 (US$9,772.72), with total expenditures of R$4,778,788.00 (US$2,172,176.36). For values composition, fixed expenses (percentage of total operational costs, e.g. equipment maintenance and depreciation, doctors multi-professional team members wages) and variable (consumables and third-parties procedures, e.g. reimbursement of daily anesthesia) were taken into account. The total annual resources designated for this project corresponds to less than 1% of the total share to the philanthropic projects sponsored by the HIAE.

Discussion

Brazilian population is almost 190 million. So far childhood cancer incidence could be estimated at 52 cases/million inhabitants. In São Paulo City’s metropolitan area, where the project’s partners “target” population is concentrated, total inhabitants number at 19 million, with approximately 988 new childhood cancer cases diagnosed every year.

Based on these data, the study shows that optimization of a preexisting physical and technical structure of a private hospital’s radiotherapy sector had allowed to extend its capacity of attendance to a total equivalence of at least 12% of the local demand of attendance in paediatric cancer care (120 patients/year), reaching a low income population and remaining economically self-sustainable. Shortage of infrastructure could be counterweighted by successful alternatives, as presented here, based on partnerships between private initiative and public health services, and with adequate legal endorsement.

REFERENCES

Cervical carcinoma in women under 25 years old

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The objective was to analyse the treatment results and prognosis of cervical cancer in women under 25 years old, because there is great controversy about the influence of young age on the prognosis of cervical cancer with papers reporting better outcomes [1], papers pointing to survival disadvantage [2] and others showing no statistical difference[3].

About 15,000 women with cervical cancer treated between 1970 and 2004 in the institution were retrospectively reviewed, 53 patients were found to be 25 years of age or less. Thirteen were excluded from the analysis: four were treated with palliative intention, three lost the follow-up and five had clear cell tumours. So, the final analysis consisted of forty patients with 14 of them having disease in situ and 26 presenting invasive tumours.

For the patients with in situ disease the median age was 24 years. Six were submitted to cervical amputation and eight to conization. After a median follow-up of 61 months (32–189), no patients have any evidence of cancer anywhere (including one positive of HIV). For the patients who were submitted to cervical amputation there was observed one treatment related complication, a case of inflammatory pelvic disease, developed 6 weeks after the procedure. For the women submitted to conization there was no related morbidity. Morbidity. The small size of the population and it’s heterogeneity do not allowed statistical inference.

For the patients with invasive the median age was 23 (17–25). The distributions of the clinical stages were: I = 5; II = 2; III = 15; IVA = 4. Five had involved the lower vagina and only four do not have bulky tumours. Six were treated with surgery and the remaining 20 were treated with combinations of external beam radiotherapy and brachytherapy (half of these with concomitant cisplatin based chemotherapy). Median dose of external beam radiotherapy and brachytherapy was 40Gy and 20Gy, respectively. External beam radiation was delivered with conventional four-field technique in linear accelerators and brachytherapy insertions were done with afterloading low dose rate applicators or high dose rate system. Just 28% of the patients achieved local control with 19% of late local failure and surprising 58% developing progressive disease or no response to the treatment. The five year overall survival involved 60% for stage I, 50% for stage II, 26% for stage III and none for stage IVA. All The 15 women with stage III were treated with at least 40Gy of external beam radiotherapy and at least 18–20 Gy of intracavitary brachytherapy but 10 do not show any significant response during the treatment evaliations, resulting in a median survival of nine months only.

We conclude that in our data, women of 25 years or less with cervical carcinoma do not have good response to treatment with radiation therapy resulting in a prior local control and worse overall survival compared with those reported of older women.
REFERENCES


PTV coverage evaluation when comparing 3-D with 2-D techniques for breast treatment planning

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The purpose of this study is to compare 3-D with 2-D breast treatment planning, using the conventional two tangential field technique, regarding target coverage and dose to organs at risk.

All treatment plans, performed on computed tomography (CT) data sets of 10 (2 right and 8 left) patients with breast cancer, was generated with 6 MV photon beams in order to evaluate the impact of treatment technique with fixed photon energy. All dose distributions were calculated using treatment planning system Eclipse v7.3.10 (Varian Medical Systems, Palo Alto, CA). Heterogeneity correction was done using Batho Power Law. The dose was prescribed at the intersection of the beam and after dose calculation was completed, all treatment plans were normalized in 95% of the dose prescription.

For each of the ten patients, two treatment plans were done. The 3-D plans created to treat patients in the institution were compared to 2-D treatment planning in this study. In both techniques the central axis is the same but the gantry angles were different for most of the cases.

To reproduce 2-D plans using CT, the tangent field entries in 2-D plan were first defined, based on radiographies, and the radio-opaque markers were put on the skin of the patient in these entries. After these, CT images were carried out and a reference straight line in the axial slice crossing two radio-opaque markers was drawn. Then the gantry angles and field sizes were chosen, so that the field limits coincided with the reference line. In another direction, the field sizes were adjusted to the PTV with edges of 0.5 cm and 0.9 cm for x and y, respectively. It was needed to use dynamic wedges to provide homogeneity of dose. This was looked only in central axis to simulate the 2-D plans.

In 3-D plans, the gantry and collimator angles were chosen for the best PTV coverage with the least exposure of the ipsilateral lung. The multi-leaf collimators were adjusted to the PTV with edges of 0.5 cm and 0.9 cm for x and y, respectively. Dynamic edges were used to improve the dose homogeneity.

In 2-D plans, the mean and median PTV volume that received 95% or more of dose prescription was 79% and 93%, respectively. In 3-D plans, the mean and median PTV volume that received 95% or more of dose prescription were 96% and 99%, respectively. The PTV coverage in both techniques is shown in Fig. 1.

The average doses in the organs at risk were 2.3, 0.4 and 3% of the dose prescription in the heart, spinal cord and lung, respectively, while in 3-D treatment planning, these values were 6.4%, 0.7% and 9%. The doses in the critical structures to each treatment technique can be visualized in Fig. 2.
Satisfactory target coverage was observed in 3-D plans where an average of 96% of the target received 95% of dose prescription. In 2-D plans, it was found that an average of 79% received 95% of dose prescription.

The doses in organs at risk in a 3-D plan are greater than in a 2-D plan because of the better coverage target. However, the doses received in the critical structures are small when compared with tolerance limits.

**FIG. 1.** The mean and median PTV coverage in 2-D and 3-D treatment techniques.

**FIG. 2.** The average dose to organs at risk for 2-D and 3-D treatment planning.
Results and complications of high dose-rate brachytherapy associated with 2-D or 3-D external beam irradiation in prostate cancer

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High dose-rate brachytherapy (HDR) for prostate cancer may be a nice treatment option for dose escalation as a boost, when associated to external beam irradiation, mainly if 3-D conformal or more advanced technology is not available.

**Purpose**

This study analyses the results and toxicities of HDR brachytherapy boost prior to localized radiation with 2-D or 3-D conformal irradiation in patients with stage T1–T3 prostate cancer. Prognostic factors associated with overall and disease-free survival, as well as to treatment related toxicity were also studied.

**Patients and methods**

Data of 454 patients treated from December 1998 to March 2006 were prospectively collected; 403 were selected for this study. All had localized prostate adenocarcinoma. According to the Mt. Sinai risk group classification, three fractions of HDR brachytherapy were delivered in the course of 24 hours, with a single implant: 5.5 Gy per fraction for low risk, 6–6.5 Gy per fraction for intermediate risk, and 6.5–7 Gy per fraction for high risk patients. The implant was performed by transperineal insertion of needles, using a perineal template, with transrectal ultrasound guidance. The interval between fractions was of at least six hours. Conventional 2-D or 3-D conformal external beam irradiation was delivered to the prostate and seminal vesicles with 25 fractions of 1.8 Gy (45 Gy), about two weeks after brachytherapy.

The studied variables were: age, diagnosis PSA, prostate volume, Gleason score, clinical stage (TNM - UICC), presence of prostate nodules, risk group, use of neoadjuvant hormone therapy, previous trans-urethral resection or urinary obstruction symptoms, conformal or non-conformal external beam irradiation, brachytherapy dose and presence of co-morbidities such as arterial hypertension and diabetes.

Biochemical failure free survival (BFFS) and overall survival (OS) were analysed. Biochemical failure (BF) was defined according to both, the ASTRO and the Phoenix consensus criteria. Acute and late urinary and gastrointestinal toxicities were evaluated according to the Radiation Therapy Oncology Group (RTOG) classification; sexual function was evaluated by the American Urologic Association (AUA) classification. Data were submitted to statistical analysis. Uni- and multivariate analysis (Cox regression model) were
performed to evaluate factors related to BFFS, OS and toxicity with the significance level set at 5% (\( p \leq 0.05 \)).

**Results**

The patients presented a median age of 68 years (range: 48 to 85 years), mean PSA of 9\( \eta \)g/ml (range: 1 to 100\( \eta \)g/ml), and mean prostate volume of 35cm\(^3\) (range: 9 to 80 cm\(^3\)). Gleason score was less than 7 in 43% of the cases and 97% presented stage T2b or lower. There were 36.1% patients in the low risk group, 42.8% in the intermediate, and 21.1% in the high risk groups, respectively. Up to six months of neoadjuvant hormone therapy was used in 64% of the cases. External beam radiation was delivered with 3-D conformal radiation in 19% of patients.

The mean follow-up was 50 months ranging from 24 to 113 months (median 48.4 months). Nine patients (2.2%) did not respond to treatment. Death from prostate cancer occurred in 4.5% of the cases in a mean period of 22 months. Biochemical failure occurred in 9.6% according to both ASTRO and Phoenix consensus criteria. However, the mean time to relapse was 13 months using the ASTRO criteria and 26 months with the Phoenix definition.

The five year BFFS using the ASTRO criteria was 94.3%, 86.9% and 86.6% for the low, intermediate and high risk groups, respectively. The five year BFFS using the Phoenix criteria was 92.4%, 88.0% and 85.3% for the low, intermediate and high risk groups, respectively (\( p = 0.109 \)). The OS was 97.1%, 95.8% and 91.6% for low, intermediate and high risk groups, respectively.

Multivariate analysis was done to evaluate unfavourable prognostic factors for BFFS. The only feature predicting biochemical failure (BF) by both ASTRO and Phoenix criteria was the presence of prostate nodules, but patients younger than 60 years presented higher chance of BF using Phoenix criteria only. Better overall survival was related to younger age and Gleason score \( \leq 6 \) in the multivariate analysis.

**TABLE 1. EARLY AND LATE URINARY AND RECTAL TOXICITIES**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary</td>
<td>23.7%</td>
<td>15.1%</td>
<td>2%</td>
<td>-</td>
</tr>
<tr>
<td>Rectal</td>
<td>14.8%</td>
<td>10.5%</td>
<td>1.3%</td>
<td>-</td>
</tr>
<tr>
<td>Late</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary</td>
<td>8.8%</td>
<td>3.9%</td>
<td>7.7%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Rectal</td>
<td>3.4%</td>
<td>1.5%</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Late sexual impotence occurred in 71% of cases treated effectively by Sildenafil in 59%.

Acute urinary toxicity was related to previous urinary obstruction and higher brachytherapy dose to the urethra. Late urethral stenosis was related to older age and higher brachytherapy dose. The risk of acute and late rectal toxicity was higher when 3-D conformal irradiation was used. Sexual impotence presented a higher incidence in older patients with one or two comorbidities, previous sexual impairment, or 3-D conformal irradiation.
Discussion

Using the ASTRO criteria, BF was detected earlier than the Phoenix criteria. The retrospective characteristic of the ASTRO criteria may explain this discrepancy. However, five year BFFS and overall survival were not influenced by this finding.

The presence of prostatic nodules, which is directly related to stage, was the main factor associated to a higher risk of BF, independent of the risk group. This could be due to the higher number of low/intermediate risk patients in this population.

Besides the fact that younger age was related to a higher risk of BF according to the Phoenix criteria, this was not reflected on OS, where younger patients and Gleason score < 7 were predictive for better survival. Salvage therapies after recurrence may be very effective, and may benefit the younger patients that usually do not present severe comorbidities that might have influenced the OS of the older patients.

Urinary toxicities were mainly related to brachytherapy dose, as expected. Interestingly, the use of conformal external beam irradiation led to a higher risk of rectal complications, even with the prescribed dose of 45Gy. Probably the better accuracy of volume definition and treatment targeting included a higher volume of rectum in the fields. However, there was a very low rate of Grade 3 and 4 toxicities in the whole population. Also, even considering a better coverage of the target volume by using 3-D conformal irradiation, BFFS was not affected by the external irradiation technique. Probably, the high conformality of HDR brachytherapy might have compensated for eventual geographic misses.

Incidence of impotence was high in this group of patients and no influence of hormone therapy was detected, only previous risk factors, mainly related to the older patients.

Conclusions

The association of HDR brachytherapy as a boost for external beam irradiation seems to be a feasible and safe procedure, with good efficacy and acceptable toxicity. Decreased overall treatment time and reducing demand on conventional external beam equipment may be cost-effective when more advanced technology to increase dose safety is not available. Factors related to survival and toxicity can help to better select and manage patients with localized prostate carcinoma.
Intense modulated radiotherapy (IMRT) in paediatric patients: When the indication is an advantage


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IMRT is the best technique to be used when the tumour is very close to the critical normal tissues. However, some risks have been imputed to its use, specially in children. Because dose distribution is very heterogeneous within the target and because the number of monitor units is often increased to deliver IMRT, some authors have suggested that the risk of radiation induced second malignancies is increased. In addition, in paediatric patients, the heterogeneity of dose can also induce more adverse developmental effects. The Centro Infantil Boldrini is the most important oncology children’s hospital in Brazil, treating ~500 new cases per year. Almost 120 new cases per year are treated with radiotherapy.

Purpose

To describe the IMRT experience in a specialized paediatric radiotherapy centre.

Methods and results

There were 112 patients of less than age 18, who were treated with radiation therapy in the Centro Infantil Boldrini from September 2007 to September 2008.

The IMRT technique was implemented in our institution in September 2007. IMRT was used to treat 18 of 120 patients (15%). Ten were male and eight female. The median age: was 6 years (range: 1–18 years). IMRT was used for the following malignancies: head and neck rhabdomyosarcoma (4), nasopharynx tumour (1), nasoangiofibroma (2), esthesioneuroblastoma (1), neuroblastoma in the pelvis and spine (1), skin cancer (1), brain stem tumour (3), other brain tumours (4), and head and neck rhabdomyosarcoma re-treatment (1).

The median number of fields was 5.5 (range 5–9). Almost all radiation treatment was delivered with concomitant chemotherapy. The targeted tumour dose was 1.8 Gy/fraction.

In some head and neck tumours with different volume prescription, the dose kept between 1.7 to 1.92 Gy/fraction. However, in those patients, we experimented increased acute side effects (mucositis) and in the last patients we decided to do different phases of treatment to keep always the 1.8 Gy/fraction in the volume prescription.

The use of dedicated moulds and masks specialized to paediatric patients are scarce and the challenge of the reproducibility in such complex treatments is a routine problem. Some patients with orbital tumours could be treated with IMRT with less morbidity to the brain and chiasma. However, some genetic defects such as the bilateral retinoblastoma have higher risk of second malignancies that IMRT is not recommended.
Conclusions

In our experience, we have observed an advantage to IMRT to deliver radiation treatment to paediatric patients with head & neck and CNS tumours.

- Lower radiation doses can be delivered to the orbit, chiasma, brainstem, salivary gland, cochlea and uninvolved brain outside the PTV and provides a distinct advantage to the patient.
- The dose/fraction should be kept in less than 1.8 Gy even if it will implicate in a treatment with different phases.
- Specialized moulds and masks should be used to deliver IMRT more safely and easily in paediatric patients.
- Hot spots in bone tissue should be avoided in children to prevent growth disturbances.
- No benefit to IMRT in paediatric malignancies in the extremities, abdominal and thoracic region was observed.
Implementation of 3-D CRT and IMRT for prostate cancer: A three year experience at the National Cancer Institute of Colombia

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A retrospective study was carried out to describe socio demographic, clinical characteristics and results on any event free survival and on acute and chronic toxicity among localized prostate cancer patients treated with three dimensional conformal radiation therapy at the National Cancer Institute in Bogotá, Colombia during the last three years.

Records of patients treated with conformal three dimensional radiotherapy between January 2003 and December 2006 were retrospectively reviewed. Time to first event analysis was employed. Descriptive data analysis was carried out and survival curves were compared using the Kaplan-Meier method taking into account relapse risk classification. Acute and chronic morbidity were also reported.

One hundred and ninety-six (196) patients with localized prostate cancer were treated with conformal radiotherapy between January 2003 and December 2006; 114 patients were included in the main analysis. The median time of follow-up was 14.4 months. In all risk groups the 30-month any event free survival was 74%. Nine patients suffered events: 6 events in high risk patients, 3 events in intermediate risk patients and 0 events in low risk patients. During follow-up, no deaths occurred. Cumulated probability of any event free survival was 100%, 73% and 63% for low risk, intermediate risk and high risk groups, respectively. The rate of non-preexistent any grade chronic urinary toxicity was 12.8%, 10.8% for rectal toxicity, and 18.3 % for sexual toxicity.

The short follow up limits the possibility of making comparisons with international series. Even though it was not possible to demonstrate statistically significant differences in any event free survival between risk groups, events did occur in accordance with the risk group. A greater sample size would have increased the power and hence would have allowed detecting the differences. Acute and chronic toxicity was not measured systematically or standardized; hence, the results on this subject are not conclusive. There is a good adherence to the radiation administration protocol, but bladder and rectal tolerance doses did not meet standards in some cases. Guidelines should be developed and implemented in order to define the optimal hormonal treatment.

After completion of this phase and with the support of the International Atomic Energy Agency we were able to implement the technique of IMRT with the advice of international experts in May 2008. So far we have treated 12 prostate cancer patients with an established protocol.

The Research Group of the National Cancer Institute of Bogotá Colombia has chosen, among the high technology projects, the IMRT technique led by the Radiation Oncology Group to begin a prospective study on long term side effects and events free survival.
Recurrent glioma: Is re-irradiation a feasible option?

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The standard care for treatment of glioblastoma multiforme (GBM) consists of surgery, fractionated radiotherapy with concomitant and adjuvant administration of the alkylating drug temozolomide [1]. However, despite modern treatment techniques and the radiochemotherapy approach, GBMs will recur in several months. The high recurrence rate of approximately 100% is due to the infiltrative growth characteristics of this tumour type with unrelenting spread throughout the normal brain. Malignant gliomas relapse in up to 90% in close proximity of the resection site, which is the post-operatively irradiated volume. In case retreatment by radiotherapy is considered, the tolerance dose of the healthy brain tissue is the limiting factor for the re-irradiation dose that can be applied with an acceptable late morbidity profile.

Aim

To give an overview of current available clinical data on re-irradiation of glioma with respect to the tolerance dose of normal brain tissue. To facilitate the comparability of the radiation schemes with regard to the total dose and number of fractions used in the different studies, radiobiological model calculations were performed to obtain appropriate normalized total dose (NTD) values. The analysis provides insight in the re-irradiation tolerance of normal brain tissue, which can be used as a guideline in the clinical practice.

Materials and methods

Twenty-one brain re-irradiation studies were identified by a comprehensive search on PubMed over the period from January 1996 to December 2006. To enable calculation of the cumulative equivalent doses in 2 Gy fractions (NTD), which is the additive of the NTD of the initial irradiation course and the NTD of the re-irradiation course, only papers with clearly stated median physical dose of the initial radiation treatment were included in the analysis. Radiobiological model calculations were performed using the linear quadratic model assuming complete repair between subsequent irradiation fractions for conventional radiotherapy, fractionated stereotactic radiotherapy and LINAC based stereotactic radiosurgery. Severity of symptoms due to necrosis is based not only on the size, but even more importantly on the location of the injury. The tolerance dose is defined as the maximum radiation dose that can be tolerated by the normal brain tissue included in the treatment field, or the biological dose that does not induce any irreversible late radiation toxicity, i.e. clinical or histopathologically proven brain necrosis.
P. Sminia and R. Mayer

Results

The NTDcumulative in conventional re-irradiation series (NTDcumulative of 81.6-101.9 Gy) was generally lower than in fractionated stereotactic radiotherapy (NTDcumulative of 90-133.9 Gy.) or in the stereotactic radiosurgery series (NTDcumulative of 111.6–137.2 Gy). No correlation between the time interval between the initial and re-irradiation course and the incidence of radionecrosis was noticed. The data show a tendency towards the NTDcumulative to be the limiting factor with regard to the induction of necrosis rather than the time interval between initial and re-irradiation, which ranged from 3 to 50 months. With regard to the irradiated volume the analysis showed that, when the re-irradiation volume was smaller, the re-irradiation dose used was statistically significant higher (p = 0.0116). The increase in prescribed NTDcumulative with decreasing treatment volume indicates that dose escalation can be considered in small treatment volumes.

Conclusion

Radiation-induced normal brain tissue necrosis was found to occur at NTDcumulative beyond 100 Gy. The applied re-irradiation dose and NTDcumulative were found to increase with a change in irradiation technique from conventional to conformal techniques like fractionated stereotactic radiotherapy to radiosurgery re-treatment, without increasing the probability of normal brain necrosis. The applied total cumulative dose was found to be the most important factor with regard to the development of radionecrosis [2]. No effect was noticed from the time interval between the initial and re-irradiation exposure, which was however three months at the minimum. Our analysis is not decisive concerning the dependency of tissue recovery on the total dose of the initial exposure, since this was generally a standard regimen of 60 Gy in 2 Gy fractions. It seems to be implicit to include quality of life data in planned re-irradiation studies including neurocognitive functioning preceding and following therapy [3]. In conclusion, current literature shows that re-irradiation is a feasible option as palliative therapy for recurrent high grade glioma.

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Design and evaluation of a national programme to increase the capacity for radiation oncology

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Estimation of the need for radiation treatment capacity in The Netherlands was made several times in the past 30 years by both government committees and the Dutch Society of Radiation Oncology (DSRO). These estimations indicated a 100% increase of the number of patients requiring radiation oncology in The Netherlands in 25 years. A demographic change — aging of the population — is the major reason for this increase.

The number of linacs and professionals did not increase accordingly during the 90s of the past era, due to a very strict policy by the Dutch government to reduce costs of health care. As a result patients were confronted with waiting lists for radiation treatments, despite prolonged business hours and the introduction of sub-optimal, but time efficient treatment schedules.

The DSRO mobilized the public opinion and the Dutch parliament, which finally led to a decision of the Dutch Minister of Health in September 2000 to solve the problems. The DSRO (!) took the lead in an alliance of hospital organizations, organizations of patients and government representatives in what resulted in an integral plan to bring radiation treatment capacity to the required level [1]. The plan was designed within two months. It was based on a balanced growth of equipment, education of radiation oncologists, medical physicists and technologists.

Technological developments were included in the capacity prognoses as one of the goals of the plan was to improve the technical quality of radiation oncology by bringing new technological developments to the general public quickly. A capacity weight factor was included in the capacity estimations, expressing required radiation capacity in terms of standard equivalent treatments (e.g. two tangential fields for breast cancer treatment, 25 fractions correspond to a standard treatment). Weight factors that were applied ranged from 0.7 (simple ‘single dose’ treatment) to 2.9 (extensive treatment, CT planning including DVHs, portal imaging). A change in technological achievements could be included as a change in the average capacity weight factor for all treatments. All capacity guidelines were expressed in terms of the number of standard equivalent treatments per year (trst/year).

The recommendations used as guidelines for estimation radiation capacity were: treatment units: 500 trst/year, radiation oncologists: 250 trst/year, medical physicists: 650 trst/year, technologists: 100 trst/year.
FIG. 1. Estimations made in 1993, 2000 and 2007 of the number of treatment series in radiation oncology and the actual registered number of these treatments.

FIG. 2. Estimations made in 1993, 2000 and 2007 of the required number of treatment units and the actual number of treatment units.

Clearly the result of the coordinated action to increase the capacity for radiation oncology can be seen [2].

The number of professionals is growing in a similar way as the number of treatment units. Enough positions were created to educate new professionals.

The growth in radiation oncology capacity was distributed over the country according to the expected number of patients per health care region in The Netherlands. Initiatives for satellites relying on existing oncology centres were included as one way to bring technological improvements rapidly to the local population.

The national programme has proven to be very succesful. Reliable prognoses for the required radiation capacity were important, and could be met afterwards. The method supports the incorporation of technological advances in the prognosis.

These methods could be used succesfully in countries were radiation oncology is developing. The approach in The Netherlands has been succesful for both the government and the professional organizations. After ten years of ‘regulated growth’ the needs and capacity for radiation oncology are balanced; there are no waiting lists and sufficient well educated personnel are available for the radiation oncology centres.

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Impact of \(^{18}\)F-FDG-PET/CT on staging and radiation treatment planning of patients with primary locally advanced pelvic malignancies

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The aim of this study was to investigate the impact of FDG-PET/CT on staging and planning of radiotherapy for locally advanced rectal (LARC) and cervical cancer (LACC) patients.

From January 2003 to December 2007 a total of 36 patients with LARC and 18 patients with LACC underwent a retrospective PET/CT study for radiotherapy planning purposes. The impact of PET/CT on staging, overall patient management decisions and radiation treatment planning was evaluated.

Target volumes (GTV, CTV, PTV) were defined according to ICRU 50, ICRU 62 reports by a blinded reader.

The GTVs for the hypothetical boost volume (GTV + 2 cm) in LARC patients were defined primarily on CT alone, and afterwards on the fused PET/CT dataset. The CT-based and PET/CT-based GTVs were quantitatively compared and the percentage of overlap (OV%) was calculated and analysed. The potential impact of PET information on formation of CT-PTV was assessed by calculating PET/CT-PTV outside CT-PTV volume.

In LACC patients the hypothetical nodal boost volume(s) for dose escalation in external beam radiation treatment planning was defined on PET/CT only (PET/CT-PTV\(_n\) = PET/CT-GTV + 1 cm).

PET/CT imaging resulted in a change of overall therapeutic approach for 3 (8%) LARC patients and 5 (28%) LACC patients.

In LARC patients PET/CT-GTVs were smaller than CT-GTVs (p<0.05). In 46% LARC patients PET/CT resulted in a need for modification of the usual target volumes (CT-PTV) because of detection of a geographical miss (PET/CT-PTV outside initially in CT slices defined CT-PTV).

In LACC patients PET/CT was useful to define the adequate extension of target volumes (in 28% LACC patients para-aortal area should be included because of PET/CT detected paraaortic nodal disease) and to precisely identify possible dose escalation areas.

Conclusions

FDG-PET/CT had significant impact on radiotherapy planning and overall treatment decisions of patients with LARC and LACC.
Future of cobalt-60 in the treatment of cancer

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Radiation therapy remains one of the main modalities in the treatment of majority of cancers. It works by damaging the DNA of cancerous cells. The challenge of radiation treatment is to deliver large enough doses to the cancer cells while minimizing the dose to normal tissues. Now with the recent development in imaging the metabolic or functional status of cancers, the position of tumours related to surrounding normal tissue can be more clearly delineated. The therapeutic dosage of radiation to the tumours can be escalated without exceeding normal tissue tolerances. Equipment based on linear accelerators as well as cobalt-60 is extensively in use though linear accelerators have largely replaced the earlier cobalt-60 teletherapy machines in the developed countries. However, cobalt-60 teletherapy machines still remain the workhorse of radiotherapy in the rest of the world. Gamma knife was introduced later for stereotactic surgery of brain tumours. Now with introduction of newer versions of cobalt-60 equipment with high radiotherapy target/normal tissue ratio, the necessity of cobalt-60 in treatment of cancer continues.

Linear accelerators are capable of prodigious output producing nearly a continuous stream of particles. These monoenergetic electron beams are directed at a high density target to produce X-ray output of varying energies. Both electrons and X-rays are used to treat the malignant tissues. The reliability, flexibility and accuracy of radiation beam produced are adoptable to both IMRT and IGRT making it score over cobalt units. In addition, the devices can be switched off when not in use. The unit as such does not need any shielding unlike cobalt machines. The disadvantages of these units are because of their dependence on power supplies which remain erratic in underdeveloped or developing countries particularly in their rural areas. The capital cost of such equipment have now come down; however, in the countries where indigenous designs of cobalt-60 units are available, the linacs are still found to be relatively expensive to buy, operate and maintain.

Cobalt-60 teletherapy units provide radiation which is ideally suitable for head and neck cancers and other superficially located tumours like breast cancers and soft tissue sarcomas of extremities. Such units are very reliable and are easy to operate even in difficult conditions prevailing in developing countries. India has now introduced its own state of the art teletherapy equipment, Bhabhatron, which is available at very competitive rates and with cobalt-60 source also being made available and disposed of locally, retaining its economic competitiveness. The advantages of their deployment very much outweigh over linacs. In China, a similar situation prevails and, India and China being two largest countries with maximum number of cancer patients, the utility of such cobalt units is going to remain important for many years to come. India has about 250 such units but, looking at the number of cancer patients in the country, a much higher number is needed for providing adequate treatment to the patients.

The concept of Gammaknife which is a static focusing equipment from a number of sources for stereotactic radiosurgery suitable for brain tumours has now been further developed to
improve their utility for use in treatment of solid tumours in the body. Two such models ‘Gyroknife’ and ‘Supergamma’ are gaining popularity. In ‘Gyroknife’, a number of inclined sources focusing at a point and housed in a body which can rotate about its axis and the body itself can revolve to access differently located tumours in the body keeping the focus to skin dose ratio very high. In the ‘Supergamma’, the same effect is produced by having a number of sources located offset to each other so that when they rotate they focus at the same point but enter the body from different portions. This new generation equipment integrates head and body treatment into one. It can also do both radiotherapy and radiosurgery. Due to multifunctional nature of these new generation cobalt machines, they promise to provide cost effective treatment.

It can be concluded that due to lower initial cost of cobalt machines as compared to their equivalent linacs, and their much less dependency on power and other working conditions, the utility of cobalt-60 machines is likely to remain for many more years to come, particularly in underdeveloped and developing countries of the world.
Intensity modulated radiotherapy for functional lung avoidance in radiotherapy of non-small cell lung cancer: An update of a planning study

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We conducted a planning study to assess a potential benefit of IMRT compared to three dimensional conformal radiotherapy (3-D CRT) in patients with non-small cell lung cancer (NSCLC) in terms of sparing functional lung (FL) defined as perfused by single photon emission computerized tomography (SPECT) scan [1]. Hereunder we report the updated results.

Twenty-five patients undergoing radiotherapy (RT) for NSCLC had planning computerized tomography (CT) and SPECT scans in the treatment position using radio-opaque markers to co-register the scans. Methods of image co-registration and RT treatment planning reported are reported in detail [1, 2]. RT volumes were delineated on CT. SPECT images were used to define FL. Two coplanar inverse RT plans were generated: 4-field 3-D CRT and 5-field segmented stop-and-shoot IMRT. Automated inverse 3-D CRT plans were created using AutoBeam optimization software, and IMRT plans were generated employing Pinnacle3 treatment planning system (Philips Radiation Oncology Systems). All plans were prescribed to 64 Gy in 32 fractions using data for 6 MV beam. The objectives for both plans were to minimize a volume of FL receiving 20 Gy (\textit{V}_{20}) and dose variation in the planning target volume (PTV). Spinal cord dose was constrained to 46 Gy. Volume of PTV receiving 90% of the prescribed dose (\textit{V}_{90}), \textit{V}_{20} and FL mean dose (\textit{MLD}) were recorded. The \textit{V}_{90}/\textit{V}_{20} ratio was used to account for variations in both measures, where the highest ratio meant the “best” plans. Dose/volume parameters were related to the disease stage and to the type of perfusion defect.

The mean values for eight patients with stage I-II disease are shown on Table 1, and the mean values for 17 patients with stage IIIA-B disease are shown on Table 2.
TABLE 1. MEAN VALUES FOR EIGHT PATIENTS WITH STAGE I-II DISEASE

<table>
<thead>
<tr>
<th>Plan</th>
<th>Type of perfusion defect</th>
<th>fV_{20}</th>
<th>fMLD</th>
<th>PTV_{90}/fV_{20}*</th>
<th>fV_{20}</th>
<th>fMLD</th>
<th>PTV_{90}/fV_{20}*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Large uniform defect adjacent to tumour (4 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-uniform heterogeneous hypoperfusion (4 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMRT</td>
<td></td>
<td>9.5</td>
<td>7.7</td>
<td>13.9</td>
<td>12.6</td>
<td>5.9</td>
<td>7.8</td>
</tr>
<tr>
<td>3-DCRT</td>
<td></td>
<td>9.8</td>
<td>7.5</td>
<td>13.4</td>
<td>14.1</td>
<td>6.1</td>
<td>7.5</td>
</tr>
</tbody>
</table>

*p – not significant

TABLE 2. MEAN VALUES FOR 17 PATIENTS WITH STAGE IIIA-B DISEASE

<table>
<thead>
<tr>
<th>Plan</th>
<th>Type of perfusion defect</th>
<th>fV_{20}</th>
<th>fMLD</th>
<th>PTV_{90}/fV_{20}*</th>
<th>fV_{20}</th>
<th>fMLD</th>
<th>PTV_{90}/fV_{20}#</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Large uniform defect adjacent to tumour (7 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-uniform heterogeneous hypoperfusion (10 patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMRT</td>
<td></td>
<td>13.8</td>
<td>7.7</td>
<td>7.8</td>
<td>17.4</td>
<td>12.9</td>
<td>6.4</td>
</tr>
<tr>
<td>3-DCRT</td>
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<td>7.5</td>
<td>7.5</td>
<td>28</td>
<td>16.1</td>
<td>4.0</td>
</tr>
</tbody>
</table>

*p – not significant; #p=0.002; +p=0.004

Discussion

IMRT has no advantage over 3-D CRT in sparing of FL in patients with stage I-II NSCLC regardless the type of perfusion defect, as well as in patients with stage IIIA-B disease and large uniform perfusion defect adjacent to tumour. In contrast, IMRT leads to significant decrease of fLV_{20} and MLD and improvement of PTV_{90}/fV_{20} ratio in patients with stage IIIA-disease and non-uniform heterogeneous hypoperfusion. We conclude that the use of IMRT compared to 3-D CRT improves the avoidance of SPECT perfused FL in selected patients with NSCLC. If the dose to FL is shown to be the primary determinant of lung toxicity, IMRT would allow for effective dose escalation by better avoidance of FL.

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CT-based planning for craniospinal irradiation

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Cranio-spinal irradiation (CSI) is employed for the treatment of tumours with the propensity to spread via cerebrospinal fluid. The most frequent indication for CSI is in the treatment of medulloblastoma. CSI is technically challenging because of the need to cover a complex clinical target volume that includes the whole brain, the whole length of the spine and the covering meninges. As most of our patients requiring CSI are paediatric and require anesthesia, we have adapted our CSI technique to treat patients in the supine position.

CT-simulation

The patient is placed in a supine position. The patient’s head is immobilized using a thermoplastic mask, and a neck rest is used to extend the neck. In choosing the neck rest, the mandible position should be considered so that the lateral cranial beams do not enter the patient through the shoulders even with junction feathering. Three BBs, one anterior and two laterals, are placed on the mask at the level of mid-brain. These BBs are our “reference point” which then will be used as the isocentre for the cranial fields. Another set of three BBs are placed at mid-trunk, this set represents the “reference point” for the spinal field(s). A scout view is taken to verify the location of the BBs and to verify the positioning of the patient, especially verifying that the patients is lying straight on the table by looking at the spine. The patient is then scanned from 2 cm above the head down to the mid-pelvis with 5 mm resolution.

The supine position is chosen for three reasons: 1) more comfortable for the patient, 2) easily reproduced on daily basis, 3) allows anesthesia for our paediatric patients. However, this position suffers from one major drawback, which is the inability of the technician to verify the junction by visual inspection. However, we use film-based QA method to verify our junction before treatment and on every fraction. This is discussed in another paper that is also to be presented at ICARO.

CTV definition

CTV is defined and contoured on every slice. Our CTV consists of the whole brain and the whole length of the spinal axis.

CSI isocentre location and field definition

We start by creating the spinal field(s) depending on the length of the patient. If the length of the spine is 38 cm or less, one field is used, otherwise, two fields are created, one for each the upper spine and the lower spine. The spinal field is connected to the spinal reference point and then the depth of the point is adjusted to get 100 cm SSD. The inferior border of the spinal field is adjusted to cover the caudal extent of the thecal sac as determined by MRI, while the upper border is abutted at the chin. The width of the spinal field is adjusted to conform to the neural foramen plus 1.0 cm expansion; this is achieved by the use of blocks. The prescription
point is placed around the mid-point of the spinal length and at a depth such that the spinal CT received 100% of the dose ±5%. The two lateral cranial fields are connected to the cranial reference point and this is defined as the cranial isocentre. The superior border of the lateral beams is extended 2 cm in air above the head, while the inferior border is extended towards the mandible. The collimator of the fields is rotated at an angle to follow the divergence of the spinal field, while the table is rotated to follow the divergence of the cranial fields. The match between the three fields is verified by inspecting the matching plane on the transverse, sagital and coronal views.

3-D treatment planning

Following the beam definitions, the treatment planning begins with the cranial fields by delivering the prescribed dose to the prescription (Rx) point, which is not necessarily the same as the isocentre. The Rx point location is chosen such that 100% of the CTV will receive at least 95%. Any isodose greater than 105% is considered a hot-area and is removed by the use of “compensator beams”. These are made by copying the lateral beams and then shaping the blocks to follow the hot area, the weight given to the compensator beams depends on the level of the hot area to be removed. Spinal irradiation planning starts by delivering the prescribed dose to the Rx point as defined by the physician and then moving it, if necessary, to allow for 100% coverage of the CTV. As the spine CTV curves with the body contour, the prescription is allowed to vary from 95%–105% along the entire length of the spine. Hot areas, larger than 105%, usually exist at the superior part of the spinal field. Wedges and/or compensator beams are used to bring these hot areas down to 105%.

Conclusion

The CT-based technique for CSI allows for:

1. Proper definition of radiation fields using anatomy.
2. Proper shaping of spinal fields blocks.
3. Proper verification of the collimator and table rotational angles by inspecting the CT scans for any slight overlap.
4. The flexibility of choosing the Rx point to allow for dose coverage of the target area.
5. The flexibility to use modifiers, such as wedges, and other beams, such compensator beams, to remove hot areas.

With the frequent use of CT-simulators in the Radiotherapy Department, even “classical” techniques, such as CSI, benefits from the accuracy of anatomical definition of CTV and field arrangements and from the accuracy of 3-D planning.
Establishing plaque therapy for ocular tumours in Jordan

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Ocular tumours are rare, distributed by age in bimodal fashion. Retinoblastoma (RB) is the most common ocular malignancy in children, and uveal melanoma (UM) is the most common ocular malignancy in adults. The general incidence of ocular tumours average at around 0.6-0.9/100,000 for males and between 0.5–0.8/100,000 for females.

Enucleation and external beam radiation therapy (EBRT) is considered a standard therapy for many ocular tumours like RB and remain an integral component in the management of these diseases. However, there are many concerns about these modalities and current treatment strategies aim to delay or eliminate the need for them and to preserve vision. To achieve this goal, plaque therapy was established in order to treat RB in children and UM in adults.

Jordan is one of the developing countries with limited resources. Before 2002, most patients with ocular tumours were treated in general teaching and private hospitals that did not advocate multidisciplinary team management. After 2002, the King Hussein Cancer Center was established with the main mission to recruit, maintain and train local expertise that manage cancer patients in Jordan and its neighboring regional areas.

After its establishment, the Ocular Oncology Programme of the centre started networking with advanced ocular oncology centres worldwide (like St. Jude Children's Research Hospital in the USA), introduced state of the art technology to perform focal therapy (such as cryotherapy, transpupillary thermotherapy and the Retcam for imaging) and started new treatment modalities (like the subtenon carboplatin injection, vision rehabilitation and 3-D conformal radiotherapy) in order to preserve eye function, globe, cosmesis and life, as much as there will be possibilities for these aims.

In 2006, we started to prepare the institution for the Plaque Therapy, and arranged a team composed of a radiation oncologist, an ophthalmologist, a medical physicist, an ocular medical oncologist and a radiation protection officer. Two of our team members attended an intensive training course on Plaque Therapy at Princess Margaret Hospital in Canada in late 2006, which was followed by the implementary steps to establish this modality in our country for the first time. After completion of the required steps, we started to establish this technique to our patients.

In March 2008, we treated the first case (adult man with UM), followed by two other cases in September 2008 — a child with RB and an adult with UM. Treatment was done after clinical discussions with our colleagues at St. Jude Children's Research Hospital in the USA and technical discussions (verification of the plan and calculation of the dose to the tumour and organs at risk) with our colleagues at Princess Margaret Hospital in Canada.

In this poster we shall present steps we took to establish this modality from clinical and physical points of view.
REFERENCES


Conformal forward radiation treatment planning using PET/CT and lymphatic Atlas based target volume definition

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It is vital to have precise diagnostic information about the local extension of the tumour and the extent of the lymphatic spread of cancer for determining the stage of the disease as well as the target volume in order to achieve conformal therapeutic dose distribution in 3-D forward treatment planning.

Despite improvements in current imaging modalities such as CT and MRI, the detection of normal or malignant lymph nodes remains a challenge due to the large variability in lymph node characteristics and the variation in imaging quality and the limited imaging resolution. The development of PET imaging, using FDG and other more tumour specific tracers, allows improved detection of involved lymph nodes.

The standard lymph node topography in our newly constructed 3-D lymph node atlas offers a detailed knowledge base of human lymphatics and topographical distribution of discrete lymph node locations in relation to surrounding organs at risk [1].

PET/CT imaging together with the computerized lymph node atlas could serve as ideal tools for target volume definition based on the distribution of normal lymph nodes surrounding the verified malignant nodes on PET/CT to improve the conformity of radiation treatment planning.

In the present work, we utilized PET/CT imaging with the recently developed lymph node atlas for selection and delineation of target volumes in the head and neck region. We have incorporated the topographical information of the atlas lymphatics with the diagnostic PET/CT information to achieve a more accurate delineation of the target volume.

When the lymph node atlas dataset is aligned to the PET/CT-verified lymph node involvement, most of the uncertainties in the lymph node locations could be eliminated [2]. As a result, a higher accuracy in target volume definition, an increase in tumour control probability and a decrease in radiation related toxicity could be achieved [3].

In conclusion, direct access and visualization of reference lymph node atlas geometry can assist in defining the involved lymph nodes and loco-regional lymph clusters that might contain possible microscopic lymphatic spread. This possibility is particularly important to estimate the likely microscopic lymphatic spread beyond what is visible on the PET/CT images. In addition, that can play an important role in improving and standardizing target volume definition in 3-D forward and inverse radiation treatment planning [3].
FIG. 1. The dose distribution of a treatment plan on a coronal view of the lymphatic atlas head and neck dataset. The Gross Target Volume GTV (white), the defined lymphatic regions (blue, red, green) and the planning target volume PTV (black) are shown.

REFERENCES


In-house low cost shield for pregnant radiotherapy patients

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A pregnant patient in her 30\textsuperscript{th} week of gestation presented to our department with soft tissue sarcoma of the right arm. She was planned to receive a total of 60 Gy in 30 fractions using 6 MV AP/PA technique. Fetal dose is recommended to stay below 100 mGy to avoid the non-deterministic nature of radiation [1]. As such, fetal shielding was discussed as per AAPM Report No. 50 [2], which recommends the use of lead-shielding devices. Due to time but mostly financial constraints, manufacturing the recommended shielding at our institution was prohibitive. Therefore, we have devised an in-house low cost attenuator for use as a fetal shield. The attenuator had to fulfil three requirements: a) Easy and quick to make, b) available and cheap material, c) tissue equivalency is preferred. The material of choice that fulfilled all these requirements was cooked rice. While the idea of using rice in radiotherapy is not new, as it is used as a cheap substitute for bolus [3], we have decided that it also fulfills our requirements and thus we came up with the “cooked rice” attenuator.

To ensure high water content, rice with high starch content was overcooked before it was filled in plastic bags. Before applying it to the patient, a rice phantom was made using a U-shaped block (Fig. 1) for the purpose of measuring the attenuation of rice as compared to water. The dose at dmax and at 10 cm was measured.

The patient was put in a prone position, with the treated arm extended above her head to create a maximum separation between the isocentre and the fetus, Fig 2. The dose reaching the fetus is expected to be mainly from head leakage. Three points were identified on the patient for the purpose of measuring the dose, these represented the centre of the uterus from the AP and PA positions (as identified by the physician) and the centre of the uterus laterally. The first two fractions were delivered without the attenuator for the purpose of measuring the dose reaching the three points. Following that on daily basis, the patient's abdominal area was wrapped with the rice bags for a thickness of 4 cm on the AP/PA and 3.0 cm laterally.

Dose was measured at the same three points after the use of the attenuator on several days. The average reduction in dose for the AP/PA and lateral points was more than 50%. The average dose reaching the centre of the uterus from the AP/PA direction was less than 0.05 cGy/fraction, while the lateral point received around 0.1 cGy/fraction. These represented the dose measured at the depth of dmax; therefore, to estimate the dose reaching the fetus, the physician estimated that the uterus is located at 13 cm from the PA point and assumed that it is centred laterally within the patient. After taking the measurements and applying the PDD for the appropriate depth, the average dose reaching the fetus per fraction was estimated to be 0.077 cGy.
FIG. 1. U-shaped block to hold the bags of rice for measurements.

FIG. 2. Schematic diagram showing the extended position of the treated arm. The patient was placed in a prone position, to make use of the central frame of the table as an extra shield for the uterus, dashed line in the figure.

REFERENCES


Transition from 2-D to 3-D conformal radiotherapy of brain malignant gliomas

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Three dimensional (3-D) conformal radiotherapy for the treatment of malignant gliomas of the brain was introduce at the Kazakh Research Institute for Oncology and Radiology in 2006. This technique was performed for 30 patients after surgery treatment (subtotal tumour resection). Earlier patients with brain tumours received conventional radiotherapy with 2-D treatment planning (Fig. 1). Conventional RT did not allow increasing the target dose more than 50–55 Gy (2 Gy fraction) and achieving full regression of residual tumour. The dose escalation led to local complications such as epidermitis and brain edema. It was important to get the exact target delineation required to increase field size to ensure target coverage and therefore increased irradiation volume of normal tissue. The implementation of 3-D conformal radiotherapy allowed to enhance total tumour dose to 65–70 Gy.

The CT images for 3-D planning were obtained for patients immobilized in treatment position with thermoplastics masks. The thickness of the slices was 3 mm. Data were transferred to treatment planning system Eclipse (VARIAN Medical Systems). The pre-operative MRI was used to help delineate target volume.

FIG. 1. 2-D plan.FIG. 2. 3-D plan, transversal.

Target volume delineation was made in accordance with ICRU recommendations (Report 62) [1]. Gross tumour volume (GTV) was defined as the area of visible residual tumour and surgical bed [2]. Clinical target volume (CTV) included the area of microscopic disease extension and was generated from GTV plus 2.5–3 cm margin. Planning target volume (PTV) was defined as CTV plus 5 mm margin to take into account patient motion and geometrical set-up uncertainties during the treatment. The normal brain, eyes, optic nerves, hiasma and brain stem was contoured as organs at risk (OAR).

Treatment plans usually consist four radiation beams (Fig. 2). The homogeneous coverage of target was achieved with use beam weighting and wedges, if necessary. In some cases
noncoplanar beams arrangement was used to decrease dose delivered to eyes and optic nerves (Fig. 3). Plan evaluation was made visually and with dose-volume histograms (DVH) (Fig. 4). The plan ensured PTV coverage within 95–105% was approved for treatment.

The increased tumour dose while minimizing normal tissue dose was achieved also with the use higher radiation beam number and creating irregular fields with multileaf collimator.

Treatment was delivered on Clinac-600C/D accelerator (VARIAN Medical Systems) with multileaf collimator Millenium-80, photon beam 6 MV. Total target doses were 65–70 Gy (2.5 Gy per fraction, 5 fractions weekly).

As a result of 3-D conformal radiotherapy we achieved improvement of tumour control for 28 patients (93.3%). The full response was observed in 16 patients (53.3%) and partial response in 12 patients (40.0%). Only two patients were without effect. The radiation induced toxicity was significantly less in comparison with patients who underwent conventional radiotherapy with a total dose 55–60 Gy.

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Tolerability of chemo-radiation in patients undergoing treatment for cervical cancer in Sarawak, Malaysia

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Carcinoma cervix is the most common cancer in developing countries. Surgery or radiotherapy alone would be the mainstay of treatment for early stage disease. Chemo-radiation of cisplatin based chemotherapy [1] given concurrently with radiation therapy has become the standard of care since the year 2000 in the Department of Radiotherapy & Oncology of the Sarawak General Hospital, Kuching, Malaysia. It is the only oncology centre providing radiotherapy treatment to the population of 2.3 million in Sarawak state. As radiotherapy is the essential treatment for cervical cancer, nearly all patients are referred to this hospital.

The purpose of this study was to evaluate the tolerability of chemo-radiation treatment for cervical cancer in our patient population treated in the years 2004–2006.

Method

Prior to treatment, all patients had a full physical, vaginal, EUA examination, chest X ray and CT scan of abdomen and pelvis including full blood count, renal and hepatic function tests to complete the staging work up. All cases were staged according to FIGO staging (1994). Data were extracted from case notes of all cases diagnosed with carcinoma cervix and treated in the years 2004–2006 using a structured format. Information on patients was collected from case notes, telephone calls and home visits.

Treatment

Radiotherapy treatments were performed according to our institutional guidelines. Conventional X ray simulator is used for planning simulation. External beam teletherapy (EBT) using a four field box technique with photon energy of 6 or 10 MV X ray from a linear accelerator is used in whole pelvic irradiation. Patients with early-stage disease (I & II) received 46 Gy of EBT in 23 fractions over 23 days and four fractions of high dose rate brachytherapy (HDR) with 6.5 Gy dose per fraction to Point A. Late-stage patients (III & IVa) received 50.4 Gy of EBT in 28 fractions over 28 days with three fractions of HDR with 8 Gy dose per fraction to Point A. An EBT boost of 10–15 Gy was added for patients with bulky parametrial disease. Radiotherapy would only be interrupted when patients have grade 3 non-haematologic and grade 4 haematologic toxities.

Cisplatin at 30–40mg/m² was administered weekly starting from week 1 for all consecutive weeks during the course of EBT. It was given 1.5 hours prior to the EBT and omitted on the days of brachytherapy treatment. EBT was given within 2–2.5 hours following cisplatin. Antiemetics such as 5HT3 antagonists and dexamethasone were given as pre-medications prior to chemotherapy. Chemotherapy was omitted if patients had haemotologic and non-
haematologic toxicities (CTCAE Ver. 3) of more than grade 2. Cisplatin was resumed when the patient’s toxicities grading changed to grade 1. Patients with poor performance status and impaired renal function were excluded for concurrent chemotherapy. Data was analysed using SPSS software.

Results

There were a total of 204 cases. Seventy-one percent (n=145) were in early stage (I & II). Of the 204 patients, 10 patients were excluded from the analysis as they did not complete the full course of RT. Concurrent chemotherapy was prescribed to 153 patients of which 69% (n=106) received 4 to 5 cycles. Treatment interruption was noted in 23% (n= 45/194) of our patients with 77% (n=149/194) completing the treatment in 58 days. Treatment interruption associated with patients was 14% (n=27/194) and, due to machine problems, was 9 % (n=18/191). The adverse effect of patients treated is shown in Table 1. Of the grade 3 toxicity, 9.2% had anaemia, 3.6 % had leucopenia, 2.5% had gastrointestinal toxicity, 2.0% had cutaneous symptoms and 1.0% has genitourinary symptoms. Treatment was interrupted for five patients due to grade 3 gastrointestinal symptoms as well as for two patients due to cutaneous symptoms.

Conclusion

The results reveal that chemo-radiation is well tolerated in our population as majority of the patients completed the full course of radiotherapy and 69% completed four to five cycles of concurrent chemotherapy with few patients having grade 3 morbidity.

TABLE 1. ADVERSE EFFECTS OF 194 PATIENTS TREATED AT THE SARAWAK GENERAL HOSPITAL, KUCHING (CHEMO-RADIATION, N = 153; RADIATION ALONE, N = 41)

<table>
<thead>
<tr>
<th>Toxicity/ Adverse effect</th>
<th>Toxicity Grading</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Anaemia</td>
<td>111</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>117</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>72</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>178</td>
</tr>
<tr>
<td>Cutaneous *</td>
<td>30</td>
</tr>
<tr>
<td>Fatigue</td>
<td>167</td>
</tr>
<tr>
<td>Weight loss</td>
<td>105</td>
</tr>
</tbody>
</table>

Note: * - RTOG toxicity grading

REFERENCE

Development of specialist training programme in clinical oncology: The Malaysian experience

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The Malaysian government has traditionally sent clinicians to the United Kingdom for postgraduate training in clinical oncology over the last 30 years. Whilst this provided an opportunity for exposure to treatment facilities and techniques in a developed country, it proved to be an expensive exercise. In addition, most of the training occurred outside the context of the local culture and pattern of malignancies. In 2000 there were only 30 practising oncologists in Malaysia to serve a population of 20 million, which was significantly lower than the ratio recommended by the World Health Organization. With the rising incidence of cancer in Malaysia, it was decided that a local university-based programme was required to train oncologists within Malaysia, to provide the necessary non-surgical cancer services for a growing population.

Groundwork

A steering committee was set up with the purpose of developing a four year structured training programme for a Master of Clinical Oncology degree, under the auspices of the University of Malaya. The aim was to produce ‘generalist’ clinical oncologists who are able to safely and competently manage a broad range of malignancies with both chemotherapy and radiotherapy. The committee of nine clinicians consisted mainly of clinical oncologists who were previously trained in the United Kingdom and was chaired by the head of department of the Clinical Oncology Unit at University of Malaya Medical Centre.

The syllabus is based largely on the Royal College of Radiologists (United Kingdom) higher specialist training programme for clinical oncology, with both summative and formative assessments, plus a dissertation in the final year of training. There were three core components of training: 1) basic sciences (radiotherapy physics, medical statistics, molecular biology, pathology, chemotherapy, radiobiology), 2) clinical training with continuous assessment, and 3) research.

There were initial concerns about the capacity of local resources to deliver a high quality training programme and to organize exams which would adequately reflect the knowledge and experience of the trainees. In order to maintain standards, it was determined that the exams would be moderated by external examiners, both locally and internationally.
Implementation and development

After the programme was approved by the university senate in 2002, three trainees were selected for the first intake of the programme. Trainees rotate through the three public cancer centres in Kuala Lumpur, namely the University of Malaya Medical Centre, Universiti Kebangsaan Malaysia Medical Centre and Hospital Kuala Lumpur, to maximize the learning opportunities. Lectures and tutorials were provided by academic and clinical staff to prepare trainees for the two part written and clinical exams. There was close cooperation and collaboration between the clinical oncologists from the universities and the Ministry of Health.

The teaching was well supported by other university departments including medical physics, pathology and statistics. The core group of external examiners provided invaluable advice to hone the existing programme. In addition, the International Agency for Atomic Energy (IAEA) provided educational support in the form of a visiting lecturer, internet-based distance learning programme and ‘training the trainers’ course. Feedback was encouraged from pioneering trainees to help improve the quality of training.

The programme has grown from strength to strength over the last six years as trainers and resources are developed. A total of 28 trainees have been admitted into the programme since its inception. Four have completed the training and are now practising as specialist staff.

Challenges and future directions

Teaching of the basic sciences remains a challenge with the lack of specialist teaching staff. Four candidates have not completed the training programme since it started and we are working towards minimizing the rate of attrition. We plan to gradually increase the acceptance of trainees as our pool of resources develop. One of the future challenges will be to retain these clinicians in the public system and to maintain a balance between specialists in the academic and clinical streams.

Conclusion

When the idea of a specialist training programme for clinical oncology was first mooted, there were some uncertainties about our ability to create a successful training programme, but over the last two years, the steering committee has begun to see the fruits of its labour. The history and development of this project have demonstrated the ability of a developing country to shape its own future in healthcare, with the support of international agencies such as the IAEA. It also reflects a successful collaborative effort between the Ministry of Health and the Ministry of Higher Education of Malaysia.

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Analysis of ethnic and regional disparities and appropriate intervention rate for the use of radiotherapy in lung cancer in New Zealand

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Due to its high incidence, the IR for RT in lung cancer is an important parameter in health service planning. Models usually predict a higher IR than reported actual IR values, for reasons that are unknown. NZ has a significant indigenous minority (Māori) and immigrants from the Pacific Islands (PI) that are over-represented by poor socio-economic status and for whom the outcomes from lung cancer are poor.

Aims

1) To determine the intervention rate (IR) for radiation therapy (RT) in the management of lung cancer in New Zealand (NZ);

2) To determine the use of RT in different ethnic groups and different health areas.

Methods

An audit of the management of 565 lung cancers diagnosed in the Auckland and Northland region of NZ in 2004, and who received a component of treatment in secondary care, provided the basis of the study. Demographic, tumour and treatment factors were obtained from multiple sources. Aspects relating to the presentation, investigations and timelines for diagnosis, staging and treatment and survival were analysed. This analysis enabled the IR for lung cancer to be determined and permitted differences in the management of ethnic groups to be evaluated.

Results

The utilization of RT was estimated at 43% (range 40–48%). A further 8% of deceased cases may have benefited from RT, to give an “appropriate” IR of 51%. All other cases were considered to have been well managed without the use of RT. Following multivariate analysis, disparities in the presentation and management of ethnic groups was identified.
Maori presented with more advanced disease than non-Maori, non-PI; although the same proportion of Maori received treatment for lung cancer, the intent was more likely to be palliative; and Maori and PI were more likely to decline RT.

Discussion

The estimated actual (43%) and appropriate (51%) IRs for RT in this study were substantially less than modelled values. Inclusion of cases of post mortem diagnosis would have further reduced the appropriate IR. The difference from the Canadian model (61%) was due to early deterioration and mortality, which is not accounted for in the models. The additional difference from the Australian model (76%) was due to an assumption of higher treatment rates for all stages of lung cancer. The high early mortality and later presentation of Maori and PI indicate the need for greater primary care initiatives to improve earlier diagnosis. The lower curative treatment of Maori requires further research, particularly regarding documentation of comorbidities. The high number declining recommended treatment is of concern and may indicate that oncology and RT services are not configured for these ethnic groups.

Conclusion

The use of RT for lung cancer in NZ was substantially less than internationally recommended rates. However a careful review of all cases suggested that the NZ estimated optimal rate was appropriate in the NZ context at that time. Further increases in the IR will depend on earlier diagnosis and reconfiguration of services to make them more acceptable to minority groups. The importance of local data for allocation of limited resources is emphasized.
Effects of radiotherapy on cancer patients infected with HIV/AIDS in Nigeria

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Cancer reduces immunity, as does human immunodeficiency virus (HIV).

Over 75\% of cancer patients undergoing radiotherapy at one stage or the other of the disease management. The overall effects of radiation therapy on cancer patients infected with HIV/AIDS were determined in order to evaluate prognosis and initiate corrective measures where necessary. The subjects of the study were cancer patients attending the five existing radiotherapy centres in Nigeria. Questionnaires were administered to patients and thirty (30) personnel involved in radiotherapy across the country in 2005. Clinical data were also retrieved from records of patients treated between 2003 and 2005. The statistical software, EPI info version 6.04b was used for data analysis. A total of 250 cancer patients were involved in this study, out of which 43 (17.2 \%) were found to be HIV positive. Radiotherapy plays a vital role in the management of malignancies in HIV-infected patients. Although the technique does not change seropositivity (HIV status), it serves the purpose of palliation if treatment is optimized. Further immunosuppression is the predominant observed effect of therapeutic radiation doses on cancer-HIV patients. Rate of local tumour recurrence and incidence of metastasis was higher in HIV positive patients than their non-HIV counterparts. Post radiotherapy, long term effects of irradiation on HIV/AIDS patients could not be established due to lack of regular follow-ups. Medical physicists involved in radiotherapy need to take stringent measures in optimizing patients’ doses particularly those infected with HIV/AIDS in order to avert risks attributable to undue exposures to radiation. For retrospective studies, it is strongly recommended that CD4 and full blood counts (FBC) should be well established, before, during and after radiotherapy to further determine the effects of radiation therapy on HIV/AIDS-cancer patients.

\begin{table}
\centering
\caption{Effects of conventional radiotherapy on HIV-infected cancer patients as observed by Nigerian personnel.}
\begin{tabular}{llll}
\hline
S/n & Effects & Freq. & \% & Cumulative \% \\
\hline
1 & Anaemia & 3 & 10.0 & 10.0 \\
2 & Risk of early complications & 1 & 3.3 & 13.3 \\
3 & Further immunosuppression & 12 & 40.0 & 53.3 \\
4 & Low survival rate via opportunistic infections & 1 & 3.3 & 56.6 \\
5 & Poor wound healing & 1 & 3.3 & 59.9 \\
6 & Reducing symptoms of cancer if ARV is properly used & 3 & 10.0 & 69.9 \\
7 & Same effects as in non-HIV patients if ARV drugs are used and FBC is in check & 5 & 16.7 & 86.6 \\
8 & Same but more severe effects as in Non-HIV patients & 4 & 13.4 & 100.0 \\
\hline
TOTAL & & 30 & 100.0 & \\
\hline
\end{tabular}
\end{table}
FIG. 1. Types, stages and incidence of cancer among HIV patients in Nigeria.

FIG. 2. General complaints of Nigerian cancer patients during and after radiotherapy.

REFERENCES


Experience and problems of managing a randomized clinical trial in a low income and a low resource country, Pakistan: A success story

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The number of cancer patients requiring treatment is increasing in low and middle income countries, therefore international, multicentre randomized clinical trials are needed to generate evidence based data for resource sparing approaches for frequently occurring cancers in these countries. Such data could only come from Phase III high powered randomized clinical trials to be carried out in an indigenous population and an indigenous health care environment.

The Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar, Pakistan, was one of the participating centres in the IAEA coordinated research project (CRP) on “A randomized multicentre study of five versus six weekly fractions of radiotherapy in the treatment of squamous cell carcinoma of the head and neck.”

The aim of this study was to examine whether reduction in overall treatment time by increasing the number of weekly radiotherapy fractions from five to six and maintaining the same total dose and fraction number would improve the tumour response and would be acceptable with regard to early and late morbidity, as well as being a suitable therapeutic principle in all therapeutic environments especially with reference to countries with low income and limited resources. Moreover, the project also looked into the biological and economic gains of such an accelerated regimen in low resource settings.

A total of 908 patients were inducted by nine cancer treatment centres of seven developing countries — Chile, Estonia, India, Lebanon, Pakistan, Saudi Arabia and South Africa — from January 1999 to March 2004. IRNUM, Pakistan inducted 209 patients [1]. This initiative of IRNUM to participate in such a trial was to take up a gigantic uphill task in the face of limited resources and so many other constraints. Moreover, the all time impressions were that in view of lack of education, of poverty, prolong treatment times, homesickness, radiation reactions, these patients tend to leave the treatment incomplete and tend not to turn up for follow-up.

The research at IRNUM in the context of the IAEA CRP was conducted with the aforementioned backdrop. The patients inducted at IRNUM had heavy tumour burden (median tumour size 5cm), with 32% in Stage III and 46% in Stage IV. Regarding the nutritional status, 22% were severely thin (BMI<17) and 16% were underweight (BMI 17–18.5). Ninety one percent (91%) were illiterate with limited affordability, and 69% had daily income of less than US$1.

On one hand this research provided us with the opportunity to work in the face of so many clinical, technical, financial, administrative, human resource, socio-economic and communication constraints. On the other hand it proved to be a milestone in providing answers to certain important questions based upon scientific evidence, such as the following.
N. Begum

- The efficacy of six fractions per week as compared to five fractions per week (fx/wk) in improving five year loco regional control rates of 41% versus 28%, p=0.01, RR: 0.68 (0.52–0.89) and the disease specific survival rates of 53% versus 39% for six versus five fx/wk, respectively, at p=0.01, RR:0.68 (0.51–0.91) [2].
- Acute morbidity in the form of confluent mucositis was significantly more frequent in six fx/wk arm but there was no difference in late radiation effects [1, 2].
- It also helped in rejecting the impressions regarding compliance to treatment completion and follow-up in the context of a developing country. By adopting certain proactive measures at IRNUM 91.4% patients completed the total planned dose in 6 fx/wk arm and 87.5% in 5 fx /wk arm, with a follow up rate of 99%.

The adoption of this accelerated fractionation regimen (6 fx/wk) in Pakistan and other countries with similar low income and low resource settings can have the following advantages:

- Biologically more effective as reflected in improved loco regional control rates and disease specific survival rates.
- Economically more cost effective, as reduction in the treatment time by seven days means a saving in direct medical costs of about US $300 per patient, which when multiplied by a large number of patients would result in substantial cost savings.
- No additional resources are required.

This experience proved the feasibility of successfully managing a randomized clinical trial in a low income and low resource setting. Based upon the conclusions of the evidence-based data generated from this trial, the management policies can be rationalized and future trials on this line could be planned and accomplished in order to further improve the treatment outcome and quality of life of these patients.

Acknowledgements: This work was supported by a grant from the IAEA. Thanks are due to the project coordinators at IAEA-ACC Trial Centre, Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark and the IAEA-ACC Study Group.

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To compare treatment outcome with ring and Fletcher type applicators in brachytherapy of carcinoma cervix

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Bino Cancer Hospital, Pakistan has treated 29 patients of carcinoma cervix since October 2005 (15 patients of Stage II, and 14 patients of Stage III), with concomitant chemoradiotherapy by using both external beam radiation therapy on cobalt-60 machine and intracavitary brachytherapy on Varian HDR. Brachytherapy System having ABACUS Treatment Planning System with different arms and protocols.

There are many aspects of comparison between ring and Fletcher applicators for treatment planning. The main aspects are the dose, position of the applicators, sources relative to the reference points and geometry of the organs during treatment on HDR remote after-loading system. Four reference points — rectum, urinary bladder, right pelvic wall and left pelvic wall were undertaken. Rectal and bladder points were marked using barium sulphate and urographin, respectively.

For each fraction dose of 5 to 9 Gys. was normalized at Point A according to the Manchester system.

Average dose received at four reference points treated with ring applicator was uniform due to a better alignment according to the Pelvic Geometry. However, reconstruction problem was seen in a Fletcher type applicator due to misalignment between Ovoid channels and the existence of extra gap between tandem and Ovoid channels.

Standard deviation (SD) of dose received by the ring applicator was near to zero, which shows a constant dose receipt at reference points with each fraction whereas Fletcher type applicator shows non-uniform dose and SD higher than zero in each patient.

Anatomical topography was obtained using orthogonal radiographs.

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The role of brachytherapy in cancer cervix experience at the Nuclear Medicine, Oncology and Radiotherapy Institute, Islamabad

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Cervical cancer remains a frequent and gruesome cause of death. Worldwide it is the second most common cancer in females after breast cancer. The incidence varies widely among different countries and cultural and social classes within the same country [1]. According to the statistics of the Nuclear Medicine, Oncology and Radiotherapy Institute (NORI) for a 14-year period, cervical cancer was found to constitute 27% of all gynecological malignancies, 4.22% of all female cancers, and 2.15% of all new cancer cases registered at NORI (Fig. 1).

More than 70% of the patients are in locally advanced stages and are therefore inoperable. Even those who are operable, majority of them do not undergo surgery because of either medical contraindications or their refusal to undergo surgery.

Chemotherapy, which is rapidly becoming the standard of care either as neoadjuvant treatment or concomitantly with radiotherapy, is not afforded by most of our patients. Radical radiotherapy therefore remains the treatment of choice in more than 90% of our cervical cancer patients. Patients with locally advanced cancer of cervix are nowadays being treated at NORI as per international practice with a combination of concomitant chemo-radiation and high dose rate (HDR) brachytherapy. HDR brachytherapy machine was installed at NORI in October, 1996. Since then a total number of 442 insertions have been done up to December, 2006. Fifteen iridium-192 sources have been installed during this period.

Out of all the gynecological cancer cases registered at NORI during this period, only 50% could be treated with brachytherapy with favourable response and mild toxicity. The cost of one iridium source is approx. US$7,000. The average number of insertions done with one source is about 29.5; therefore, the estimated cost for one patient comes out to be very high.

Besides cost of the source, other problems that we encounter are that there is no X-ray or fluoroscopy facility inside the treatment room and, although treatment time is short, planning takes very long. Moreover treatment plan has to be made for each insertion of one patient as position of applicators is not reproducible due to non-availability of proper fixators. Therefore only one patient can be managed to be treated in one day. Furthermore there are frequent breakdowns in the machine and at times the patients do not report in spite of prior appointment.

Keeping in view the results of brachytherapy, it is strongly recommended that, to fully utilize the source, brachytherapy needs to be done in non-gynecological malignancies and the patients for brachytherapy from other oncology centres with no brachytherapy facilities should be referred to NORI. Moreover, an X-ray facility should be available inside the treatment room and treatment plan made at the time of first insertion for an individual patient should be made reproducible for subsequent fractions for the same patient if significant change in anatomy is not expected.
FIG. 1. Incidence of different gynaecological malignancies at NORI, Islamabad.

REFERENCE

Image-guided IMRT for prostate cancer: Influence of organ motion correction associated with acute toxicity and quality of life

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Purpose

Internal organ motion is a limiting factor for the success of dose-escalated irradiation of prostate cancer [1, 2]. We assessed the effect of an online field-based verified motion error correction method related to acute toxicity and quality of life for prostate IMRT.

Materials and methods

Forty-two localized prostate cancer patients were prospectively treated with IMRT and escalated doses of from 72 to 80 Gy. A margin of 5 mm was used to generate the treatment planning volume (PTV).

A recently developed dual kilovoltage on board imager (Fig. 1A) was used for the daily documentation, registration and correction, on real time, of a gold marker implanted into the gland (Fig. 1B).

The intrafractional motion error of a patient was incorporated into the IMRT plan for recalculation and to estimate dosimetric effects. Dose volume histograms (DVH) were used to evaluate mean doses to treatment volumes. The Radiation Therapy Oncology Group (RTOG) glossary was utilized to assess acute toxicity. Quality of life (QOL) changes were assessed using the QOL-ACD questionnaire for cancer patients.

Results

The impact of isocentre shifts on the clinical target volume (CTV) dose was +1%. In our study, doses to rectum were increased by inferior and posterior shifts by as much as 5% while doses to bladder were seen reduced up to 2.76% with inferior and posterior shifts.

High-dose IMRT was well tolerated acutely; five patients (12.1%) experienced grade I urinary toxicity, one patient (8.33%) rectal toxicity grade I and no >grade II toxicity was observed.

An improving tendency was observed in all items of the QOL questionnaire, with trouble from urinary symptoms (P= 0.05) and face scale of mood (P <0.001) reaching statistically significant improvement after six months of post-treatment.
Conclusions

In this study, clinical and dosimetric effect of organ motion on target and clinical structures could be ameliorated safely by incorporating a field based repositioning approach in the settings of high total dose prostate IMRT. Acute morbidity was seen to be low and benefits in patients’ general QOL scales were seen at six months after treatment. Therefore, if long follow-up outcomes persist satisfactorily, routine use of image guided field based target verification techniques should become necessary for high precision prostate radiotherapy.

FIG. 1 A/B. Scheme of the clinical implementation of a dual kilo voltage fluoroscopy and flat panel system on the gantry of the Linac (Clinac 23EX, VMS) for real-time target positioning.

REFERENCES


Definitive radiotherapy in young patients newly diagnosed with nasopharyngeal carcinoma

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Cancer of the nasopharynx (NPC) is an NIH listed rare tumour that children and adolescents of 0–19 years of age have a crude rate calculated at 0.6 cases per million by the North American Central Cancer Registry (NACCR) based on data published in 2003. According to the International Agency for Research on Cancer (IARC) the worldwide crude rate for NPC in children, 0–14 years of age, is 0.1 per 100,000. As of 2002, the most affected continent is Asia with 891 cases, followed by Africa: 469 cases, America: 167 cases and Europe: 45 cases.

Objective

This is a retrospective, single, institutional review of the management and results of locally advanced nasopharyngeal cancer in childhood and adolescents in Chiang Mai, Thailand.

Materials and methods

From January 2000 to December 2005, there were 16 nasopharyngeal cancer patients receiving treatment at the Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University.

Five patients were excluded from this analysis because they were presenting with distant metastasis or diagnosed with non-Hodgkin’s lymphoma. A total of 11 locally advanced nasopharyngeal cancer patients were entered onto this study. The median age was 18 years, ranging from 10 to 19 years. The majority (90.9%) were male with the male-to-female ratio of 10:1. Two patients were in stage 3, five patients in stage 4A and four patients in stage 4B, according to the 1997 AJCC staging system. Treatment approaches include seven concurrent radiochemotherapy + adjuvant chemotherapy and four neoadjuvant chemotherapy + concurrent radiochemotherapy. The Median radiation dose at primary site was 7,000 cGy (6600–7000 cGy) and the median radiation dose at regional lymph node was 7,000 cGy (5000–7000 cGy). The chemotherapy regimens were cisplatin + 5-fluorouracil in eight patients and carboplatin + 5-fluorouracil in three patients. Ten patients achieved complete response and one patient got partial response. The median follow-up time was 51 months (6-86 months). Six of 11 patients (54.5%) have been followed for more than 50 months. There was only one patient (9.09%) who developed distant bone metastasis of pelvis eight months after treatment completion.

Conclusion

This review demonstrated that the definitive radiotherapy integrated with systemic chemotherapy is the effective treatment for locally advanced nasopharyngeal cancer in the young. This combination also yields the prolonged survival in this retrospectal population.
Total lymphocyte count in HIV/AIDS patients with carcinoma during radiation therapy

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The purpose of the study is to determine the effects and factors associated with total lymphocyte count in HIV-infected carcinoma patients during radiation therapy.

A retrospective study of HIV infected carcinoma patients during RT was conducted in the Department of Therapeutic Radiology and Oncology, Rajavithi Hospital during January 1995–December 2006. All patients received conventional radiation therapy (200 cGy per fraction, five fractions per week). With a weekly lymphocyte-report during treatment, at least four weeks were reviewed. Patients who received radiation in more than one region were excluded. Generalized linear model was used to determine the association of lymphocyte count with different radiation dose and age. Independent T-test was used to determine the association of reducing lymphocyte and antiretroviral treatment (ART).

Twenty-three HIV infected carcinoma patients, with ages ranging from 27 to 67 (median 37) years were included in this study. Ten patients (37.3\%) received ART during radiation. Lymphocyte was significantly decreased on higher total radiation dose (p 0.000), see Fig. 1. The reduction of lymphocyte was significantly associated with higher age (p 0.033) and not receiving ART (p 0.050). Seven patients (70\%) who received ART during radiation reached a two-year survival. Nine patients (52.9\%) who did not receive ART had to undergo follow-up within 6 months.

The conventional radiation therapy significantly reduced lymphocyte count on HIV-infected carcinoma patients. ART during radiation improved long term survival and made slower decrease of lymphocyte count. More consideration about age and specific laboratory tests including CD\textsubscript{4} count and viral load are needed to determine whether ART should be initiated during radiation treatment.

\textbf{FIG. 1. Radiation dose and total lymphocyte count.}
A randomized trial comparing between two fractionation schedules in the treatment of metastatic bone pain

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Purpose

To compare the efficacy and side effects of two different dose fractionation schedules, which are equal in biologically effective dose (BED) in the management of painful bone metastases.

Material and methods

In a prospective trial, 95 patients with a total 124 sites were randomized to receive either 30 Gy given in ten fractions daily (BED 32 Gy$_{10}$) or 17 Gy given in two fractions, every other day (BED 30 Gy$_{10}$). The primary tumour was in 28%, 23%, 16%, 11% and 22% of patients with breast, lung, prostate, colorectal, and other cancer, respectively. Outcome measures were pain relief, as measured by the visual analogue scale (VAS), patients’ assessment of treatment and analgesic consumption, especially in the first month.

Results

A total of 114 treatment sites were evaluable for response. The two groups did not differ with respect to age, sex, primary tumour, metastasis location, performance status, degree of pain and analgesic consumption. The treatment was completed as planned in 96% of patients. The degree of pain relief did not differ between the two treatment groups. In the first month, the overall response rate was 94% in two treatment groups. Nevertheless, arm 2 achieved significantly faster relieve on the pain symptom than arm 1 (p=0.007). There was neither any significant difference in the duration of pain relief nor the need for re-irradiation. There was no toxicity in the two groups.

Conclusions

This preliminary randomized study showed that 30 Gy given in ten fractions daily was as effective as 17 Gy given in two fractions every other day in relieving pain from bone metastases.
Vaginal vault brachytherapy in low risk endometrial cancer


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Purpose
To evaluate the efficacy and side effect profile of adjuvant vaginal vault brachytherapy alone after surgery in stage I endometrial cancer.

Methods and materials
Between May 2005 and May 2008, a total of 41 patients with early endometrial carcinoma treated with vaginal vault brachytherapy alone after surgery were identified. Patients were treated using a single line source vaginal stump applicator (Varian Medical Systems a donation from the IAEA under the national technical cooperation project TUN/06/010) to deliver a dose of 5 Gy per fraction at a depth of 5 mm from the applicator surface. A total of four fractions were delivered treating once a week to deliver the total dose of 20 Gy in four fractions.

Results
There were two stage IA and 39 stage IB. Immediate reactions are grade 1 urinary tract symptoms occurring in almost all patients after the first fraction probably in relation with the use of bladder catheter. Diarrhea occurred in two patients and resolved spontaneously. Late morbidity was rare except vaginal stenosis and mild bleeding seen in two patients. There were neither deaths nor local recurrences in this series. Two patients developed other primary cancers (breast and colon).

Conclusion
This study confirms that vaginal vault brachytherapy is associated with a high rate of pelvic control for low risk endometrial cancer with minimal toxicity.
Evolution from 2-D to 3-D: Craniospinal irradiation

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This study is prospective. It is about the evolution — the craniospinal irradiation from 2-D to 3-D at the Hospital Universitario de Caracas (HUC). Since two years this institution has made 3-D techniques. The children received both treatments.

The objective of the study was to describe the steps and to confront results during the period from 2006 to 2008.

The traditional CSI techniques that were utilized opposed lateral cranial fields and one more posterior spinal field depending on the patient size. Junctioning of monoplanar fields in the cervical region is potentially hazardous because of the risk of overlap resulting in radiation myelitis. Consequently, great attention needs to be paid to precise immobilization and variety of immobilization devices. Image guidance during radiotherapy can help in ensuring day-to-day reproducibility. The prone positions permit direct visualization of the light field from the linear accelerator on the patient thereby allowing daily adjustments of the junctions. However, if anesthesia or sedation is required as may be the case with young children, a supine set-up may be considered safer.

In this study ten cases were analysed with simulation 3-D and 2-D, and the techniques used were explained.
Retinoblastoma: Treatment of one eye. Comparative analysis of external radiotherapy techniques

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Retinoblastoma is the most common intraocular malignant tumour in children. The incidence is the same all over the world (1:15000–30000 live birth) and it is the second intraocular tumour in any group of ages after melanoma. The external beam radiation therapy (EBRT) has been used for decades as a conservative treatment alternative for selected patients, to avoid surgical enucleation. Despite the use of focal therapies as photocoagulation, cryotherapy, transpupillary thermotherapy, episcleral brachytherapy, chemotherapy, the EBRT has had an important role and is still one of the most effective therapies.

The aim of this study was to develop a comparative analysis of three EBRT techniques: lateral collimated D-shaped photon field, 3-D CRT and IMRT.

The ideal treatment should be able to generate a homogeneous coverage of the entire retina avoiding subdosage to the ora serrata retinae and protecting the lens.

We use 3-D volume from CT images of two patients with retinoblastoma diagnosis and we applied the three different techniques through our treatment planning system (Eclipse). The prescribed dose was 45 Gy in 25 fractions of 180 cGy/day in the same target volume. All these techniques were compared through the dose volume histogram using 6 MV photon beam from a linear accelerator (Clinac 23 EX-S with multileaf collimator) by an isocentric technique at a source-to-axis distance of 100 cm [1].

We analysed the three following techniques:

1) The lateral D-shaped collimator (described by Schipper), modified by adding a conformal multileaf collimator to the D-shaped external block [2].

2) 3-D CRT treatment with three arc fields with a lens block.

3) IMRT radiation treatment planned with six treatment fields with constraints in the lens using an algorithm of optimization with dose volume histogram (DVH).

In all cases, isodoses in the three dimensional reconstructed volume from CT images were analysed in axial, sagittal and coronal views. In each treatment plan, the volumes (V) and the average doses (D) were analysed in the following structures: eye and irradiated lens, contralateral lens, hypophysis and central nervous system (CNS).

Table 1 shows our results.
TABLE 1. RESULTS OF THE COMPARATIVE ANALYSIS OF THREE EBRT TECHNIQUES

<table>
<thead>
<tr>
<th>Techniques</th>
<th>With lens protection</th>
<th>Without lens protection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eye/lens</td>
<td>Contra-lateral lens</td>
</tr>
<tr>
<td>D-Scipper</td>
<td>4500 cGy</td>
<td>366 cGy</td>
</tr>
<tr>
<td></td>
<td>1700 cGy</td>
<td></td>
</tr>
<tr>
<td>3-D CRT</td>
<td>4500 cGy</td>
<td>1117 cGy</td>
</tr>
<tr>
<td></td>
<td>2100 cGy</td>
<td></td>
</tr>
<tr>
<td>IMRT</td>
<td>4500 cGy</td>
<td>10 cGy</td>
</tr>
<tr>
<td></td>
<td>3057 cGy</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions

Taking into account that most of the patients are less than two years old, we considered that the lateral D-shaped collimator is the best alternative, since it reduces significantly the radiation doses in hypophysis and CNS, followed by IMRT and 3-D CRT techniques. For paediatric patients dose distributions must be evaluated in relation to the tumour control probability (TCP), late effects and the development of secondary tumours associated with low radiation doses (integral dose) case by case.

REFERENCES

Experience in total body irradiation in one institution

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Total body irradiation (TBI) combined with intensive chemotherapy plays an important role in conditioning patients with hematologic malignancies before bone-marrow transplant (BMT). The goal of TBI in this setting is threefold: destroying residual neoplastic cells, clearing the host marrow to allow repopulation with the donor marrow cells, and providing a sufficient degree of immunosuppression to avoid allograft rejection by immunologically active cells in the host. This is the reason why in 1994 the technique of total body irradiation in the Radiation Therapy Department of “Professor Dr. Juan P. Garrahan” Children’s Hospital was developed. The objective of this work is to analyse the dosimetric results of TBI and evaluate the results of BMT in patients undergoing allogeneic BMT with acute lymphoblastic leukemia.

Between November 1994 and January 2006, 46 eligible patients with acute lymphoblastic leukemia in first or greater remission were analysed. Fourteen (69.9%) patients were female and 32 (30.4%) were male. The median age was 8.7 years (2–21). Twenty-four (52.2%) patients with ALL were in 1st remission, 17 (37%) in 2nd remission and 5 (10.8%) were in 3rd remission. Forty-five patients were transplanted with grafts from HLA-identical family related donors while one with umbilical cord. The pre-transplant conditioning regimen included cranial and testis boost, TBI and chemotherapy. The doses of radiation for cranial and testis was 6 Gy. TBI was delivered in every case before conditioning chemotherapy with six equally divided fractions over three days, twice daily, with a 12 Gy as a total dose, and after TBI chemotherapy with etoposide. During each TBI session, the dose was monitored in vivo using semiconductor diodes or ionization chamber placed directly on the central axis (pelvis) and off-axis anatomic sites (head, lungs and legs). In our case we use the laterolateral irradiation, with the patient seated or laid down, with photons of 10 MV of linear accelerator or with a cobalt unit. Aluminum compensators are used to produce a uniform dose throughout total body regions to within ±10% of the dose specified at the pelvis.

Out of 46 patients analysed, 20 patients died and 26 are alive (23 are alive, free of disease and 3 are in partial remission), with 40% disease-free survival at 134 months, being relapse the more common cause of death (13 patients). The toxicity was: VOD 3 patients; encephalopathy 2 patients; kidney 8 patients; mucositis 5 patients; cistitis 1 patient; pneumonia 1 patient; GvHD acute 35 patients; GvHD chronic 9 patients; and other: 2 patients. Fourteen patients relapsed, 20 patients dead and 26 patients alive.

All measurements were analysed. The percentage relative error, that is to say, the difference in percentage between the dose measured with respect to the prescribed one in the different points is observed (Table 1).
TABLE 1. ANALYSIS OF MEASUREMENTS

<table>
<thead>
<tr>
<th></th>
<th>Cobalt Unit</th>
<th>Photon 10 MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head</td>
<td>Mean: 0.31% SD=3.37</td>
<td>Mean:-3.23% SD=2.10</td>
</tr>
<tr>
<td>Lung</td>
<td>Mean: -3.07% SD=4.70</td>
<td>Mean:-7.52% SD=2.69</td>
</tr>
<tr>
<td>Pelvis</td>
<td>Mean: -1.58% SD=2.95</td>
<td>Mean:-1.20% SD=1.95</td>
</tr>
<tr>
<td>Legs</td>
<td>Mean: -1.42% SD=4.93</td>
<td>Mean:-2.98% SD=2.15</td>
</tr>
</tbody>
</table>

Conclusions

The technique of TBI in 12 years of experience has demonstrated, based on the dosimetric aspect, to be effective in the delivery of prescribed dose. The BMT in children with ALL remains an important treatment option for the patients in second remission or in ALL-high risk after first remission.

REFERENCE

Adapting the linear accelerator room to perform electron intraoperative radiotherapy for early breast cancer

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The standard treatment for early breast cancer consists of conservative surgery, sentinel lymph node biopsy or axillary lymph node dissection followed by six week external radiation to the whole breast.

Long term follow-up showed low local recurrence rate and, when it occurs, is in the vicinity of the tumour bed [1]. So, it could be feasible to give irradiation limited to a smaller volume. Some techniques had been proposed, especially the electron intraoperative therapy (ELIOT). The method delivers a high dose single fraction of irradiation to the tumour bed during surgery.

Some advantages with this method are the avoidance of external daily irradiation, direct visualization of the tumour bed and low acute toxicity. Possible disadvantages are the long term cosmetic damage such as telangectasis and fibrosis, the selection of the patients, etc.

The number of new cases of breast cancer expected in Brazil in 2008 was 49,400, with an estimated risk of 51 cases per 100,000 women. In Fortaleza, the estimated number of newly diagnosed patients is 640. Although considered to have a relatively good prognosis if diagnosed well, mortality rates from breast cancer remain high in Brazil, most probably because the disease continues to be diagnosed at advanced stages. Worldwide, the mean five year survival rate is 61% [2].

On 1 November 2007 dosimetric measurements of the electrons energies of the Varian 21EX were performed with a Wellhoufer in a water phantom. Since 15 November 2007 we performed seven ELIOT treatments with the most common energy 6 MeV and the cone diameter of 57 mm inside the linear accelerator room, adapted to the collimator machine.

The selection of patients was, as follows: over 45 years old: tumours lesser than 3 cm, negative axillary lymph nodes, negative margins and no extensive intraductal component.

The procedure is feasible with a modest prolongation of the surgical time, low cost, low incidence of acute toxicity. The major advantage is the reduced irradiation time.
FIG. 1. Med-Tec non-docking intracavitary electron cones.

FIG. 2. View of the cone during the procedure.

REFERENCES


Image guided high dose rate brachytherapy as salvage for recurrent prostate cancer after definitive external beam radiotherapy

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Purpose: HDR brachytherapy, as salvage of local-only failure after previous radiation, has limited data reported to date. This is to report our results in using high dose rate (HDR) brachytherapy for salvage of local-only failure, after external beam radiation.

Methods and materials: The data of charts of patients with biopsy proven local-only failure after conventional external beam radiotherapy (EBRT) for prostate cancer, treated with salvage HDR brachytherapy at our institution, was retrospectively reviewed. Information was gathered from chart review and questionnaires completed at follow-up visits.

Results: From January 2002 to January 2006, 174 patients had local-only failure defined by transrectal biopsy, after a median EBRT dose of 68 Gy (66–70 Gy). Median follow-up was 47 months (range, 15–65). All but three patients had gleason score equal to six. The HDR prescribed dose ranged from 34 to 36 Gy, given in four fractions BID. At the moment of failure all patients presented PSA value of <10 ng/ml. The crude biochemical control rate (PSA ≤ 0,1 ng/ml) is 70.5% (12/17). There have been no further local failures. There were 8/17 (47,1%) Grade 2 and 1/17 (5.9%) Grade 3 late rectal injuries. Symptomatic urethral structures grades 3 and 4 were observed in 17,6% (3/17) and 5,9% (1/17), respectively.

Conclusions: The disease control rates and complications using HDR brachytherapy as salvage compared very favourably with those reported using other modalities. This approach shall be for further investigation.

REFERENCES


**TABLE 1. DISEASE SPECIFIC SURVIVAL**

<table>
<thead>
<tr>
<th>Patient ID#</th>
<th>Time (months)</th>
<th>Status</th>
<th>Cumulative proportion surviving at the time estimate</th>
<th>Number of cumulative events</th>
<th>Number of remaining cases</th>
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<td>2</td>
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<td>DPC</td>
<td>93.8%</td>
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<td>17</td>
<td>81.9</td>
<td>NED</td>
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</table>
Collaboration with the IAEA to improve cancer care in Estonia

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The collaboration between the IAEA and North Estonia Regional Hospital has started more than 10 year ago. During this time, the major impact of the cooperation has been seen on many aspects of radiotherapy including: radiation safety, upgrade of radiotherapy equipment, improvement in treatment quality and patient access to radiotherapy, implementation of new radiotherapy techniques and methods as well as training of the staff.

Each technical cooperation project cycle has been planned to tackle the most urgent needs A step-by-step approach has been followed. The training provided to the departmental staff by the IAEA, i.e. scientific visits, both before and after the purchase of equipment includes the smooth transition from 2-D to 3-D conformal radiotherapy.

Since the implementation of 3-D conformal radiotherapy, the voluntary incidence reporting system was implemented. The number of reported non-compliances increased as the complexity of radiation therapy rose with subsequent reduction of reported incidents after additional quality control procedures and training were put in place. The one year data will be shown.

The additional time required to prepare the treatment plans as well as increase in the number of staff members for the same amount of patients as consequences of the move from 2-D conventional to 3-D conformal radiotherapy would be presented. The set-up uncertainty estimation using EPID for previously used and current immobilization devices has allowed the reduction of margins and gained confidence in set-up reproducibility.

For the next TC cycle the hospital has plans to implement advanced radiotherapy techniques to further improve the therapeutic ratio. The new project will focus on implementation of intensity modulated radiotherapy), IGRT (image guided radiotherapy) and stereotactic radiotherapy.

There are still a lot of things which need to be worked out to improve the radiotherapy service at North Estonia Regional Hospital. The best indicator for our collaboration with the IAEA would be the independent QUATRO audit which will take place early next year.
Robotic extracranial stereotactic radiotherapy in lung, liver and head and neck tumours: The role of the CyberKnife®

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In the field of radiation oncology, equipment for fractionated radiotherapy and single-dose radiosurgery has become increasingly accurate together with the introduction of robotized treatments.

A robot is a device that can be programmed to carry out accurate, repeated and adjusted tasks in a given environment. Treatment of extracranial lesions involves taking account of organ mobility (tumour and healthy tissue) whilst retaining the ability of stereotactically locating the target.

New imaging techniques (spect MRI, PET) provide further relevant information to slice images (CT Scan, MRI) for defining targets. Hypo-fractionated treatments can only be used for curative treatment if the target is accurately defined and tracked during treatment. The CyberKnife® is a non-invasive system of radiosurgery and fractionated stereotactic radiotherapy. For intracranial lesions treated by single dose radiosurgery, it has been used to treat meningioma, acoustic neuromas, pituitary adenoma, metastases, arteriovenous malformations and refractory pain (trigeminal neuralgia). More than 10,000 patients have been treated worldwide.

Currently, the most significant developments are in the field of extracranial stereotactic radiotherapy (lung, liver, re-irradiation, prostate…). For example, from June to September 2007, nine patients with hepatocarcinoma and ten patients with liver metastases, with ages ranging from 23 to 84 years old (median: 69 years), have been treated in Lille with HSRTH. Treatment options and indications were discussed at the multidisciplinary gastro-intestinal (GI) oncology panel. Seventeen of the 19 lesions were solitary and two were bifocal, with largest diameters ranging from 15 to 100 mm (median 48 mm). All hepatocarcinomas had developed from cirrhosis of alcoholic origin. The Child scores before treatment were A5 to B7. Lesions were classified as Okuda I or II, BCLC A1 to C, T1 to T4. Two patients had portal thrombosis.

Patients treated for metastatic lesions were followed for colorectal cancer (8/10), breast cancer (1) or pulmonary blastoma (1). All had been previously treated by surgery and/or by lengthy chemotherapy. Treatments were delivered over a period of ten days. Doses consisted of 45 Gy delivered in three fractions for hepatocarcinomas and 40 Gy in four fractions for the metastases. All treatments were delivered as planned without any technical failure. All 19 patients were assessed for acute toxicity (CTC AE v3.0 scale). Eight patients had grade 1 nausea after treatment (8/19, 40%), two patients had grade 1 vomiting and one patient reported grade 1 asthenia.
Two grade 2 biological toxicities were observed: one elevation of liver enzymes and one exacerbation of diabetes, possibly caused by corticosteroid therapy. Neither clinical nor biological toxicities of grade 3 and grade 4 were observed. At six week follow-up, the child scores of 3 assessed cirrhotic patients were stable.

Clinical results obtained in the Cyberknife Nord Ouest programme in lung tumours and for re-irradiation in head and neck tumours will be presented.
Train the trainers

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*Train the Trainers* is a new initiative taken by the European Society for Therapeutic Radiobiology and Oncology (ESTRO) in conjunction with the International Atomic Energy Agency (IAEA). It has been increasingly recognized that insufficient time and focus are given to the practice of radiation therapy as an integral part of the education of RTTs. This has an impact on both recruitment and retention of staff in the clinical departments and in the level of additional training required following qualification.

To try to address this issue ESTRO and the IAEA have designed this new course aimed at providing participants with the skills to be able to design, prepare and deliver a short course on a topic that they identified as an important area for RTTs in their own country. The course was designed to cover all aspects of course preparation and delivery including the definition of academic content and the practical issues such as venues, cost, faculty, etc.

The course has been designed in four phases:

- the first week is an introductory workshop during which the participants define the topic and begin to prepare their individual course;
- the second phase, the delivery of the first short course in their own country monitored by a member of the teaching faculty;
- the third, a three day feedback session for the full group; and
- the fourth is the delivery of two further short courses.

It is also hoped that the topic can subsequently be integrated into the curriculum for RTTs.

The first course was held in Vienna from 31 August to 4 September 2008, attended by 24 participants representing eight countries. Three participants from each country were invited ideally representing clinical, academic and the professional organization. It was felt that this would give weight to the courses designed and delivered and ensure that all interested parties would support the initiative.
M. Coffey, et al.

This course was a mixture of lectures, workshops and interactive feedback sessions. The lectures focused on preparation of academic content and how best to approach this, as well as on the factors that must be considered from a practical perspective when organizing to deliver a local course. This course is a learning experience for both the participants and the faculty and was therefore flexible in terms of ensuring the maximum benefit gained.

The participants identified the topics most appropriate for their country and, together with the faculty, agreed how this could be best constructed within the confines of a three day course. In some instances the aim was to develop and deliver a single course three times to different participants. For others, the three courses developed would be delivered as a continuum to the same audience. The topics covered a wide range of subjects including practical implementation of patient management systems, site specific management and professional development.

The participants approached their task with enormous enthusiasm and all succeeded in preparing a skeleton outline of a three day course to be delivered in the first seven months of 2009. In some instances there was a synergy between the courses being developed, and it may be possible for two or more countries to share courses and thereby increase the potential in the longer term. This would also be very important in influencing changes in the core curriculum for RTTs in the individual countries.

The Dokeos e-learning system kindly provided by ESTRO will be of great help in enabling the faculty and students to continue to work together on the course preparation in the coming months.
Strategy of the system physicotechnical development of radiation oncology in Russia

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Radiation oncology has been in stagnation for a long time in Russia. Its technical equipment is more than 30 years behind the developed countries. 75% of clinics are on the dramatically low level of equipment which could not afford the satisfactory treatment quality. The efficiency of the sophisticated radiologic equipment does not exceed 10%. The number of the expensive, out-of-service and inefficient equipment is increasing. Practically there are no domestic developments and manufacturers of the therapeutic and diagnostic equipment although the material and technical basis for radiopharmaceutical elaboration and manufacture is available, but needs serious modernization. Insufficient financing from the Government resulted in the long term stagnation in this field. There are no proper specialists and education system, legislation base, after-sales service fund, etc.

It is essential to elaborate a special federal programme with the aim to eliminate the 30 year retardation from the developed countries. The programme consists of two stages:

1) during the first stage (8–10 years), retardation should be halved on the basis of the world’s achievements and simultaneous intensive domestic developments in this field;

2) during the second stage (10–12 years) we should enter the world market with the domestic technologies and products.

Adequate financing should be given to the therapeutic radiology (photon, electron, radionuclide, hadron therapy) and the diagnostic radiology (radionuclide diagnostics, PET, radiopharmaceuticals, radiodiagnostics, intervention radiology). Development of radiation therapy without diagnostic radiology is a strategic mistake.

Success of the programme is guaranteed if the scientific and systematic approach is provided. The activities should be made in three directions:

- creation and development of conditions (or environment) of high technology radiology centres in clinics: staff education, legislation issues, after-sale service organization and financing, etc.

- creation and development of the science based system of radiology complexes in medical centres and big clinics (oncology clinics in the first place)

- elaboration of the domestic radiology equipment, technologies, radiopharmaceuticals; creation and development of domestic production, scientific research, physicotechnical and clinical schools.
Without the above-mentioned conditions it is useless to invest money on the creation of medical centres, equipment and manufacturing. The most important mission is the creation of the modern system of the continuing professional development (CPD) of medical physicists and radiotherapists. The chairs and departments for medical physics should be organized in universities for the base education, and the leading medical centres should have training centres for CPD. Teachers should be prepared. Training courses, manuals, training equipment, teaching aids should be elaborated.

During 20 years, modernization will be needed for the present 140 departments and future 460 radiation oncology departments with stereotactic radiosurgery and brachytherapy. There should be a minimum of 20 clinical centres of hadron (proton, ion and neutron) therapy, more than 50 targeted radionuclide therapy centres, 150 PET centres. Serious modernization or creation of 300 radionuclide diagnostic and 300 radiodiagnostics departments should be effected. Development of equipment, radiopharmaceuticals and clinical technologies should be done. More than 40 different workshops, plants should be built. New medical physics and engineering institutions, laboratories should be organized.

Modern radiation oncology consists of a high efficient system of hardware and software, a perfectly coordinated team of qualified specialists, radiologists, medical physicists and engineers, a wide range of treatment and diagnostic technologies, quality assurance and safety, competent management system, i.e. a sort of a “competence centre”.

The realization of this programme will result in:

- high quality treatment leading to the 30% decrease of the death rate from severe diseases;
- return on investment and equipment efficiency increase up to 8–10 times;
- development of competitive domestic radiology equipment entering the world market;
- elaboration of more efficient radiation diagnostic and treatment technologies of cancer and other severe illnesses.

REFERENCES

Implementing IMRT for head & neck – the steps of the process

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The process of implementing IMRT for head & neck patients at the Oncology Centre IPOCFG, EPE, in Coimbra (Portugal) is described, highlighting the strategies and the detailed steps.

IPOC-FG, EPE is a public hospital with a very busy radiotherapy department treating around 1500 new patients per year, with three linacs and also a brachytherapy (BT) sector. After a period of two years (2004–2006) when all the equipment and the building were modernized, the new linacs (2 Oncor Avant-Garde, Siemens both with MV-CBCT) were installed at the end of 2006. One of the main goals of this large modernization project was to establish a treatment process in an integrated, efficient, accurate and safe way, both in external beam radiotherapy (EBRT) and BT.

The main objective in 2007 was to start treating patients with the new equipment and taking advantage of all the new technological features. During this period the delineation of new techniques like IMRT, radiosurgery and fraccionated stereotactic radiotherapy was also done.

Concerning the implementation of IMRT for head & neck patients the delineated strategy involved different phases:

1. Getting a postdoctoral student having her Ph.D. in a reference European centre (Karolinska Institut, Sweden) with a full time dedication to the project.

2. Starting from January 2007 an improved forward treatment planning technique was introduced in clinical practice which included around 20 beams from five or six incident directions and a single isocentre. With this intermediate optimized technique the introduction to structures delineation, dose-volume conditions and optimization has been smoothly introduced into clinical practice.

3. Efficient procedures and protocols for IMRT verification were established, including both equipment related tests and patient specific verification procedures — an exhaustive quality control of the flatbed scanner Epson Expression 10000XL was done using GafChromic EBT (GEBT) films [1] and a method for a dosimetric based calibration of the double focused 82-leaf Optifocus MLC of an Oncor Avant-Garde (Siemens) accelerator was developed [2]. Relative and absolute comparisons between planned and delivered dose distributions are made for every patient. The EPID Optivue 1000 is used to measure planar doses for each beam. Verification of the dose delivered by the plan calculated by the Konrad TPS is made with film dosimetry in an IMRT head phantom from PTW(Freiburg). Films are placed at the isocentre plan and in other two relevant axial plans. RIT113 v.5 software is used for film dosimetry analysis. Absolute dose is measured
with an ionization chamber placed at the isocentre in the head phantom. For each treatment plan an independent MU calculation is done through EqualDose v.2.0 (a QA tool developed within ESTRO). MV-CBCT reconstructed images are compared with planning CT images for the first three treatment fractions and then weekly. The tolerance level is 3 mm in each direction. Also a control CT is made in the 3rd week of the treatment to verify changes in the dose distribution due to weight loss or tumour shrinkage.

4. A retrospective planning study to compare the conventional treatment technique with the improved forward planning technique (IFP) and two IMRT techniques using different fractionation schemes has been carried out in order to evaluate the quality improvement of the successive implemented techniques [3];

5. Finally, a structured follow-up form for treatment outcome evaluation was proposed.

The IMRT treatments for patients with head & neck tumours started in February 2008. After almost one year of experience the results of treatment verification are presented.

In the relative comparisons 95% of the points on average passed the gamma criteria of 3%/3 mm. The average absolute dose deviation was -0.04±1.75%. Considering all the uncertainties involved, the criteria of 3%/3 mm for more than 90% of the points in the complete treatment film was regarded as acceptable.

Concerning the retrospective study of treatment techniques, significant improvement in the quality of the dose distribution was obtained by the IFP technique compared to the conventional treatment for head & neck. A dose escalation in the PTV of more than 5 Gy was thus prescribed. Also, a significant reduction in the mean dose in the parotids was obtained with the IFP technique, which reduced the probability of severe complications from 63% to 42% in the ipsilateral parotid and from 50% to 20% in the contralateral parotid. As expected, the largest benefit of IMRT was by further reducing the dose in the parotid glands. This significantly reduced the probability of complications in the ipsilateral parotid by 25% relative to the IFP technique and by more than 10% in the contralateral parotid. Only a slight increase in the probability of tumour control was obtained with IMRT compared to the IFP technique.

The follow-up of patients in the next years will hopefully confirm these predictions.

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The dermatoradiotoxicity during radiotherapy

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The first displays of dermatoradiotoxicity were fixed immediately after the opening of X ray beams in November 1895, which have turned to a serious problem after the beginning of the wide application of X rays for medical and diagnostic purposes. The various degrees of skin damages were shown as radiation dermatitis to the researchers, physicians and patients. It was continued until the middle of the 20th century, per era of X ray treatment, when the radiation injuries of skin were treated practically in all patients five years after the treatment. The amount of radiation dermatitis has dramatically decreased after the introduction of teletherapy gamma units; however, depending on topographo-anatomical localization of an irradiation target, new types of radiation damages have appeared (myocarditis, pericarditis, pulmonitis, cistitis, colitis, etc.). The listed beam damages were connected with the absence during those years of the necessary equipment for pre-irradiation procedures — CT scans, simulators, planning systems, immobilization facilities, necessary dosimetry equipment, etc.

Now, due to existing modern radiotherapy hardware, performance of the requirements of radiation therapy quality assurance (QA) became possible, that has resulted in sharp reduction of frequency and severity of radiation injuries. However, the problem of radiotoxicity is not solved yet. The dermatoradiotoxicity occuring during the irradiation of the breast by conventional techniques is one of the most actual problems in the developing countries. The results of numerous researches showed that the following factors influence the frequency of occurrence and degree of dermatoradiotoxicity: total irradiation dose, size of breast, amplitude and frequency of respiratory movements, irradiation of both breasts, index of weight of the body, high blood pressure, system diseases of a connective tissues, high sensitivity to ionizing radiation, etc. For prediction of possible skin toxicity, different methods can be used: punch biopsy (to determine the changes of skin fibroblasts and collagen), investigation of integral blood for definition of lymphoblastic cell lines, etc. It is necessary to mention that the history of publications dedicated to the given question covers many decades and continues up to now, thus emphasizing the pendency of a problem.

In this presentation, the prediction of dermatoradiotoxicity, reasons of its occurrence, its prevention and treatment by the method offered by us are considered. In the research group involving patients who received treatment since 1996, to define the degree of a radiation injury we used the EORTC toxicity scale that was recommended in the same year. In the group that recruited 1896 patients with breast cancer (BC), the patients received radiotherapy (RT) in 1996–2005. Thirty-eight of them had neoadjuvant RT with large fractions 5–6 Gy per fr., and total dose of 24–25 Gy, followed by surgery within 72 hours after RT. A total of 256 patients underwent curative RT using different fractionation schemes, with the total dose equivalent to 60–70 Gy. Adjuvant RT was prescribed to 1602 patients, including 915 patients after breast-conserving surgery. With the purpose of preventive maintenance of dermatoradiotoxicity offered by us, oil extract of medicinal plants (patent of Republic of Armenia, No. 893 from 10.04.01) has been used externally for 452 patients from 1896. With the medical purpose (after development of dermatitis) the skin surface was treated by the same oil extract from medicinal plants (OEMP) for 273 patients. The median age of the patients was 48 years.
In the group of neoadjuvant RT with large fractions (38 patients) the cases of acute radiation toxicity of skin were not fixed. In the group of curative RT (256 pts) the OEMP was prescribed with preventive purpose to 103 patients, out of whom only 43 patients (42%) were affected by dermatoradiotoxicity like local erythema and pigmentation of skin, dry desquamation of skin, including 4 patients (4%) who have developed moist desquamation. It is necessary to note, that 31 patients out of 43 (including four with moist desquamation) received previous or concomitant chemotherapy. Other 153 patients with curative RT have not received OEMP with preventive purpose. Out of these patients, 92 (60%) who have developed dermatoradiotoxicity and moist desquamation (grade 2 by EORTC scale) was treated at 14 (9%). In 79 cases the patients received concomitant or induction chemotherapy. Thus, in the group of curative RT (256 patients) the cases of dermatoradiotoxicity grades I–II were revealed at 135 patients (52.7 %). The preventive use of OEMP reduces the specified parameter to 42%, whereas without preventive maintenance, the parameter grows up to 60%.

More frequently, radiotoxicity of skin was shown in the patients during the adjuvant RT, despite smaller values of total dose of 10–15 Gy (comparing with curative RT). The different manifestations of dermatoradiotoxicity were fixed in 1025 (63.9%) out of 1602 patients who received adjuvant RT. For preventive purpose, OEMP was prescribed to 349 patients out of whom 164 (47%) developed dermatotoxicity, including 36 (10.9%) with grade II toxicity. The skin surface was not handled by OEMP with the preventive purpose during the adjuvant RT in 1253 cases, out of whom 839 (67%) were fixed skin injuries, including grade II in 123 patients (14.7%). The treatment was temporarily interrupted in 171 patients (9%) because of severe dermatotoxicity. In such cases, the OEMP was administered for medical purpose (142 patients out of 171). The break lasted 2–7 procedural days, excluding rest days. When the severity of injury was not decreased during four days, the low intensive magnetic radiation and standard pharmaceuticals were administered concomitantly. It is necessary to note, that in patients with prophylactic or medical OEMP administration, the maximum break was three procedural days.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total dermatotoxicity (%)</th>
<th>Dermatotoxicity after preventive OEMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curative RT</td>
<td>52.7%</td>
<td>42%</td>
</tr>
<tr>
<td>Adjuvant RT</td>
<td>63.9%</td>
<td>47%</td>
</tr>
</tbody>
</table>

Such significant difference in parameters of the skin injuries, revealed between the patients received curative RT (52.7%) and adjuvant RT (63.9 %) has forced us in more details to study the reason of paradox, because the total doses for adjuvant treatment were, on the average 10 Gy less.

We have unequivocally concluded that there is crucial influence of surgical intervention on the increase of frequency of dermatoradiotoxicity during adjuvant irradiation. The given fact is caused by the damage of tegumental tissues integrity, resulting in failure of local blood flow, by intra and post operational handling of wound surface by chemically active substances. The moist desquamation has occurred in 100% cases of patients with delayed healing of an operational wound (more than three weeks) and presence under generated operational scar of infected liquid component. For the curative RT, three main factors had the influence on the frequency of dermatoradiotoxicity occurrence: inductive or concomitant chemotherapy, large sizes of breast, sensitivity to solar exposition and hot weather.

As shown in the given data offered by us, OEMP has a certain efficiency with regard to preventive maintenance and treatment of acute dermatoradiotoxicity. Despite the copyright protection, we are ready to give the interested clinics formulation of this extract. It is necessary also to mention that the medicinal plants used have wide natural habitat of growth, can be easily and quickly reproduced, are allowed to be used in medicine and do not enter into the Red Book of Armenia.
Experience of transition from 2-D to 3-D radiation therapy in a centre of a developing country

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A total of 6,926 new patients were treated in the year 2007 in the National Institute of Cancer Research & Hospital (NICRH), where the male-female ratio was 57:43. The topmost malignancy among both sexes was lung cancer, followed by breast cancer. The most prevalent cancer among the paediatric age group was retinoblastoma [1]. Of the total, 3,082 patients (44%) were taken to the radiation oncology department (ROD) where 107 were in the paediatric age group. The most common cancer was head & neck cancer (792) followed by lung cancer (525) and, among children, retinoblastoma.

TABLE 1. TOP FIVE MALIGNANCIES OF PATIENTS REPORTING TO THE RADIATION ONCOLOGY DEPARTMENT

<table>
<thead>
<tr>
<th>Site</th>
<th>Number with Percentage</th>
</tr>
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<tbody>
<tr>
<td>Head &amp; neck</td>
<td>792 (25.7%)</td>
</tr>
<tr>
<td>Lung</td>
<td>525 (17 %)</td>
</tr>
<tr>
<td>Cervical</td>
<td>454 (14.7%)</td>
</tr>
<tr>
<td>Breast</td>
<td>365 (11.8%)</td>
</tr>
<tr>
<td>Esophagus</td>
<td>169 (5.5)</td>
</tr>
<tr>
<td>Others</td>
<td>777 (25.2%)</td>
</tr>
</tbody>
</table>

Only about 35% to 40% of the attending patients at the ROD received treatment with curative dose. Most of these patients were of head & neck cancer, breast cancer and some sarcoma patients. In accordance with the European Dynarad consortium, NICRH is providing treatment delivery at level-0; in the transition stage to levels 1 and 2, 3-DCRT would be started [2]. 3-D CRT is accepted as the standard practice in the developed world to treat many types of cancer with curative intent. Most of the clinical evidences are available in favour of clinical superiority of 3-D CRT in cases of nasopharyngeal carcinoma, lung cancer and prostate cancer. It is possible to achieve about 30% to 50% reduction in the treated volume in 3-D CRT by conforming the dose with the target volume [5, 6], where the reduction includes only normal tissues. Local control can therefore be improved by increasing the dose delivered to the tumour, without unacceptable toxicity. In case of many tumours there are available data supporting the dose-response relationship [4]. Dose escalation makes better local control of tumour possible, leading to improved survival that can help change the treatment approach in many tumours from palliative to potentially curative.

In accordance with IAEA-TECDOC-1588 a total of eleven steps are required to fulfill the approach to conformal radiotherapy [3]. The first six steps have been completed, which
include: defining the scope of the programme, development of staffing needs for the programme, identifying the necessary space and equipment, development of a programme budget, preparation of space and purchase equipment and hiring of new staff. At present the centre is equipped with three dual energy linear accelerators with MLC, one simulator and three treatment planning systems: 1.5 Tesla MRI, Multi slice CT scanner. Procurement of a CT simulator and a PET CT is under process.

The centre is struggling for lack of budget and adequate experience to ensure proper training of the staff, proper acceptance testing and commissioning of the new equipment, development of necessary policies and procedures and development and implementation of a comprehensive QA programme.

IAEA supported RCA Project No. RAS/6/048 is contributing to support the training component. In addition, Technical Project No. BGD/2007/03 will also support staff training and upgrade of one linear accelerator with IGRT facility. Even these steps are not enough to fulfil the total requirement of this centre.

The government of Bangladesh should allocate adequate budget to ensure optimum training of manpower. Additional support from the IAEA, UICC and WHO could be sought to supplement the government’s effort by arranging more training opportunities and sending expert missions. Creation of the post of medical physicist in government hospitals should be implemented with the highest priority.

REFERENCES

Establishing a quality assurance programme in radiosurgery

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Radiosurgery is a very specialized radiotherapy technique. The main goal of this work is to describe the expected difficulties and to point out the critical issues which are important to implement a radiosurgery division.

The ideal condition is a specialized team in radiosurgery. The treatments of benign diseases like AVM, acoustic neurinomas, trigeminal neuralgia are specialized medical concepts. It is essential to know what we have to draw, which doses are necessary to treat each disease, when it is better to fractionate the dose, the management of the follow up, the results and side effects, when it is possible to re-treat a patient, which constraints are used in fractionated, single dose treatments and re-treatments.

In this work, we will present the results of the acceptance and commissioning from a linear accelerator Varian 6EX associated with a BrainLab micro-multileaf collimator system (m3) at Clinicas Hospital. For the acceptance tests, several checklists have been provided by the manufacturers (Varian and BrainLab) in order to apply the AAPM recommendations [1]. These tests include the following parameters: stereotactic target positioner, CT-X ray localizer, diagnostic data acquisition (CT, MRI and angiography), treatment planning systems (BrainScan and iPlan) – hardware and software, and Winston-Lutz test, among others.

For the commissioning of dosimetric tests [2], measurements for non-reference conditions have been performed in order to verify the algorithm effectiveness (pencil beam). Measurements were performed for depth dose distributions for square fields from minimum to maximum field sizes (from $6 \times 6$ mm$^2$ to $100 \times 100$ mm$^2$), scatter factors (with and without the mMLC), diagonal radial fields (mMLC unmounted and jaws retracted). The main issue was to select the proper size of the detector for some types of measurements: for instance, for field sizes smaller than $12 \times 12$ mm$^2$, a stereotactic diode was employed additionally to a pin point ionization chamber (0.01 cm$^3$). All absolute absorbed dose measurements were performed by making use of a Farmer cylindrical chamber (0.6 cm$^3$) which was calibrated in terms of absorbed dose to water according to IAEA TRS-398 [3]. The lack of charged particle equilibrium is the main task for the dosimetry of small fields.

Due to the complexity of the radiosurgery and fractioned stereotactic radiotherapy processes, it is mandatory to establish a proper quality assurance programme for each patient to be treated with this treatment modality [1]. In this work, such programme will be described with its respective results covering the following aspects: QA of stereotactic target localization with all image modalities, basic dosimetry, treatment planning, absolute dose output calibration and delivery dose. These tests require a proper phantom (an IMRT phantom for
example) as well as appropriate dosimetric equipments such ion chambers and diodes with small sensitive volumes, solid water phantom, radiographic films in order to perform all periodic tests.

Since the most important QA test in radiosurgery is the periodic verification of the mechanical stability of the nominal isocentre, a checklist for the treatment procedure was elaborated for each individual patient. Once those tests are performed, the patient is then positioned for treatment and the following steps terminate the whole process [4]: the patient is positioned in the stereotactic assembly, the localizer box is then attached to his/her head, the couch is moved up in order to realign the lasers at the isocentre, a fine adjustment is performed with the stereotactic base, the localizer box is removed; and finally, the treatment is initiated.

In order to evaluate the set-up errors, the difference among these parameters are given in Table 1. Fifteen patients who submitted to either radiosurgery or fractioned stereotactic radiotherapy were considered in this preliminary study.

**TABLE 1. MEAN VARIATION BETWEEN COORDINATES OF ISOCENTRE LOCALIZATION AND ISOCENTRE POSITION + MEAN VARIATION BETWEEN COUCH COORDINATES RELATING TO ISOCENTRE AND CALCULATED COUCH COORDINATES**

<table>
<thead>
<tr>
<th></th>
<th>Mean value – 15 patients</th>
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<tbody>
<tr>
<td>ISO_DIF AP</td>
<td>-0.098 mm</td>
</tr>
<tr>
<td>ISO_DIF VERT</td>
<td>-0.077 mm</td>
</tr>
<tr>
<td>ISO_DIF LAT</td>
<td>-0.014 mm</td>
</tr>
<tr>
<td>COUCH_DIF AP</td>
<td>2.878 mm</td>
</tr>
<tr>
<td>COUCH_DIF VERT</td>
<td>-0.115 mm</td>
</tr>
<tr>
<td>COUCH_DIF LAT</td>
<td>0.819 mm</td>
</tr>
</tbody>
</table>

From these results, one verifies a larger variation of the isocentre localization for antero-posterior orientation. Regarding the couch coordinates, a major difference was found for the antero-posterior orientation. However, the results from the Winston-Lutz test are within expected variations.

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Efficacy evaluation of prophylactic low energy laser application in patients with chemotherapy and radiotherapy-induced oral mucositis

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Oral mucositis is a frequent and severe acute side effect of radiotherapy and chemotherapy that increases morbidity and mortality of treatment in patients with head & neck tumours. The analgesic effect of laser on the treatment of mucositis has been described by some authors; however, its prophylactic use to prevent mucositis has only few uncontrolled reported studies in literature.

Purpose

To evaluate the:

- prophylactic low-energy laser application in preventing or delaying severe oral mucositis in patients with head & neck cancer treated with radiotherapy and chemotherapy concomitantly, and
- impact of its use to pain relief and the necessity of brakes during radiotherapy.

Methods

A phase III, prospective, comparative, randomized, double-blind study was conducted on patients with head & neck tumours submitted to radiochemotherapy in our department. The estimate was 40 patients in each group (experimental and controlled) to detect a 30% reduction in the incidence of oral severe mucositis in the experimental group (EG), with an alpha error of =5% and a beta error of =20%. The group included patients with head & neck cancer who received radiotherapy and chemotherapy weekly with cisplatin concomitantly. The patients were randomized in two groups. In the experimental group (EG), the patients received laser and in the control group (CG), the patients received placebo-laser application before each fraction of radiotherapy during all the treatment (five days/week during seven weeks). Both groups were permitted to receive care, orientation and analgesic medicine for mucositis. Mucositis severity was scored by an oral toxicity scale (OTS) and pain severity, by visual analogue scale (VAS) (National Cancer Institute).

Preliminary results

Included in the study were 54 patients during the period from March 2007 to April 2008. The squamous cell carcinoma was the most frequent, with 24 patients in CG and 21 in EG (p=0.3). The primary sites were: oral cavity (4 CG versus 1 EG), hypopharynx (2 CG versus 2 EG), larynx (3 CG versus 4 EG), oropharynx (11 CG versus 12 EG), nasopharynx (4 CG versus 5 EG), others (1 CG versus 1 EG) (p=0.8). The mean dose of radiotherapy was 67.76 Gy for CG and 69.28 Gy for EG (p=0.09). The mean of fields involving all the oral cavity was 4.2 CG versus 4.3 EG (p=0.94). In the OTS analysis, a non-significant difference in severe
mucositis at the 10th radiotherapy was observed: 5 CG versus 3 EG (p=0.7). At the 20th session, the difference was almost significant: 8 CG versus 2 EG (p=0.07) and at the end of the 30th radiotherapy session, seven patients were observed with severe mucositis in both groups (p=1.0) (Fig. 1). Evaluation of the OTS revealed that the laser group presented lower mean scores during all radiotherapy sessions (Fig. 2).

FIG. 1. Incidence of severe mucositis.

In the CG, it was observed that five patients had a break of radiotherapy because of severe mucositis while no patient was with interruption in the EG (p=0.05) (Fig. 3). The breaks occurred at about the 18th session of radiotherapy and during approximately seven days.

FIG. 3. Number of breaks of radiotherapy due to severe oral mucositis.
In the VAS analysis, at the $10^{\text{th}}$ session of radiotherapy severe pain was observed in five and in three of CG and EG, respectively (p=0.7). At the $20^{\text{th}}$ session, severe pain was observed in four patients of CG and seven of EG (p=0.4) and at the $30^{\text{th}}$ session, it was 7 and 8, respectively (p=1.0) (Fig. 4). In the evaluation of pain relief, the laser group presented lower mean scores only at the $10^{\text{th}}$ radiotherapy (Fig. 5).

**FIG. 4. Incidence of severe pain.**

**FIG. 5. Mean scores of pain.**
Preliminary study of genes related to the concomitant chemoradiotherapy sensitivity in advanced uterine cervical squamous cell carcinomas

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Tumour intrinsic chemoradiotherapy sensitivity is one of the crucial reasons for concomitant chemoradiotherapy failure in advanced uterine cervical squamous cell carcinomas (UCSCC). This study aims to identify a set of genes and molecular function pathways related to the concomitant chemoradiotherapy sensitivity in UCSCC.

Materials and methods

Forty cases of UCSCC patients in FIGO stage IIb or IIIb treated with platinum based concomitant chemoradiotherapy in our hospital from October 2006 to October 2007 entered this trial. The chemoradiosensitive group and chemoradioresistant group each included 20 cases. The clinical pathology characters in two groups of patients were summarized in Table 1. Tumour tissues were obtained by biopsy before treatment and total RNAs were extracted. 22k Human Genome Oligonucleotide Microarrays carrying 21522 oligonucleotide probes were used to identify differentially expressed genes correlated with concomitant chemoradiotherapy sensitivity between the two groups (three cases for each group). Molecular biology functional pathways analysis of differentially expressed genes was performed. Expression differentiations of genes involved in several important pathways were further determined in next semiquantitative reverse transcription polymerase chain reactions (RT-PCR) in 40 cases.

Results

Oligonucleotide Microarrays identified 108 significantly differentially expressed genes. Fifty-six genes were relatively higher expressed in resistant group and 52 relatively higher expressed in sensitive group (Fig. 1). The functional pathways classes analysis of these genes demonstrated many related pathways such as DNA damage repair, apoptosis, cell circle, Mapk signal transduction, anaerobic glycolysis and glutathione metabolism. We determined 14 genes involved in these pathways in RT-PCR. Seven of these 14 genes showed the same significant mRNA expression differention results with that in the microarray analysis: PDGFRA and PRKAR1A were significantly higher, expressed in chemoradiosensitive group ($P<0.05$), while, LDHA, BAK1, BNIP3, SMUG1, CDK7 were higher, expressed in chemo- radioresistant group ($p<0.05$). The other 7 genes, CAST, IL1R1, RAN, TGFB3, GSTM3, HRAS and ATM showed no significant expression differention ($p>0.05$) between the two groups (Table 1). The coincidence of predicted groups by combination of seven genes and clinical groups was 87.5%.
FIG. 1. Tree diagram of the 108 genes expression in two groups.
TABLE 1. FOURTEEN GENES INVOLVED IN THESE PATHWAYS IN RT-PCR

<table>
<thead>
<tr>
<th>Genes</th>
<th>RT-PCR relative expressions</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitive group</td>
<td>resistant group</td>
</tr>
<tr>
<td>ATM</td>
<td>0.378±0.220</td>
<td>0.534±0.268</td>
</tr>
<tr>
<td>BAK1</td>
<td>0.798±0.271</td>
<td>1.13±0.274</td>
</tr>
<tr>
<td>CAST</td>
<td>1.125±0.296</td>
<td>1.140±0.390</td>
</tr>
<tr>
<td>IL1R1</td>
<td>0.332±0.131</td>
<td>0.256±0.088</td>
</tr>
<tr>
<td>PDGFRA</td>
<td>0.549±0.251</td>
<td>0.249±0.098</td>
</tr>
<tr>
<td>HRAS</td>
<td>0.605±0.299</td>
<td>0.729±0.214</td>
</tr>
<tr>
<td>PRKAR1A</td>
<td>0.991±0.549</td>
<td>0.500±0.292</td>
</tr>
<tr>
<td>SMUG1</td>
<td>0.365±0.197</td>
<td>0.742±0.579</td>
</tr>
<tr>
<td>BNIP3</td>
<td>1.347±0.342</td>
<td>1.642±0.405</td>
</tr>
<tr>
<td>RAN</td>
<td>1.698±0.362</td>
<td>1.745±0.425</td>
</tr>
<tr>
<td>CDK7</td>
<td>0.503±0.278</td>
<td>0.737±0.369</td>
</tr>
<tr>
<td>TGFB3</td>
<td>0.907±0.323</td>
<td>0.757±0.277</td>
</tr>
<tr>
<td>LDHA</td>
<td>1.151±0.322</td>
<td>2.201±0.813</td>
</tr>
<tr>
<td>GSTM3</td>
<td>2.005±0.476</td>
<td>1.900±0.338</td>
</tr>
</tbody>
</table>

* p<0.05

Conclusion

Seven genes of PDGFRA, PRKAR1A, LDHA, BAK1, BNIP3, SMUG1 and CDK7 are related to the concomitant chemoradiotherapy sensitivity in UCSCC. Combination of these seven genes might be primary predictors for concomitant chemoradiotherapy sensitivity in UCSCC.
Concurrent chemo-radiotherapy versus radiotherapy with boost in locally advanced unresectable rectal cancers. A randomized phase II study


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In India 50% of the patients of rectal carcinoma is in the locally advanced stage which is technically unresectable, or that is beyond the realm of a potentially curative surgical resection. The evaluation of treatment approaches for these tumours is hampered by the absence of any substantial randomized studies and the heterogeneous nature of the tumours at presentation. The management of these tumours has changed over the years. There is emphasis on neoadjuvant chemo-radiation therapy (CTRT), trying to convert a tumour that is initially unresectable to one that is potentially curable by surgery. But only 70–80% of the patients is able to complete this treatment without any significant treatment breaks. Dose escalated treatment with radiotherapy (RT) in locally advanced and unresectable rectal cancers have been tried in many small series with good results and lesser toxicity.

Aim

This study was undertaken to compare the rate of resectability between the patients treated with neoadjuvant concurrent chemo-radiation versus boosted radiotherapy alone.

Materials and methods

Ninety patients of previously untreated locally advanced non-metastatic rectal cancer who were deemed unresectable by two independent gastrointestinal oncosurgeons were randomized to the following arms. These patients were treated between July 2006 to June 2008.

- Arm-1 (46 patients) – patients received external beam radiation therapy (EBRT) to pelvis (45Gy over 25 fractions) + concurrent chemotherapy with Tab Capecitabine (850 mg/m2 twice a day 1–14 and day 21–35 with EBRT.
- Arm-2 (44 patients) – patients in this group received EBRT to pelvis alone and an additional dose of localized radiotherapy boost to the primary tumour to a dose of 20 Gy over 10 fractions.

All patients were assessed at six weeks clinically and by CT scan and underwent surgery if the tumour was resectable.

Results

The two groups were well balanced according to pre-treatment characteristics. Of the 90 patients one patient (Arm 1) died of intestinal perforation prior to starting EBRT and two patients (1 in Arm 1 and 1 in Arm 2) refused to undergo radiotherapy after randomization.
The rest all the 87 patients (44 in Arm 1 and 42 in Arm 2) could complete the prescribed treatment with acceptable grade 1–2 toxicity. No patient had grade 3 or 4 toxicity. and one patient died of myocardial infarction four weeks post CT + RT(Arm 1). Operability was assessed at 6–8 weeks after completion of radiotherapy, clinically or examination under anesthesia and CT scan, and were taken up for surgery subsequently. Four patients (3 in Arm 1 and 1 in Arm 2) refused to undergo surgery inspite of being deemed resectable. Overall: 36 of the 82 (44%) patients who received RT and were willing to have surgery underwent the procedure. An R0 resection was performed in 22 patients (55%) in the CRT group and in 14 patients (33%) in the RT group (P=0.05).

Conclusion

EBRT plays a major role in downstaging of locally advanced unresectable rectal cancers. More than 50% of the initially unresectable tumours can be deemed resectable with chemoradiotherapy. Addition of chemotherapy is definitely superior to dose intensified radiotherapy alone.

**TABLE 1. PATIENT CHARACTERISTICS**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Chemoradiotherapy (n=46)</th>
<th>Radiotherapy (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>41</td>
<td>39.8</td>
</tr>
<tr>
<td>Range</td>
<td>20-74</td>
<td>19-70</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>34 (73.9%)</td>
<td>36 (81.8%)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (26%)</td>
<td>8 (18.2%)</td>
</tr>
<tr>
<td>Serum CEA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>Range</td>
<td>(1-89)</td>
<td>(1-193)</td>
</tr>
<tr>
<td>Stage group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>8 (17.4%)</td>
<td>6 (13.6%)</td>
</tr>
<tr>
<td>IIIB</td>
<td>34 (73.9%)</td>
<td>30 (68.2%)</td>
</tr>
<tr>
<td>IIIC</td>
<td>4 (8.7%)</td>
<td>8 (18.2%)</td>
</tr>
<tr>
<td>Invasion of adjacent structures/bones</td>
<td>25 (54%)</td>
<td>27 (62%)</td>
</tr>
<tr>
<td>Performance status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18 (39%)</td>
<td>15 (34.1%)</td>
</tr>
<tr>
<td>1</td>
<td>23 (50%)</td>
<td>27 (61.4%)</td>
</tr>
<tr>
<td>2</td>
<td>5 (11%)</td>
<td>2 (4.5%)</td>
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</tbody>
</table>

**TABLE 2. SURGERY AND PATHOLOGICAL RESPONSE**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Chemoradiotherapy (n=46)</th>
<th>Radiotherapy (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operated</td>
<td>22 (55%)</td>
<td>14 (33%)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAR</td>
<td>6 (13%)</td>
<td>1 (2.2%)</td>
</tr>
<tr>
<td>APR</td>
<td>16 (34.7%)</td>
<td>13 (29.5%)</td>
</tr>
<tr>
<td>Type of resection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>18 (39.1%)</td>
<td>13 (29.5%)</td>
</tr>
<tr>
<td>R1(CRM +ve)</td>
<td>4 (8.6%)</td>
<td>1 (2.2%)</td>
</tr>
<tr>
<td>Pathological response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>3 (6.5%)</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>Partial response</td>
<td>19 (41.3%)</td>
<td>10 (22.7%)</td>
</tr>
</tbody>
</table>
REFERENCES


Locally advanced inoperable carcinoma pancreas and gall bladder treatment with concurrent chemoradiation using tomotherapy based IMRT and IGRT: Case series


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Optimal management of carcinoma pancreas and gall bladder has always remained a challenge and the improvement in survival, an illusion. Even with radical resections in the early stage, the disease’s five year overall survivals are only 10–20%. For patients with locoregionally advanced disease multimodality treatment using chemotherapy and radiotherapy (RT) can be offered with the aim of downstaging the disease and symptomatic relief.

The rationale of upfront concurrent chemo radiation (CCRT) entails that:

1) RT is more effective in well oxygenated tissue in the presence of intact vasculature,
2) borderline unresectable tumours might become resectable after downstaging
3) there is a decrease in chances of tumour implantation during surgery
4) patients with biologically aggressive disease suggested by presence of visceral metastasis on repeat imaging after RT can be identified and can avoid unnecessary surgery.

The aim of this study was to evaluate feasibility and tolerability of CCRT with dose escalated intensity modulated radiotherapy (IMRT).

Materials and methods

We treated six patients with locally advanced carcinoma pancreas and gallbladder with CCRT using Helical Tomotherapy (HT) based IMRT/IGRT at Tata Memorial Centre, Mumbai in 2008.

All six patients had inoperable disease, three had carcinoma pancreas, two had periampullary carcinoma and one with gall bladder cancer. All patients underwent diagnostic contrast enhanced CT scan abdomen and biopsy as part of staging workup. Three patients underwent PET CT scan to rule out distant metastasis. These patients were deemed inoperable by virtue of infiltration of adjacent major vessels, matted portal LNs or extensive duodenal infiltration. All patients had good performance status and total serum bilirubin was <3mg/dl. Three patients had endobiliary stents placed prior to RT.

All patients were positioned and immobilized using standard vaclocs or abdominopelvic thermoplastic moulds. Planning CT scan of abdomen with 5 mm slice thickness was obtained using IV non-ionic contrast and only water given orally was used as bowel contrast. Contouring of target and organs at risk (OAR) was done following standard ICRU 62 guidelines. Two separate planning target volumes (PTV) were contoured. Gross tumour volume (GTV) was given a uniform margin of 1 cm all around to form SIBV (simultaneous
integrated boost volume). GTV, areas of subclinical extension of disease and enlarged lymph nodes (LNs) were given a 1 cm margin all around to generate clinical target volume (CTV) and PTV primary was generated by giving appropriate margins to it. A conscious effort was made to avoid inclusion of radiologically uninvolved portion of duodenum out of CTV. The dose prescription varied in these patients as it was our initial experience and also keeping in mind the dose tolerances of various organs. One patient was treated with PTV prescription dose of 56 Gy in 28 fractions (without simultaneous boost). The rest of the patients received 50 Gy in 25 fractions to PTV with simultaneous boost dose of 55–60 Gy/25 fraction @2.2–2.4 Gy/fraction. All patients underwent daily MVCT imaging coregistration prior to RT. Two patients received concurrent capecitabine (1700 mg/m2) and four received gemcitabine (weekly 350 mg/m2) as radiosensitizer. All patients were regularly monitored for acute GI toxicities, weight loss, CBC and RFT.

Results

1) Dosimetric patterns – mean PTV volume in these patients was 371.19 cc and boost volume was 157.23 cc. Mean SIBV, V95 % and V100% (volume receiving 95% and 100% dose) was 99.6% and 93%. Mean conformity index was 0.9948 for PTV and mean homogeneity index was 4.166 for PTV boost volume. Mean duodenal dose was 51.23 Gy with mean V50 Gy and 60 Gy at 75.23 and 5.51%, respectively. Mean small bowel dose was 18.97 Gy and mean bowel V50Gy was 6.49%. Mean right and left kidney doses were 17 and 11.1Gy, respectively. Doses to all other adjacent OARs were well within standard acceptable limits.

2) Acute toxicities – All patients tolerated treatment well with no grade 3-4 haematological or GI toxicity. None of the patients required admission or treatment interruption due to acute toxicities. Mean weight loss on CTRT was <5%.

3) Response – Four patients who had presented with abdominal pain and backache were completely off analgesics at the end of RT. All patients underwent PET CT scan after four weeks of RT for response assessment and evaluation for surgery. Two patients had distant metastases and were offered palliative chemotherapy. One patient had CR and three patients had PR on PET CT scan. Two of these patients were still deemed inoperable, while two underwent exploratory laprotomy. However, the disease was resectable in only one patient with overall resectability rate of 16.6% .

Conclusion

Dose escalation with IMRT with concurrent chemoradiation is both feasible and well tolerated in locally advanced carcinoma pancreas and gall bladder. It provides good symptom relief to all patients. Its impact on resectability rates and durability of symptom relief needs evaluation in larger cohort of patients.
Role of the Board of Radiation & Isotope Technology (BRIT) in combating cancer in India

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The Board of Radiation & Isotope Technology (BRIT) is a unit of the Department of Atomic Energy, India. BRIT is actively engaged in propagating the widespread application of radiation and radioisotopes in areas as diverse as industry, agriculture, research and healthcare. Cancer diagnostics and treatment occupy a very important role in the healthcare sector. To ensure that the benefits of cancer treatment reach the large population, it is important that the different equipment and services are available at affordable prices. BRIT is engaged in the development, production and supply of various radiopharmaceuticals for diagnosis and treatment, sealed radiation sources used in teletherapy, brachytherapy equipment and blood irradiators. BRIT also produces radiolabelled biomolecules for research related to cancer and drug discovery. The products are supplied to all major hospitals and nuclear medicine centres.

Radiopharmaceuticals in cancer treatment and diagnosis

Radiopharmaceuticals find extensive use in diagnosis (including prognosis and follow-up of treatment), therapy and management of cancers. BRIT has been manufacturing and supplying radiopharmaceuticals since its inception in 1989.

Diagnostic radiopharmaceuticals

BRIT supplies $^{99m}$Tc generators and various cold kits for use with the $^{99m}$Tc labeled compounds, which are useful in diagnosis of many diseases including cancer. For example, a cold kit of MIBI labeled with $^{99m}$Tc is useful for myocardial perfusion scan and early detection of breast tumours using BSGI (breast specific gamma imaging). The sensitivity of the latter is reported to be better than mammography. $^{99m}$Tc-MDP, which specifically localizes in the skeleton, is used for bone scintigraphy to diagnose the metastases of various primary cancers arising from lung, prostate, breast, etc. $^{99m}$Tc labelled pentavalent DMSA is routinely used for medullary carcinoma of the thyroid. Na$^{131}$I, when administered orally or intravenously, is preferentially taken up by thyroid and is widely used for diagnosis and treatment of thyroid cancer and its metastases. BRIT is producing and supplying this radiopharmaceutical in both capsule and solution forms. BRIT is also producing and supplying $^{131}$I-mIBG (meta iodo benzyl guanidine) which is used for imaging tumours of neuroendocrine origin like pheochromocytoma and neuroblastoma.

Therapeutic radiopharmaceuticals

In therapeutic radiopharmaceuticals, the range of penetration of radiation is restricted to a few abnormal cells so that only tissues/cells, which are very close get affected, thus selectively killing the cancer cells and largely sparing the healthy tissues. Doses (50 mCi to 250 mCi) of $^{131}$I as NaI are routinely supplied for the treatment of thyroid cancers. It is used for ablation of
remnant thyroid tissue after thyroidectomy and for treatment of metastatic lesions from well differentiated thyroid carcinoma. Another important radiopharmaceutical is $^{131}$I mIBG, which in higher doses (100–200mCi), is used to treat patients of pheochromocytoma and neuroblastoma, and is particularly useful in paediatric patients. The modern approach towards treatment of cancer/tumour is to couple desired radioisotope with specific biomolecules like antibodies. The antibodies specifically target the cancer cell and bind to them. They also carry along radioisotopes to the cancer cell. The radiation emitted by the isotope inactivates the cancerous cells. BRIT is collaborating with a premier US pharmaceutical company for production of their $^{131}$I labelled monoclonal antibody chTNT-1/B, which is currently undergoing Phase II clinical trials for treatment of brain tumours like glioblastomas.

**Palliative radiopharmaceuticals**

Many of the cancer patients are diagnosed at an advanced stage and very quickly experience extreme pain in bones due to occurrence of pressure metastasis. Painkillers at this stage become ineffective to alleviate the pain. $^{32}$P-sodium orthophosphate and $^{153}$Sm-EDTMP are the radiopharmaceuticals, which are found extremely useful for palliation and are being produced and supplied by BRIT. These radiopharmaceuticals help to improve the quality of life for such patients.

**PET radiopharmaceuticals**

In India positron emission tomography (PET) technology is fast growing and becoming an important tool in the field of cancer imaging and diagnostics. BRIT is operating India’s first 16.5 MeV medical cyclotron. $^{18}$F-FDG is the most commonly used PET radiopharmaceutical and is supplied to nine PET centres. About 74 GBq (2.0 Ci) of FDG is supplied everyday catering to about 40–45 patient doses per day. Already more than 31,500 patients have benefited from this. Initially the application of $^{18}$F-FDG was limited to study glucose metabolism in vivo to map the regional cerebral functions under various conditions. Today it is one of the most useful tracers for the detection and management of cancer.

BRIT has also commenced production of $^{18}$F-NaF, a very useful diagnostic agent for bone metastases, especially in carcinoma of breast cases. Large numbers of patients suspected for metastatic bone involvement have been assessed using bone scintigraphy with Na$^{18}$F, which has a high sensitivity. The production of $^{18}$F-FLT (fluorothymidine), which is considered a better alternative to image cancer cells, is being planned. Another $^{18}$F labeled compound FMISO is widely used for imaging hypoxic cells. The synthesis procedure for this is under the final phase of standardization. Quality control and biodistribution studies are also being carried out to enable this for routine clinical studies.

**Molecular diagnostics**

Molecular diagnostics is becoming popular very fast. BRIT has been producing $^{32}$P and $^{33}$P labelled nucleotides, which are building blocks of the hereditary materials DNA (deoxynucleic acid) and RNA (ribonucleic acid, the template for protein synthesis) of all living organisms. These isotopically labelled molecules are an important tool of modern biology and biotechnology. Cancer is a complex disease, and yet to be understood very well. A great deal of scientific research is going on in India and abroad to understand the disease mechanism, to detect the disease at an early stage, and clinical diagnosis of different stages and types. The above isotopically labelled nucleotide molecules are being regularly used by various research institutes involved in cancer research. BRIT also produces kits for fluorescent labeling of the probes used in histopathological detection of cancer. Such diagnosis
allows much early detection, better or finer typing of different forms of cancer, knowledge of the source of primer tumour, prognosis, and personalized treatment. The latest molecular diagnosis of cancer is based on measurement of gene expression in cancer tissue. Gene expression is measured either by DNA chip technology or by qPCR technology. The former gives the relative quantity while the latter gives the absolute quantity. BRIT has developed qPCR technology based on which kits for the detection of oral cancer and breast cancer are being developed.

**Sealed sources for radiotherapy**

In India cobalt teletherapy equipment is widely used for radiotherapy. The Department of Atomic Energy has developed state of the art teletherapy equipment “Bhabhatron” which is now being supplied to various hospitals in the country. The sealed sources for all the teletherapy machines imported as well as indigenous are being made and supplied by BRIT. BRIT is also in the process of developing low cost high dose rate brachytherapy equipment. BRIT also makes a $^{137}$Cs manual brachytherapy applicator that is being utilized for a large number of cervix cancer patients. Platinum coated $^{192}$Ir wire for interstitial brachytherapy is being made for many years now. Blood irradiator for the prevention of TA-GVHD for the benefit of immunodeficient cancer patients are also being manufactured by BRIT.

BRIT is actively involved in the production and supply of sealed radiation sources and a variety of radiopharmaceuticals, both of diagnostic and therapeutic value in cancer management. The range of products includes a wide spectrum of radioisotopes which are designed to meet specific applications. In addition to conventional $^{99}$Tc$m$ based radiopharmaceuticals, BRIT has made its presence felt in the supply of various other radioisotope based products and has also made a pioneering contribution in the field of PET radiopharmaceuticals in India. There has been an attempt to address the needs of basic researchers investigating cancer by providing molecular biology tools. In the last few decades BRIT has been constantly reorienting its focus to meet the societal obligations and also to provide a human touch to radiation technology.
A Phase II randomized trial comparing IMRT with conventional radiation therapy in stage IIB carcinoma cervix: An audit


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Carcinoma cervix is the commonest malignancy in Indian women and a leading cause of cancer mortality in India. Radiotherapy — external beam radiotherapy (EBRT) and intracavitary brachytherapy (ICBT) — forms the mainstay of treatment for cancer of the cervix. In the recent past, concurrent chemo-radiotherapy schedules have shown an increase in loco regional control rates and overall survival but at the cost of increase in hematological and GI toxicities.

The emerging newer precision radiation techniques, especially IMRT, have shown potential for better critical structures sparing and dose escalation to the target. Our pilot study showed a 15–22% reduction in high dose regions to rectum, bladder and small bowel region. To evaluate these potentials systematically, we undertook a phase II randomized in carcinoma cervix with a hypothesis of increasing the total dose through IMRT and reduction in acute grade III radiation enteritis from 25–35% to 10–15% and grade II bladder and rectal late sequelae to less than 5% and accrual of 200 patients.

Materials and methods

Eligible patients, after obtaining informed consent, were randomized to conventional EBRT [40 Gy /20#/4 weeks (midline block in antero-posterior portals) or IMRT arm [50 Gy/25#/5 weeks]. All these patients received five weekly insertions of high dose rate ICBT (7 Gy to point A)] and 5# of concurrent weekly cisplatin (40 mg/m²). The trial will be stopped if the difference in toxicities is significant with p< 0.001 and p<0.01 for 50% and 75% event rates, respectively.

Results

In this study, until December 2007, 58 patients were randomized and had completed treatment. The compliance rates were comparable in both the arms. Acute Grade II/III gastrointestinal and genitourinary toxicities were seen in eight and three patients in conventional arm as compared to four and one patients, respectively, in IMRT arm. Similarly, Grade II/III neutropenia was seen in three patients in conventional versus one patient in IMRT arm. The response rates were similar in both the arms. With a median follow-up of 14 months (2–24 months) four patients have had recurrences, two in each arm so far. Two patients in IMRT while one patient in conventional arm had grade III radiation proctitis. All these patients improved symptomatically with steroid enema and argon plasma coagulation. The rectal doses in all these three patients were within normal limits. None of the patients have radiation cystitis so far.
Conclusion

In this ongoing Phase III randomized trial in carcinoma cervix FIGO IIB, the audit so far suggests that moderate dose escalation with IMRT is tolerated well. The acute gastrointestinal and hematological radiation toxicities are fewer with IMRT. The comparison of late radiation sequelae and loco-regional control rates needs completion of accrual and further follow-up. Integration of IGRT with the current study would aid in precise treatment delivery and more meaningful interpretation of the toxicity and outcome data.
Comparison of gross tumour volume and planning target volume with 3-D conformal radiotherapy planning versus 2-D

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The National Cancer Center (NCC) is the only centre in Mongolia for cancer service throughout the country. About 4000 new cases (3852 in 2007) of cancer were diagnosed per year. Most of them received radiotherapy (984 in 2007) on account of the fact that more than 60% of new cases were diagnosed in advanced stages (III or IV) and those patients have no chance to have surgery at the moment. The history of radiotherapy in Mongolia was established in 1959 and since that time we use 2-D treatment planning only. However, during the last two years CT simulator machine (Siemens, Somatom Emotion 6) (Fig. 1) and 3-D treatment planning system (Nucleotron, XiO) have been installed in NCC. Transition from two dimensional (2-D) to three dimensional (3-D) treatment planning for a radiotherapy development in Mongolia was an important step for accessing to the world level. Apparently, this kind of method has already been implemented in the developed country level; however, it is an innovative treatment strategy and a good basic step for the transition to the next radiotherapy methods as IMRT and IGRT in a low income country like Mongolia.

FIG. 1. Three dimensional view of patient M, 27y with lung cancer using the CT slices of Siemens, Somatom Emotion 6 in NCC.

Purpose

To define the advantages of three dimensional conformal radiotherapy (3-D CRT) method and introduce the innovative approach of radiotherapy services in Mongolia.
Methods and materials

1) Patient selection: Twenty patients with different kinds of cancer were randomly evaluated for 3-D CRT clinical treatment planning by using CT-simulator “Siemens Somatom Emotion-6” in the Radiotherapy Department, National Cancer Center of Mongolia.

2) Volume calculation: Firstly, we calculated the gross tumor volume (GTV) and treated volume (TV) by cm$^3$ in 3-D and 2-D treatment planning in all patients. We then analysed the volume of the surrounding normal tissue ($V_d\%$) based on the difference of volume of treated volume (TV) and gross tumor volume (GTV).

Results

The mean age was 47.5 (range, 3–74). Eight patients (40%) were male; nine (45%) patients were with head & neck cancer; five (25%) patients were with thorax cavity cancer and six (30%) were with abdominal cavity cancer.

The treated volume (TV) significantly decreased for 3-D CRT plans compared to 2-D as indicated by $V_d\%$ (average 46.6 vs. 26.7) and treated volume (TV).

![Graph showing comparative treated volume (TV) of patients.](image1)

**FIG. 2.** Comparative treated volume (TV) of patients.

![Graph showing linear regression analysis.](image2)

**FIG. 3.** Linear regression analysis shows a for 2-D and 3-D treatment planning correlation between in the treated volume and normal tissue volume.
The volume of the surrounding normal tissue ($V_d\%$) is different, depending on tumour site. The $V_d\%$ means were relatively low (42.32 vs. 19.17) in 2-D and 3-D treatment planning in both as compared to the others where tumour localization is in the head & neck region. The $V_d\%$ means were relatively high (54.0 vs. 40.3) and 3-D mean is lower than 2-D where tumour was located in the abdominal region.

The mean $V_d\%$ (46.6%) is relatively high in 2-D treatment planning compared with 3-D CRT; however, it connected with cancer specific that contains a gross tumour volume and subclinical microscopic malignant diseases. Furthermore, this innovative treatment method could potentially benefit for treatment and improve overall survival (OS) and disease-free survival (DFS) in patients with cancer.

Results show that 3-D CRT is a safe and more effective method for the patients with cancer receiving radiotherapy treatment. However, we need to implement the next effective approaches (IMRT, IGRT, etc.) of radiotherapy into our own practice based on obtaining 3-D treatment planning and to do a more detailed study and research in this site.

Acknowledgement: The authors are thankful to doctors L. Tumurbaatar, G. Odontuya, N. Sansar, M. Bayarmaa and the Radiotherapy Department, National Cancer Center of Mongolia.

REFERENCES


Adjuvant radiotherapy in ‘peculiar’ African breast cancer

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‘Peculiar’ African breast cancers may have the following characteristics:

- They are large breast cancers bigger than 25 cm diameter.
- They occur in young, parturient mothers.
- They present late with locoregional involvement.
- They are operable tumours.

They are a source of contemporary challenge to radiation oncologists practicing in low-resource countries.

Adjuvant irradiation in such tumour may require modification of standard/conventional techniques to ensure adequate coverage and optimal locoregional irradiation of tumour volume and bed.

The aim of the study is to highlight acute morbidity in ‘peculiar’ African breast cancer with large tangential field-separation (greater than 22 cm) treated with Co-60 megavoltage teletherapy machine in low resource country.

Between 2004–2007, 74 patients with the ‘peculiar’ large African breast cancer, who received adjuvant radiotherapy at the Radiotherapy and Oncology Centre, Ahmadu Bello University Teaching Hospital, were reviewed. The patients had modified radical mastectomy and completed six courses of chemotherapy (CAF). The histology was invasive ductal carcinoma. They received a total of 50 Gy in 25 fractions over five weeks using a bi-tangential chest wall and an anterior supraclavicular/axillary portals. Chest wall was bolused in one-third of the treatment period. No patient had simulation.

The mean age was 34.5 years. The age range was 28 years to 41 years. The mean tangential separation was 23.2 cm (range 22 cm–25 cm).

Overall morbidity involved dry desquamation, patchy desquamation, moist desquamation and ulceration occurring in 25%, 37.8%, 29.7% and 6.7% cases, respectively. No significant difference was observed in tangential field-separation of 22 cm when compared with 25 cm. Similarly, field separations of 22 cm and 23 cm (population A) when compared with 24 cm and 25 cm separations (population B) showed no significant difference in morbidity.

Conclusion

Adjuvant radiotherapy morbidity in the ‘peculiar’ African breast cancer, treated on Co-60 machine may be acceptable. Tangential field separation 22 cm versus 25 cm showed no statistical difference. Also 22 cm and 23 cm (population A) versus 24 cm and 25 cm (population B) showed no statistical difference in the study.
Radiation dose optimization and risk estimation to patients undergoing HDR brachytherapy with ring applicators

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In the treatment of malignancy of the cervix using intracavitary radiotherapy, rectum (R) and bladder (B) are the primary organs at risk because of their proximity to the target organ. Radiation doses to these duo calculated by two high dose rate (HDR) brachytherapy treatment planning systems (Genie and BrachyVision) were compared to estimate risk and report discrepancy with different sets of ring applicators.

Between August 2007 and February 2008, a total of 130 HDR applications involving 65 patients undergoing brachytherapy for carcinoma of the uterine cervix at Johannesburg Hospital, South Africa were entered into this study. Forty (40) of these subjects were treated with Nucletron’s micro-selectron HDR unit and 25 with Varian’s gammademed afterloader. The applications were classified into 13 groups based on applicators’ dimensions and prescribed doses.

Following treatment, rectal and bladder doses were calculated for the first two fractions in all patients receiving point ‘A’ prescribed dose of 8.0 Gy (92 applications of 46 patients) or 6.5 Gy (38 applications of 19 patients) in three or four fractions, respectively. The average ‘B’ doses in all but one group are higher than the corresponding ‘R’ doses.

Variations in radiation doses to the rectum and bladder using applicator of ring diameter 32 mm, intra-uterine length of 6 cm and curvature 60° (R32IU66) are shown in Figs 1 and 2 for prescribed doses of 8 Gy and 6.5 Gy, respectively. As shown below, there is no specific trend in dose variation between these two given organs. For HDR applications of 6.5 Gy fractionation dose, mean doses received by the rectum and bladder reference points were 3.37 Gy (51.85%) [SD 0.85 Gy] and 4.92 (75.69%) [SD 1.52 Gy], respectively. Meanwhile for brachytherapy fractions of 8.0 Gy each, these values were 4.54 (56.75%) [SD 0.98 Gy] and 5.99 (74.88%) [1.97 Gy] in the same order. Dose constraints are taken as 75% (R) and 90% (B) of the prescribed dose based on ICRU-38 recommendations. In 120 (92.31%) applications, rectal doses are less than 75% (<75%) while others (7.69%) record R doses within 75–100%. Bladder doses are grouped into three: 98 (<90%), 11 (90–100%) and 21 (>100%). There is a significant difference in ‘R’ and ‘B’ doses with all ring applicators under study. Greater discrepancy in-between HDR fractions are observed with the bladder and the considerable number of applications (24.62%) in which its doses exceed the maximum radiation dose tolerance level is of concern and calls for dose-reduction measures. Whenever it is possible, calculated rectal and bladder doses should be verified by other dosimetric methods. Further investigations of ‘R’ and ‘B’ dose variations would be undertaken at the University College Hospital, Ibadan, Nigeria; using Bebig’s HDR brachytherapy facilities and treatment planning system (HDR Basic).
REFERENCES


Treatment outcome of 3-D conformal radiation therapy for localized prostate cancer: Preliminary experience

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We reviewed retrospectively the radiation therapy for patients with locally advanced prostate cancer. In recent years we have made a shift from 2-D radiation therapy to 3-D conformal therapy in our service. We compared the results of prostatectomy with radiation therapy and the combined treatment with or without hormonal therapy for local prostate cancer in the post-era of RT conformal therapy in our department.

From January 1995 to January 2006, 1020 patients with prostate cancer were evaluated retrospectively after being referred by the Urology Department to the Radiation Therapy Service. The radiation therapy consisted of 7000 cGy delivered in fractions of 200 cGy per day, five days per week. In some cases radical prostatectomy was performed before the start of RT. The primary end points were collateral side effects and overall survival. Also we evaluated the total overall time of treatment, the prostate specific antigen (PSA) and the Gleason score.

The collateral side effects were 12.2% and 1.8% in case of mild and severe enteritis, respectively; and 15.1% and 2.2% in case of mild and severe disuria, respectively. The three year overall survival and biochemical relapse-free survival rates were 93.5% and 89.6%. We have not found Grade 3 or 4 acute toxic effects.

Conformal radiation therapy, as compared with radical prostatectomy, has excellent tolerance and was associated with reduced toxicity. The combination treatment, hormonal and radiation treatments, was the most effective therapy in our study.

REFERENCES


FIG. 1. Evaluated cases according to Gleason score and modality of therapy.
Hypofractionated external beam radiotherapy and interstitial HDR brachytherapy for intermediate and high risk prostate cancer

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Purpose

High dose rate brachytherapy (HDR-BT) for prostate cancer (PC) is an accepted method to boost external beam radiotherapy. Its main advantage is the ability to deliver a relatively high dose of radiation within a well defined volume, with a rapid fall-off of dose outside the implanted area. This approach is ideal for the treatment of prostate cancer, where the gland lies very close to critical normal tissues, in particular the anterior rectal wall and bladder neck. Several retrospective studies with more than five year follow-up have previously described the outcome of patients treated with a combination of external beam radiotherapy (EBRT) and HDR-BT, but data from prospective randomized trail comparing results of this combination with dose escalation RT3-D or IMRT are still missing.

Furthermore, due to the relatively low alfa-beta ratio of prostate cancer, the use of hypofractionation could result in an increased therapeutic ratio with reduced associated morbidity.

Based on the above, we started an institutional FASE II protocol to investigate acute and late toxicity with the combination of image guided HDR-BT and 3-D conformal hypofractionated external beam radiotherapy for intermedium (IR) and high risk (HR) prostate cancer.

Our reasons for assembling the current report are to provide technical detail and show how patients tolerate the treatment.

Methods and materials

Between March 2006 to August 2008, 21 patients considered IR or HR were treated with localized hypofractionated EBRT and HDR-BT at the Department of Radiation Oncology, Hospital AC Camargo, São Paulo, Brazil. Patient’s age, Gleason score, clinical stage, initial PSA, risk group for biochemical failure, use of neoadjuvant androgen deprivation (NAAD), doses of EBRT and HDR-BT were also evaluated.

Results

All patients completed the treatment with no deviation. The biochemical control rate was 100%. Acute complications: 1/21 macroscop ic hematuria, 5/21 and 2/21 rectite G1 and G2, respectively. No Grade 3–4 nor late complications were observed. Despite this, it is not the primary end point, the biochemical control rate is 100% to date.
Conclusion

We conclude that prostate HDR-BT combined with hypofractionated EBRT is a viable and efficient procedure, both from the standpoint of resource utilization and personnel time.

REFERENCES


Treatment of malignant pheochromocitoma with high dose (800 mCi) of $^{131}\text{I}$ MIBG in a young female. How to prevent and manage secondary side effects

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Malignant pheochromocytoma is a rare disease with a five year survival of 44%. Surgery with complete resection or debulking of the primary tumour is the standard treatment. External radiotherapy and chemotherapy are usually scarcely effective. An alternative treatment is $^{131}\text{I}$-MIBG therapy. In order for $^{131}\text{I}$-MIBG therapy to achieve a remission for patients with malignant pheochromocytoma, sufficient doses of $^{131}\text{I}$-MIBG must enter tumour cells. Lower dose of $^{131}\text{I}$-MIBG therapy (<300 mCi) had shown rarely partial or complete remissions. It is now possible to treat these patients more aggressively with high doses of $^{131}\text{I}$-MIBG since peripheral blood stem cells may be collected in advance such that they may be reinfused in the event of prolonged myelosuppression following high dose therapy.

We report our experience in a 22 year old female with malignant pheochromocytoma treated with a single high dose of 800 mCi of $^{131}\text{I}$-MIBG. She was diagnosed of left suprarenal pheochromocytoma at 16 years of age. The primary tumour was removed by surgery. Fourteen months later a second surgery was performed due to ipsilateral hilar renal recurrence. During follow-up, due to an increase in normetanephrine as well an abnormal diagnostic $^{131}\text{I}$-MIBG scan, which showed lymphatic abnormal uptake in four lymph nodes, a $^{131}\text{I}$-MIBG therapy with high dose was given (18 mCi/kg; total single dose of 800 mCi). Before the treatment marrow stimulation with granulocyte colony-stimulating factor allowed successful peripheral blood stem cell leukapheresis and cryopreservation. Biochemical marker, neutrophil count (>1.000/uL), Platelet count (>80.000/uL) SGOT (<2.5x ULN), total bilirubin (<2.5x ULN) and creatininine (<2x ULN) was required. Ovaric, thyroid and cardiac functions were normal. The patient was non-pregnant. Thyroid block was performed with lugol (five drops/day until 10 days after and two days before). All medications known to interfere with MIBG uptake were suspended. The day of the therapy, two intravenous lines were established: one for hydration and the other for $^{131}\text{I}$-MIBG infusion. A bladder cathether was placed, kept open into a continuously flushing toilet three meters from the bedside during the following 72 hrs in order to reduce irradiation to bladder, uterus, ovaries and rectum. Anthemetic drugs were administered during the first days (ondansetron 8 mg every 8 h) in order to avoid vomiting and nausea. Intravenous hydration was maintained during the first days days in order to ensure a high diuresis. Laxatives since the three days after were used in order to eliminate gut activity. Sour candies were used in order to prevent sialoadenitis. $^{131}\text{I}$-MIBG was infused intravenously over four hours, pumped from a shielded vial. Blood pressure and pulse were measured remoteley every 15 minutes. Myelosuppression was observed four weeks after treatment and the patient required platels transfusion and infusion of autologous cryopreserverd peripheral blood stem cells. She also developed a transitory anorexia and alopecy. Transitory mild elevation of liver markers was observed. No other complications were observed. Two out of four lymph nodes were eliminated with $^{131}\text{I}$-MIBG. The remaining two were surgically removed.
She had undoubtedly benefited from the high dose $^{131}$I-MIBG treatment. Now, five years after the treatment, she is free of disease and has two healthy daughters.

With proper measurements, high dose of radiopharmaceutical can be used for therapy without serious and permanent side effects. High-dose $^{131}$I-MIBG appears to constitute a relatively inexpensive, non-toxic, and widely available drug, offering new hope for these unfortunately stricken patients.

**FIG. 1. Metanephrine evolution after 800 mCi $^{131}$I-MIBG therapy.**

**FIG. 2. Platels suppression after 800 mCi of $^{131}$I-MIBG therapy.**

**REFERENCES**


Angiogenesis of VEGF-A and MVD as the predictor of accelerated fractionation radiotherapy efficacy on nasopharyngeal carcinoma

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The object of the study is to compare the radiotherapy planning strategy between accelerated fractionation and conventional fractionation in relation to the angiogenesis expression VEGF-A and MVD on nasopharyngeal carcinoma (NPC).

Consecutive randomized sampling of 66 patients stage IIa-IVb NPC divided by two arms radiotherapy planning within the same equivalent BED calculation [1]. Thirty patients in accelerated fractionation 150 cGy/fraction, two fractions/day, five days/week, and 33 patients in conventional fractionation 200 cGy/fraction, one fraction/day, five days/week. Radiotherapy treatment was performed by Linac Elekta Precise. Due to radiation time consistency daily, all patients in accelerated fractionation group (AFG) were given first radiation at 7.00–8.00 a.m. and second radiation at 11.00–12.00 a.m. All patients in conventional fractionation group (CFG) were given radiation treatment at 9.00–10.00 a.m.

Radiotherapy responses were evaluated by clinical, nasopharyngoscopy and SPECT/CT imaging according to WHO criteria [2].

Angiogenesis expression level of VEGF-A and MVD were performed by immunohistochemical examination from nasopharyngeal tumour biopsy. Microvessels immunostained of VEGF-A using VEGF (A-20); sc-152 marker (Santa Cruz Biotechnology, Inc.), and MVD marker using Factor VIII-related antigen-concentrat-F8/86 (Biomedia catalog number v1180).

VEGF score consists of two values of results, which are positive - semi-qualitative calculation and positive distribution value in the form of semi quantitative calculation:

VEGF-A’s positive value is a value resulting from brown color intensity in cytoplasm of tumour cells which is visible in microscope. That value is divided into the category of grade 1 if the image of color intensity equals with negative control (inexistence of primary antibody), grade 4 if color intensity equals with positive control (normal epitel nasopharynx), grade 2 and grade 3 if color intensity is between grade 1 and grade 4. Here are the illustrations: Grade 1 = none (negative, no brown color); Grade 2 = faint/focal (weak positive: weak brown); Grade 3 = moderate (medium positive, medium brown); Grade 4 = strong (strong positive, strong brown).

Positive distribution value of tumour cell is semi quantitative value in the calculation of distribution percentage for brown color intensity per field of view of tumour cells under 400 × microscope. Here are the illustrations: Grade 1 = negative; Grade 2 = 1%–20% (brown tumour cell stained; less distribution); Grade 3 = 21%–50% (brown tumour cell stained; weak
distribution); Grade 4 = 51%–80% (brown tumour cell stained; medium distribution); Grade 5 = >80% (brown tumour cell stained; strong distribution).

MVD score was determined, qualitative intensity of microvascular around tumour cells has brown color on its endotel cells in order to form tubulus image. WF VIII coloring was executed per field of view 400 × microscope (×40 object×10 ocular lens 0.785 mm² per field of view).

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Comparison of patients’ characteristics under ‘sex’ shows a p-value of 0.09 due to randomized sampling.

The statistics were analysed by Pearson chi-square and correlation. Local-regional complete response of accelerated fractionation arm and conventional fractionation arm are 81.8% and 69.6%. Patients treated with accelerated fractionation have better local-regional response than conventional fractionation (p=0.251) but corresponded significantly only on stage IVb.
S. Soetopo, et al.

Expression level of VEGF-A marker has correlated with MVD, but expression angiogenesis VEGF-A and MVD are not correlated with tumour stage. Efficacy of accelerated fractionation radiotherapy if VEGF-A marker has strong expression level and distributed more than 80% (p=0.053) or MVD marker more than 10 microvessels identified within tumour cell in any single 400× fields (p=0.053), but combined these markers as an angiogenesis expression to efficacy of accelerated fractionation radiotherapy definitely significant in NPC stage III–IVb (p=0.014).

Conclusion of this study is combining angiogenesis expression marker of VEGF-A and MVD very useful as efficacy predictor of local-regional radiotherapy response in strategy accelerated fractionation radiotherapy of nasopharyngeal carcinoma.

REFERENCES


Benchmark use of 3-D conformal planning dose-volume histograms to predict use of intensity modulated radiotherapy under resource constraints

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Under a binding resource constraint, the relative proportion of intensity modulated (IM) to three dimensional conformal (3-C) planning depends on statistical and economic parameters unique to each locale. We undertook an analysis of data at Credit Valley Hospital (CVH) in prostate cancer to demonstrate how an organized approach can accommodate parameters, which may improve cancer control, reduce toxicities, and minimize economic costs.

Between 2005 and 2007, 168 consecutive low- and intermediate-risk patients underwent 3-C planning with fiducial gold-seed markers and identical PTV expansions. All contours were by consensus of two oncologists. Rectum was contoured for 11 cm in length (median vol. 64 cc). Prostate was contoured from apex to 1 cm of seminal vesicles (median vol. 65 cc), intending 78 Gy in 39 fractions. In the event, 61 had dose adjustments to meet dose-volume histogram (DVH) constraints, particularly for rectum. IM might have been a better option. For analysis, DVHs were re-normalized to 78 Gy. Rectal DVH shape was positively associated with prostate vol. (Fig. 1), but negatively associated with rectal volume. Logistic regression confirmed that the 61 cases could be partly predicted by these two volumes ($p=0.019$). Bladder and rectal volumes were independent. Bladder DVH were reduced with bladder filling (oral water intake). Bladder vol. did not predict dose compromise with 3-C ($p=0.8$). Rectal and prostate volume deciles were used to construct a simple IM-probability nomogram.

A receiver operating curve (ROC) had a naive optimum at 0.37 (i.e. 37% or greater chance of IM vs. 3C), assuming equal costs of misclassification (‘likely 3-C’ vs. ‘likely IM’). Costs differ in type of staff involved, and time spent in planning and quality assurance (e.g. greater physics staffing for IM). Calculus modelling demonstrated that if the cost of IM exceeded twice that of 3-C, an ROC cut-off of 0.5 was best; otherwise 0.25 was best. These attempt to reduce the risk of double planning patients who cannot meet dose constraints with 3-C.

To test the volumetric model and confirm improvement in rectal DVH with IM, the next seven consecutive cases were double planned after IM was commissioned at CVH in early 2008. Rectal DVH was improved over the range of 25 to 75 Gy by 2 to 20% (the maximum difference 45 to 50 Gy). Average reduction was 12% ($p<0.05$) across the entire DVH for rectum (Fig. 2) and it was 7% for bladder. Since March 2008, all cases have been planned with IM if fewer than four cases/week. A composite of IM DVH’s will be compared to those 168 historical, 3-C, normalized DVHs that now constitute a CVH benchmark of performance.

Limitations of this study include not considering clinical parameters known in advance of CT simulation, which might predict for IM, but those may be redundant to, or less accurate than contoured volumes. We did not contour rectal and bladder walls, but we do this on all IM plans.
prospectively, which may improve the ROC. Rectal preparation intends an empty rectum, but rectal fullness might be explored using these predictive methods for IM.

In summary, it is possible to use a local clinical series of representative prostate 3-C plans to develop the distribution of local population based DVHs. The summary (mean or median across dose) provides a home-made or local benchmark for future reference when commencing an IM program [1]. Not all patients may benefit from IM vs. 3-C, though many will. Under budgetary constraints, it is best to anticipate who might benefit from IM, relative to 3-C, meaning to reduce the DVH of the rectum while ensuring 78 Gy at the prostate. Using CT simulation and immediate contours and related parameters (volume, possibly inter-centroid distances) prior to planning could triage patients for IM, thereby minimizing double planning. Triage depends on the prevalence of needing double planning, an appreciation of local economic costs, and the extent to which DVH optimization reduces acute and chronic toxicities. Following our methods, each centre can develop their own unique, though similar solutions. We demonstrated this with prostate cancer, but it may be possible with other anatomic sites. Outside of a budget constraint, we further found that IM will allow dose escalation at the prostate to 84 Gy, while keeping rectal DVH very similar to that derived from 3-C plans. Also, planning MRI fusion and daily CT verification may lead to smaller prostate PTVs, further separating prostate and rectal doses for a better therapeutic ratio.

![rectum DVH by psv quintiles (n168 total)](image1)

**FIG. 1.** Rectal DVHs per quintile prostate vol.; 168 cases with 3-C plans normalized to 78 Gy=100%; shows systematic worsening of rectal DVH with greater prostate volumes.

![median rectal DVH, same patients, by plan](image2)

**FIG. 2.** Better rectal DVHs with IM vs. 3-C plans (in seven cases with 78 Gy=100%) especially between 30 and 60 Gy.

**REFERENCE**

Development of indigenous HDR brachytherapy equipment: An effort towards affordable cancer treatment in India

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Although there is sharp rise in cancer cases in India, the fact remains that its treatment is still inaccessible to the large section of the society resulting in cancer becoming a leading cause of death. One of the important causes of suffering of cancer patients is the paucity of modern technology particularly in rural India. After the introduction of fully indigenous teletherapy equipment named Bhabhatron, there was a need for having indigenous intracavitary treatment equipment. Development of remote operated High dose rate (HDR) brachytherapy equipment is in progress, which is expected to work in tandem with Bhabhatron to provide cost effective radiotherapy treatment in India.

In India statistics reveal that female cancer patients are largely suffering due to cervical (~21%) and breast cancer (~17.5%). Males are suffering largely due to lung & throat (~30%) and prostate & colon (~17%) cancers. These statistics indicate that the country needs a versatile, inexpensive and multiple utility equipment that can take care of the above type of cancers. HDR brachytherapy equipment is the most appropriate one because of much lower treatment time needed and making it an outpatient treatment.

Presently HDR equipment available in the country are all imported and, because of prohibitively high cost of the equipment as well as the routinely required source change cost, the number available is much smaller than what is needed. Only about 75 such units are available whereas the number required is much larger. An indigenous HDR brachytherapy equipment and capability to furnish replacement $^{192}\text{Ir}$ sources periodically is the need of the hour. Keeping the above in view the Board of Radiation & Isotope Technology (BRIT) decided to take up development of such equipment.

The first and foremost challenge was to have an equipment with features not inferior to what the existing imported models have. The production of up to 15Ci of miniature source was the major challenge. Due to limited neutron flux ($1.8\times10^{14}$ n/cm$^2$/sec) available in Indian PHWRs, it is not possible to produce activity of an order of 15Ci in natural $^{191}\text{Ir}$ pellets. This has been overcome by the use of enriched $^{197}\text{Ir}$ pellets which enable matching the activity with the specifications of existing models.

The fabrication of source assembly involving machining of miniature components and then remote assembly/laser welding, which has to be done inside hot cells, was the other challenge. Several trials were carried out for this for getting proper results.

The number of sample source assemblies have now been made that are being subjected to qualification testing for checking conformance to ISO 2919 requirements. The electro mechanical unit of the equipment with all the necessary instrumentation is under fabrication by a private industry which already has been credited with fabrication of the state of the art Bhabhatron units. The HDR brachytherapy equipment will conform with all the relevant
standards of IEC and DIN and will meet the stipulations of the Atomic Energy Regulatory Board of India.

For development of a radiation treatment planning software, expertise from Indian industry is also being employed to ensure that it meets the requirements of ISO 13485, IEC 62083 and FDA 510(K). Initially two types of applicators viz. vaginal and cervical are being developed and will utilize the standard catheters available in the market. Extensive trials are planned to be carried out with the help of Tata Memorial Hospital, Mumbai in evaluation of the unit before being placed into regular service.

The HDR brachytherapy equipment is a very versatile device for treatment of many types of deeply located tumours. Because of short treatment time it converts many of the treatments from in-patient to out-patient. With the additional benefit of an equipment which will be made available at much lower cost than the current international price and the fact that source replenishment costs will be much lower because of sheer logistics, the treatment costs of many of the cancers is expected to be vastly reduced with the introduction of such units.

The indigenous HDR brachytherapy equipment along with Bhabhatron will enable the radiotherapy treatment available at very affordable prices in India in the years to come.
Dose-fractionation sensitivities of low/middle/high risk prostate cancer deduced from eight international primary institutional datasets

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Objective

There are reports of a high sensitivity of prostate cancer to radiotherapy dose fractionation, and this has prompted several trials of hypofractionation schedules. It remains unclear whether hypofractionation will provide a significant therapeutic benefit in the treatment of prostate cancer, and whether there are different fractionation sensitivities for different stages of disease. In order to address this, multiple primary datasets have been collected for analysis.

Material and methods

Seven datasets were assembled from institutions worldwide. A total of 5120 patients was treated using external beams and daily (five per week) dose fractions, where the overall treatment time ranged from one to eight weeks. Standard fractionation (1.8–2.0 Gy per fraction) was used for 38% of the patients, and hypofractionation (2.5–6.7 Gy per fraction) for the remainder. Patients were divided into three risk groups: low risk (T1-2a, GS<7, PSA<10), intermediate risk (T2bc-3a, GS=7, PSA 10-20), and high risk (T3b, GS>7, PSA>20). Low risk patients comprised 25% of the total, intermediate risk 45%, and high risk 30%. Direct analysis of the primary data for tumour control at five years was undertaken, using the Phoenix criterion of biochemical no-evidence-of-disease, in order to calculate values in the linear-quadratic equation of k (effective target cell number), \( \alpha \) (dose-response slope using very low doses per fraction), and the ratio \( \alpha/\beta \) that characterizes dose-fractionation sensitivity.

Results and conclusions

There was a significant difference between the results for the three risk groups, and there was an expected tendency for a decrease in control as the risk group increased from low to intermediate to high. The value of \( \alpha/\beta \) for the pooled data was 1.6 (95% CI: 1.3–1.8) Gy. There was a trend for the value of \( \alpha/\beta \) to be slightly higher for higher risk patients (low risk 1.3 Gy, intermediate risk 1.6 Gy, high risk 1.8 Gy), but all these values were within the low range generally reported for prostate cancer. In contrast to a literature report, the present analysis showed no evidence in the case of high risk patients of a kinetically higher value of \( \alpha/\beta \) than the appropriate values for late normal-tissue morbidity. Hence the fractionation
sensitivity differential (tumour/normal tissue) favours the use of hypofractionated radiotherapy schedules for all risk groups, which is also very beneficial logistically in limited-resource settings.

Acknowledgement: The data used for this analysis were kindly provided by P. Kupelian, F. Leborgne, J. Logue, H. Lukka, B.L. Madsen, R. Miralbell and E. Yeoh.
Session 5b:

Poster Session

POSTERS RELATED TO MEDICAL PHYSICS
Establishing the efficacy of radiation oncology – standardizing the collection and validation of 3-D treatment planning data

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The collection of digital treatment planning data during radiotherapy clinical trials serves several important roles. Collection of this data allows:

1. Assessment of the quality of each patient’s treatment planning.
2. Identification of any departures from the treatment planning protocol of the trial, with the opportunity to correct these before the patient’s treatment begins.
3. An ability to undertake detailed prospective analysis of treatment planning technique including volume definitions.
4. A possibility to account for potential sources of variability, such as differences in volume calculation between planning systems.
5. An ability to correlate complex dose and volume related features with treatment outcome.
6. An ability to examine patterns of treatment planning techniques and resulting dosimetry.

Development of software systems to support trials through collection of multi-centre treatment planning data has been happening for well over a decade. Most notably, the National Cancer Institute in the USA supports the Advanced Technology Consortium which has developed significant infrastructure for such data collection [1]. Current international efforts to develop systems for collection of planning data shall be identified.

In Australia and New Zealand, a need to collate treatment planning data for quality control and trials support has led to the development of a software platform known as SWAN [2]. Programming of SWAN has taken place at the Sir Charles Gairdner Hospital in Perth, Western Australia. The intention in developing SWAN was to provide a platform that can be operated on multiple platforms with minimal software costs. The Java language was employed utilizing freely available runtime libraries.

SWAN incorporates two principal components. The first is a tool (the ‘viewer’) that allows for the import of raw treatment planning data (in RTOG or DICOM-RT formats), the viewing and manipulation of said data. The second is a database which accepts (possibly altered) treatment plan data from the viewer (the original raw data not being altered). The viewer can also be used to retrieve plan data from the database. An html interface also allows access to the database providing a web based front-end for querying the database and extracting reports that utilize user-defined fields. The SWAN platform is continually undergoing refinement and validation. The results of several validation tests, relevant to the quality assessment of trials data shall be presented.
The SWAN system is currently being used for quality control purposes for several trials being undertaken by the Trans Tasman Radiation Oncology Group, as well as several trials managed by individual trial investigators. Examples of the effect of data review with SWAN shall be presented, in relation to trials being undertaken for prostate and pancreatic radiotherapy. The prostate trial (TROG 03.04 ‘RADAR’) involved the collection of over 750 external beam treatment plans over five years from 26 separate institutions. Fig. 1 summarizes some of the protocol violations discovered with SWAN during the RADAR trial.

**FIG. 1. Summary of protocol violations discovered during assessment of treatment plans for RADAR prostate radiotherapy trial.**

Efforts are underway to coordinate the efforts of international groups to ensure consistency in the minimum standards met in collection of treatment planning data, and to facilitate the exchange of the formats of archived data. It is envisaged that datasets from separate trials groups may one day be able to be pooled in order to achieve significant statistical power in the derivation of evidence relating radiotherapy to outcome.

Acknowledgements: We are grateful to the Trans Tasman Radiation Oncology Group for their support. The development of SWAN has previously been funded by the Cancer Council of Western Australia and Abbott Pharmaceuticals, and is currently supported by Cancer Australia and the Department of Health and Ageing of the Commonwealth of Australia (NH&MRC grant number 501106).

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Value of whole body bone SPECT for metastatic work-up in clinical oncology: A study with 120 patients

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In routine nuclear medicine practice the conventional planner bone scan is usually being performed in metastatic work-up followed by whole body bone SPECT, but there could be confusion in abnormal bone scan findings particularly involving patients of older age group to differentiate degenerative and inflammatory lesion from bony metastasis. In comparison to planner image, SPECT scan can increase image contrast and has better capability of lesion detection along with proper localization.

To evaluate the role of whole body bone SPECT in metastatic work-up of cancer patients and to overcome the confusion of lesion detection and localization arising in conventional planner images, one hundred and twenty cancer patients were evaluated with SPECT whole body bone scan. All patients initially were scanned with routine \(^{99}\)Tc\(^m\) MDP planner image followed by SPECT imaging of the body from vertex to mid thigh. Both planner and SPECT bone were acquired by Siemens E.CAM dual headed SPECT Gamma Camera using low energy high resolution (LEHR) collimator. Imaging data were processed by using a standard SPECT reconstruction software.

Out of 120 patients studied there was a concordance of lesion detection between planner and SPECT studies in 54 cases (45%). However, in the other 66 patients (55%), the lesions were observed with better certainty, indicating enhancing better lesions detection for the appropriate diagnosis. This suggests that although planner images can indicate the presence of disease, SPECT images can provide additional information that not only could confirm the abnormality but also could help in the localization of lesions and enhance the certainty of the diagnosis.

Out of 66 cases where SPECT improved the quality of reporting, 62 cases confirmed the presence of positive diagnosis lesions. Four cases confirmed absence of lesions and, in two cases, new lesion was detected on SPECT which was not seen on planner images; thus SPECT study has a better resolution and more useful in the detection of vertebral abnormalities because of the additional value of three dimensional images, which are responsible for high sensitivity and specificity in comparison to planner imaging.

Identification of lesions pattern, i.e. body pedicle, facets or spinous process of vertebrae can help in differentiating benign and metastatic diseases. Out of 120 patients a total of 225 lesions were on SPECT. Out of these, 175 were located on the vertebral column and the rest were outside of the vertebrae. Further analysis of vertebrae abnormalities with distribution pattern vertebral body 105 (60% ) showed facets: 49 (28%), spinous process: 14 (8%),
pedicles 7 (4%). Extra vertebral sites were sternum, ribs, humerus, femur, tibia, iliac crest, pubic ramus, skull, etc. There were also five lytic lesions in vertebrae which were observed on SPECT images.

Bone scintigraphic findings are usually non-specific for the detection of skeletal metastasis in the evaluation of cancer patients but it is important to differentiate the metastatic lesion from other benign diseases which is essential for the proper oncological management. SPECT whole body bone scan can play a significant role which provides additional information particularly about lesion pattern and proper localization of the lesions with great certainty. The focal or diffuse uptake of tracer in only vertebral body is usually found to be benign, while lesions having uptake of the body and in the pedicle vertebrae are most likely to be malignant. Our results revealed the whole body SPECT imaging of the spine in metastatic work-up, and provided useful information in different benign and malignant lesions in the vertebrae.

In our study we have found that SPECT whole body images have a better resolution in detection of vertebral lesions because of their ability to provide three dimensional data information. Moreover, SPECT imaging has better sensitivity and specificity than the planner image; it can even detect the missing lesions in planner images.

It can be concluded that bone SPECT may be considered as one of the primary investigating modalities in the metastatic work-up of clinical oncology.

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Absorbed dose to water FeSO₄-based standard for ¹⁹²Ir HDR brachytherapy


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Following the general trends of modern dosimetry the quantity absorbed dose in water is the one mostly needed in clinical practice. A few attempts have been reported to establish this quantity for HDR brachytherapy and potential good results of two novel techniques have been reported, firstly by Sarfëñia, et al. (2007) using a water based calorimeter and secondly by Austerlitz, et al. (2008) both with uncertainties still high, 5% and 8%, respectively; as well as de Almeida, et al. (2008) with uncertainties smaller than 3% both using ferrous sulphate-Fricke dosimeter.

Fricke dosimetry is by defintion regarded as an absolute method for measuring the quantity absorbed dose in water. Fricke dosimetry, ionization chambers and both water and graphite calorimetry have formed a coherent dosimetry system of standards of absorbed dose to water as clearly described in the IAEA Code of Practice TRS#398 (2000).The main objective of this paper is to demonstrate the potential usefulness of extending this technique for the standardization of the quantity absorbed dose in water for ¹⁹²Ir HDR clinical sources.

A molded double walled spherical balloon was made with 5.540 cm of outer and 4.500 cm inner diameters intercalated by a shell of 0.293 cm fitted with a 0.106 cm sleeve all made of PMMA. The FeSO₄ solution was made of 0.392 g ferrous ammonium sulphate, 0.060 g sodium chloride and 22 ml sulphuric acid. The centre of the balloon is filled with water, the shell is filled with FeSO₄ solution and the whole balloon is placed in a water phantom with 30×30×30 cm³. Five balloons were casted in two halves and glued. One of the balloons was left in parts in order to have all dimensions measured with a traceable micrometer. Measurements were conducted using the Nucletron microSelectron-HDR ¹⁹²Ir source previously calibrated by a well type chamber traceable to the UW-ADCL and the Nucletron TPS was used to calculate the nominal dose. The irradiated solutions were transferred from the balloon to a quartz cuvette with a 1.00 cm light path length and the optical densities measured using a Micronal spectrophotometer at 304 nm UV light.

As result of the Monte Carlo (PENELOPE) calculations performed, dividing the balloon in 36 sectors, 12 sectors above and below the source anisotropy values varying from 3% to 10% wee found. The calculated values for the wall attenuation have introduced a correction smaller than 0.5%.
Chemical dosimetry using standard FeSO₄ solution in a containing vessel with uniform geometry relative to the source has shown to be a feasible absorbed dose standard for HDR ¹⁹²Ir source.

The overall uncertainties that includes the ones calculated by Monte Carlo as well as the ones related to the vessel dimensions, wall thicknesses, dose calculation algorithm, UV light band, cuvettes light path, signal fading, distance source solution, dose rate constant, timing, signal fading repeatability of reader, G value, the source transit time, the effect of the PMMA in the solution, and temperature measurement of the solution during irradiation and readings are smaller than 2.5%.

Improvements are now in progress with the installation of a new spectrophotometer that includes a thermal bath, re-measuring the G values using ionometric system and using a better thermoprobe.

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Contrast materials influence at computed tomography in 3-D radiotherapy planning for thorax tumours

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The use of contrast agent in treatment planning systems (TPS) of radiation therapy allows more accurate target volume contouring. However, the contrast presence increases the Hounsfield units (HUs) due to its high atomic number. In thorax treatment plan, the employment of heterogeneity correction is essential due to the low density of lung [1]. For this correction the TPS uses the HUs thus the variations in contrast-enhanced CT can modify the dose distributions. Ramm, et al. [2] have shown that the contrast influence depends on its concentration and when a high concentration of contrast is used the effect on dose calculation in treatment planning is very critical. Almost always the usual concentration in clinical settings is not so high to have significant influences on dose calculation; this fact was demonstrated for tumour of head and neck, lung and pelvis, but for situations where beams pass through the liver, spleen or kidneys, organs that have to receive more contrast, the influences are significant [3–5].

This study was undertaken to evaluate the influence of computed tomography (CT) contrast agents on the dose distributions of 3-D treatment planning for patients undergoing radiotherapy for the thorax.

The treatment plans of eight patients, who underwent conformal radiotherapy for tumour of thorax, were collated for this investigation. There were four patients with lung cancer (patients A, B, C, D), one with Hodgkin lymphoma (patient E), two with esophagus cancer (patients F and G), and one with thymoma (patient H).

All patients received both unenhanced and contrast-enhanced CT scans. These were acquired on the GE Medical Systems Highspeed with the following parameters: 120 kV, 200 mA, tube-rotation time 1 revolution per second, slice thickness 5 mm, and slice pitch of 1.5. For the exam, 80 ml of the commercial contrast Optiray 320, with a concentration of 320 mg/ml, was intravenously injected at a rate of 1.5–2.0 ml/s. The interval between injection and starting scan was 45 s, in accordance with protocol in our institution.

Scan data were transferred to the Eclipse treatment planning system (v. 7.3.10; Varian Medical Systems, Palo Alto, CA). Treatment planning was performed on unenhanced CT scan, and after, was transferred into contrast-enhanced CT, both with Batho Power Law Algorithm for heterogeneity correction. The values of MUs and DVHs, of target volume and organs at risk, were collected.

Table 1 summarizes the patients’ data with the differences in MU by contrast administration. In general, the mean percentage difference shows an increase in values of MUs, as expected.
TABLE 1. EVALUATION OF CHANGES IN MU BY CONTRAST ADMINISTRATION FOR EACH PATIENT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Number of fields</th>
<th>Prescription dose (Gy)</th>
<th>% mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>60</td>
<td>-0.31</td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>50</td>
<td>0.30</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>60</td>
<td>0.00</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>61.2</td>
<td>0.76</td>
</tr>
<tr>
<td>E</td>
<td>4 (P1:2; P2:2)</td>
<td>30.6 (PTV:25.2; PTV2:5.4)</td>
<td>0.19</td>
</tr>
<tr>
<td>F</td>
<td>7 (P1:3; P2:4)</td>
<td>50.4 (PTV1:45; PTV2:5.4)</td>
<td>0.89</td>
</tr>
<tr>
<td>G</td>
<td>4</td>
<td>45</td>
<td>0.86</td>
</tr>
<tr>
<td>H</td>
<td>5</td>
<td>60</td>
<td>-0.40</td>
</tr>
</tbody>
</table>

P1, phase 1; P2, phase 2; PTV1, planning target volume in phase 1; PTV2, planning target volume in phase 2.

The mean percentage differences in MU were less than 1% for all patients. The dose distribution for each plan was very similar on two CT scans. These results were founded by analysis of DVHs. In general, the variation on percentile volume, in function of dose to PTV and organs at risk, was less than 10%, except in a few points, where the non-significant small volumes start with larger differences.

It is necessary to point out possible differences between the non-contrast CT scan and contrast CT scan due to the patient movement. Despite this both were acquired together, small variations should be considered. This fact may have caused discrepancy between organs at risk volume and isocentres. Therefore, the related differences in two configurations for treatment planning may result partially from such factor.

In conclusion, the use of contrast materials on CT scans for radiotherapy treatment planning does not present high influence on dose calculations and distributions for thorax tumours.

REFERENCES


Integration and commissioning of the cobalt unit Terabalt 80 ASC into TPS Oncentra MasterPlan

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The Terabalt 80 ACS has been installed in 2008 at the National Oncological Hospital in Sofia. At the same time the Treatment Planning System (TPS) Oncentra MasterPlan was commissioned for linear accelerator and we had to find means to integrate all our treatment machines with one planning system for external beam radiotherapy.

All measurements for the TPS were performed in an isocentric set-up. Because of the small distance between the machine’s head and the isocentre, the main patient treatment set-up has to be at source-to-surface distance (SSD) of 80 cm.

The aim of this study was to prove the usage of Oncentra for the patient planning and irradiation on Terabalt 80 ACS and to check the accuracy of the calculation algorithm of the TPS. This is of great importance for preventing errors in the dose calculation for patient treatment.

The measurements have been performed in water, using single channel dosimeter Unidose with both a Farmer type and 0.3 cm² ion chamber for absolute dose measurements, and Markus type ion chamber, for relative dose measurements with the beam analysing system MP3.

To verify the complex treatment plan (more complex geometry combination) [2, 3], three type phantoms using acrylic and cork plates were created.

The tests were performed for open fields: 4×4, 8×8, 10×10, 15×15, 20×20, 30×30 and 36×36 cm²; for wedged fields with wedge angles, as follows: 15°, 30°, 45° and 60° for fields 4×4, 8×8, 10×10, 15×15 and 22×18 cm² at SSD 80 cm. For more complex geometry tests involving asimetric, wedged beams and combination of beams, five types of customarily used patient treatment plans were created as follows: two opposed fields, three fields representative for bladder irradiation, four fields in a box technique, two tangential fields for breast irradiation and three fields for lung irradiation.

The measurements and calculations made by Oncentra MasterPlan, with applied pencil beam mode have been compared, as follows:

1) the central axis depth dose distributions, normalized at 5 cm depth.

2) the beam profiles at 1.5, 5.0, 10.0 and 20.0 cm depth, normalized to the dose on the central axis for the corresponding depth.

3) the absorbed dose values at normalization point (ICRU point) for complex treatment plans (more complex geometry). The planning, verification and irradiation procedure for a real patient was followed.
The criteria of the acceptable levels for TPS accuracy for simple geometry is deviation 20\% of the buildup region after 2 mm from the surface, 2\% of the central axis depth dose, 10\% or 2 mm profile displacement in the high gradient region, i.e. in penumbra region from 90\% up to 20 \% points for all measured and calculated profiles, 2 mm in beam width between 90\% and 50\% dose points of the profiles, 20\% or 4 mm displacement of the points after 20\% beam profiles. For the treatment plans, i.e. more complex geometry, we accepted 3\% for the measured dose in normalization point [1, 2].

Deviation between results of calculations and measurements was expressed as a percentage of the locally measured dose according to $\delta = 100\% \times (D_{\text{calc}} - D_{\text{meas}})/D_{\text{meas}}$ [2], and the results obtained are:

- The differences between measured and calculated points for the buildup region after 2 mm from the surface are in 10\% up to 20 cm$^2$ field size and up to 15\% for a bigger fields;
- coincidence of the measured and calculated depth dose distributions has been found in the frame of 1.5 \% for open and wedged field;
- in the penumbra region, the deviation between measured and calculated profiles is within 8\%. Greater differences were found for open field 30 and 36 cm$^2$.
- Non-acceptable deviations have been found for beam width between 90\% and 50\% points of beam profiles for all depths and field size 36×36 cm$^2$ up to 5 mm and the measured values being lower than the calculated. The profile displacement in the high dose gradient region for the fields lower than 30 cm$^2$ is up to 2 mm;
- the differences in the profiles for dose points lower than 20\% of the maximum dose are within 18\%, but for the bigger field is 35\% and the profiles displacement is up to 6 mm.
- the deviation between measured and calculated dose values are in the acceptable limits for all checked treatment plans, as for the phantoms with air equivalent material the differences are smaller. In all cases the measured dose is lower than calculated.

Conclusions

The TPS Oncentra MasterPlan can be applied with confidence for patient planning and irradiation on Terabalt 80 ACS with the exception for fields over 30 cm$^2$. The calculated doses in the patient outline, the skin and in the organ at risk, would be lower than the real ones.

REFERENCES

Radioisotopic therapy for neuroendocrine tumours with radiolabelled-somatostatin analogues in Chile

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Neuroendocrine malignancies usually present a high degree of therapeutic difficulties, mainly if they are disseminated, because they are poor responders to chemo and radiotherapy, even though they are considered as slow growing neoplasm. Most of them express specific receptors for amines and peptides, as somatostatin receptors. Tumours with superficial somatostatin receptors could be treated specifically with their analogues labeled with beta emitters. We have available in our country \(^{90}\)Y-dotatoc/dotatate since 2004 and lately \(^{177}\)Lu.

**Objective:** It was to evaluate our initial experience with this newly acquired therapeutic approach performed to 17 patients in two institutions (76% at Dipreca Hospital).

**Method**

**Population:** They corresponded to 65% males; ranging between 29 to 74 years old (mean: \(53\pm12\)). All have metastatic disease. The immunohistochemical and histological diagnoses were: 14 carcinoids and one (1) medullary thyroid cancer, one (1) ACTH-like and one (1) unknown neuroendocrine. Patients were, beforehand, all submitted to surgery in their primary location and some to chemotherapy, radiotherapy and/or Sandostatin\(^{\circledR}\), this latter medication was withdrawn before isotopic diagnosis and therapies. All patients included (a) normal or near normal renal hematological, and hepatic function prior therapy and (b) initial positive diagnostic test with \(^{111}\)In-dotatate/dotatoc, *Octreoscan*\(^{\circledR}\) or \(^{68}\)Ga-dotatate PET imaging. \(^{90}\)Y was used in 95% of the cases, labeled locally with dotatoc or dotatate, as available. \(^{177}\)Lu was selected recently in cases with smaller lesions. The same protocol was used in both institutions — briefly: in-hospital renal protection with hydration i.v. using amino acids infusion pre, during and post-beta therapy. Steroids and antiemetics were also included. In all patients we acquired bremsstrahlung images\(^{90}\)Y or \(\gamma\)-\(^{177}\)Lu for in vivo biodistribution quality control.

**Follow-up:** Liver hematological and renal function surveillance were performed every two weeks and cross-sectional anatomical imaging for tumour response evaluation, every two months.
Results

The patients received sequential therapy ranging between 1 to 7 doses, with a mean of 3.2±1.6 doses/each. The total activity received varied between 100–375 mCi at the University of Chile and between 75–525 mCi at Dipreca. The follow-up ranged from 0.4 to 44 months. Two/17 patients recently entered in the protocol. Lesion size remains stable in 7/17 cases, progression was observed in 5/17; three patients died during the follow-up; another presented renal chronic failure posterior to his third dose. A transient delayed hipokalemia was observed in another. No WHO grade 3–4 toxicity was observed as other adverse effect. After therapy carcinoid syndrome ameliorated in 4/5 patients and lesser mass effect was observed in mediastinal and abdominal lesions in two.

Conclusions

Neuroendocrine cancer therapy with labeled somatostatin analogue is safe and diminishes disease progression. The protocol should be performed within a multidisciplinary team to obtain maximal benefits for the patients.

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Dosimetric characterization of an aSi-based EPID for patient-specific IMRT QA

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The Electronic Portal Imaging Devices (EPID) has become mature technology after more than 10 years of clinical use, to verify patient set-up with respect to the radiation beam. However, the use of EPIDs as a dosimetry device has not been widespread, although there are many articles on the subject.

The feasibility of using an aSi-based EPID was evaluated for QA of an aperture-based, segmental IMRT system, with a small number of segments per beam.

Dosimetric parameters such as linearity of dose/pixel response, field size output factors and off-axis sensitivity were determined. The reported oversensitivity of the indirect detection method with standard aSi-based EPIDs [1] was investigated.

For absolute measurements, the linearity of the EPID’s dose-response was obtained at beam axis for 10×10 cm fields, yielding to a value better than 1.1 and 1.5% for 6 and 15MV photon beams, respectively, for exposures in the range from 2-500 MU. Also, the dose response field-size dependence of this device was studied and compared with phantom scatter factors at different depths in water, resulting in good agreement for the factor measured at 5 cm depth, Scp(z=5cm), as shown in Fig. 1. This indicates that the EPID’s own scatter and energy response produces a combined effect equivalent to water output factors (collimator and phantom), as reported elsewhere [2, 3].

![Diagram](image_url)

FIG. 1. Comparison of scatter factors of iViewGT EPID versus factors in water.

The EPID’s off-axis sensitivity was assessed comparing the measured profiles for 5×5, 10×10 and 20×20 cm² fields versus the same fields’ profiles at several depths in water obtained with
ion chambers. A better correspondence was observed at 5 cm depth, where the EPID off-axis response underestimates the dose up to 4% for all field sizes at flat, high dose region, as shown in Fig. 2.

\[ \text{FIG. 2. iViewGT EPID off-axis sensitivity. Comparison versus profiles a 5 cm depth in water.} \]

Results showed that iViewGT can be used for evaluation of beam dosimetric parameters, provided the dose is considered at a specific depth, which in our case was 5 cm in water, where energy dependence of EPID response is compensated in acceptable range (max. 4%).

These results encourage further research for implementing the use of this EPID for machine and patient specific QA.

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Dosimetric verification of radiotherapy treatment planning systems in Hungary

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The methodology developed by the IAEA for dosimetric quality control of treatment planning systems has been tested in ten Hungarian radiation oncology centres in a study applying the requirements of the IAEA TRS-430 [1]. The aim was to reveal the differences between planned and delivered doses in conditions similar to the real patient treatments.

We have used for the test measurements the semi-anthropomorphic CIRS Thorax phantom (CIRS Inc., Norfolk) lent by the IAEA. The properties of the CIRS Thorax phantom can be found in the IAEA TECDOC-1583 [2] and in the paper of Gershkevitsh, E., et al. [3]. The CIRS Thorax phantom was scanned always on the local CT scanner (PET-CT, CT simulator, common CT). The following treatment planning systems (TPS) were tested:

- CMS XiO TPS Multi grid superposition and Fast Fourier Transformation Convolution model
- Varian CadPlan TPS Pencil beam convolution algorithm with Modified Batho Power Law, EqTAR algorithm without inhomogeneity correction
- Oncentra MasterPlan TPS Collapsed Cone algorithm and Pencil Beam model
- ADAC Pinnacle adaption convolution model
- PrecisePLAN TPS adaption convolution model
- Nucletron Helax TPS pencil beam convolution algorithm
- Nucletron Plato TPS pencil beam convolution algorithm

We have tested all the eight test cases [3] on cobalt units, and on low and high energy linear accelerators of different manufacturers (Elekta, Siemens and Varian).

For the measurements we used in all centres our PTW Unidos (PTW, Freiburg) electrometer and the NE 2571 Farmer chamber. The chamber and electrometer have a calibration traceable to Hungarian primary standard dosimetry laboratory. Calibrated barometer and thermometer were used for the barometric correction. We evaluated the measurements according to the IAEA TRS-398 [4]. In Fig. 1 the relative electron densities are plotted against the CT numbers for the CT scanners used. In most cases the CT numbers were within the prescribed ±20.

In Fig. 2 the results are shown for the different test cases for 6 MV. The numbers beside the column of different colours refer to the place of the measuring points 1–5 being in the soft tissue, 6–9 in lung and 10 in the bone. It can be seen that the four TPSSs in the figure fulfil the requirements stated by the IAEA. We received relatively good agreement in the case of high energies (15 and 18 MV). One can conclude, however, that the different algorithms are fitted rather to the low energies than to the higher ones. In the case of 60Co units we received the best results with CMS XiO TPS Multi grid superposition and ADAC Pinnacle adaption convolution model. The older TPSSs like Helax and Plato had problems in dose calculation in the inhomogeneity correction especially in the lung.
Technical comments on the usability of the CIRS Thorax phantom: more precise fixation on the table top should be used, e.g. interlock bar of the IPPS (indexed patient positioning system) would be better instead of the tape. The edges of the lung inserts for the ionization chamber are mouldering during usage. The treatment set up would be easier if the centre of the inserts were marked with a crosshair.

Acknowledgement: The authors are grateful to the International Atomic Energy Agency for lending the phantom, to Dr. Eduard Gershkevitch for his expert mission and to the Hungarian Atomic Energy Authority for its support. Thanks for the voluntary contribution to the following radiation therapy centres: Aladár Petz County Hospital, Győr, Department of Oncotherapy, Medical School, University of Pécs, Department of Radiation Therapy, University of Debrecen, Health Centre of the Kaposvár University, National Institute of Oncology, Budapest, Onco-radiological Department of the County Hospital Bács-Kiskun, Kecskemét, Oncoradiology of County Hospital Borsod-Abauj-Zemplén, Miskolc, Oncoradiology of Kálmán Pándy County Hospital Békés, Gyula, Oncoradiology of the Markusovszky County Hospital Vas, Szombathely.

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The dosimetry of small photon beams is a challenging task due to non-equilibrium conditions created as a consequence of the secondary electron track lengths and the source size projected through the collimating system that are comparable to the detector size [1] and steep dose gradients exist in a large portion of these fields. This fact adversely affects the measurement accuracy in regions where the gradient varies across the detector [2]. Thus, the most important factor in the choice of a beam measuring device is its size with respect to the beam diameter and the properties of selected detector. In this work, output factors of small circular photon beams are evaluated in a homogeneous medium (water phantom) with two different detectors, radiocromic film GafChromic EBT (International Specialty Products, USA) and a shielded solid diode detector PDF3G (IBA-Dosimetry, Germany). These results were compared with Monte Carlo radiation transport calculations.

The GafChromic film EBT® were handled in accordance with the procedures outlined in the AAPM TG-55 report [3] and those proposed by Buston and Lynch [4–5]. Film digitizing was performed using a commercial document Microtek scanner model ScanMaker 9600XL, in transmission mode with 100 dpi, 36 bits RGB colour depth. Data analysis was performed only with the red channel. Film calibration was performed by placing the film on a water phantom at 1.5 cm depth using the SSD technique (SSD=100 cm). The film was irradiated with a field size of $3\times3$ cm$^2$ covering a dose range between 1 to 420 cGy. (Fig. 1a) A strict scanning protocol was employed to ensure the reproducibility of the measurements.

A 6 MV photon beam produced by a linear accelerator Novalis system (BrainLab, Germany) was used to irradiate the radiocromic films in the water phantom using circular collimators projecting fields at isocentre with diameters ranging from 4.0 to 20.0 mm. All films were placed in a water phantom using the SAD technique. The measurements were performed at 1.5 depth according to the accelerator operation manual. Monte Carlo radiation transport calculation were performed using BEAMnrc and DOSXYZ user codes. Linac geometry and materials were provided by the manufacturer.

Results are shown in Fig. 1b. There is no statistical significant difference between the radiation detector measurements for circular collimator from 6.0 to 20.0 mm ($p=0.834$). Nevertheless, the greater difference between measures with EBT film and diode happens to a circular field with 4.0 mm diameter.

Diode response becomes gradually steeper with decreasing field size. This is due to partial volume averaging. PFD3G has a pSi ship of 2.0 mm diameter, half the size of the 4.0 mm beam. On the other hand, PFD3G it is not water equivalent, perturbing the beam in a region of non-electronic equilibrium. The results shown in this work suggest that GafChromic EBT film is an adequate detector to determine output factors of small beams with an accuracy of 2.0%.
FIG. 1. (a) Calibration curve of the EBT film using field size of $3 \times 3$ cm$^2$ covering a dose range between 1 to 420 cGy; (b) Output Factors as obtained with EBT, PFD$^{3G}$ diode and Monte Carlo simulations. The average standard deviation is indicated for each measuring device (2%).

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Commissioning of IMRT for small intracranial lesions

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It is well demonstrated that beam-let size directly affects the quality of intensity modulated radiation therapy (IMRT) plans based on multileaf collimation (MLC) delivery [1]. Beam-lets of 1.0 or 2.0 mm improve dose conformity and organs at risk (OARs) sparing. Intracranial lesions treated with stereotactic radiosurgery or radiotherapy could be benefited by this kind of IMRT optimization due to which tumour typical sizes are less or equal than 3.0 cm. However, these beam-let sizes are close to the tolerance limits of MLC leaf accuracy (±1.0 mm) making its commissioning imperative. In the present work, the accuracy of MLC based IMRT dose distributions generated using small beam-lets was evaluated with GafChromic EBT (International Specialty Products, USA) film.

All the irradiation experiments and dose calculations were performed using a 6 MV photon beam of a Novalis linear accelerator (linac) and iPlan RT 3.0.2 treatment planning software (TPS). The linac has a micro-multileaf collimation (μMLC) system (\textit{μ}-mMLC, BrainLAB, Germany) with 26 tungsten leaves of variable width: 14, 6 and 6 pairs of 3.0, 4.5 and 5.5 mm width, respectively. Dose calculations and film irradiation were performed in an in-house cylindrical water phantom (Fig. 1a). Film management was carried out according to the recommendation of Task Group 55 [2] of the AAPM. Films were cut into 6×6 cm\textsuperscript{2} pieces and calibrated from 1 to 600 cGy at isocentre plain in a Lucite slab phantom at 1.5 cm water equivalent depth. Film digitizing was performed using a commercial flatbed scanner in transmission mode at 72 dpi (~0.35 mm) spatial resolution with post-processing options turned off. For film analysis, only the Red component was used.

Lesion and OARs were simulated using the treatment planning system (iPlan RT 3.0.2, BrainLAB, Germany). The lesion simulates a pituitary adenoma near to the optical apparatus (optical nerves, chiasm and optical tracts). The dimensions of the simulated lesion did not exceed 2.0 cm in any direction. The minimum distance between lesion and OARs was 2.5 mm. Three IMRT plans with seven fields using beam-let sizes of 1×3 mm\textsuperscript{2}, 3×3 mm\textsuperscript{2} and 6×6 mm\textsuperscript{2} were designed. Each plan has the same objectives and restrictions: 2.0 Gy at isocentre, 95% PTV coverage and a total dose ≤ 45 Gy in 25 fractions for optical apparatus. The generated dose distributions were exported for posterior analysis. Films were placed at the phantom middle plain for irradiation (Figs 1a and 1b). Each IMRT beam-let plan was irradiated five times using different films. Measurements and TPS dose calculations were compared using 2.0mm/2.0% gamma index criteria by means of DoseLab v. 4.11.

In terms of dose conformity and OARs sparing, 1×3 mm\textsuperscript{2} plan shows greater advantages compared to 3×3 mm\textsuperscript{2} and 5×6 mm\textsuperscript{2} plans (Table 1). The plans generated with 3×3 mm\textsuperscript{2} and 6×6 mm\textsuperscript{2} beam-lets shows better accuracy in calculated and delivered dose with ≥95% of points passing the gamma index criteria (Table 1). For 1×3 mm\textsuperscript{2} beam-let size there is a statistical significative difference (\(p < 0.05\)) with a mean of 90.1% passing the gamma index criteria. As it is expected, the 1×3 mm\textsuperscript{2} plan is less accurate due to the leaf positioning...
accuracy limits of the µMLC system. Special care must be taken if it is intended to use IMRT plans generated with such small beam-let size. An individual analysis of each case is encouraged to see if the errors and dose differences affects directly the OARs.

FIG 1. (a) In-house phantom picture. The phantom is a two piece Lucite cylindrical tubes (16 cm diameter) filled with liquid water. (b) Gafchromic EBT film post-irradiated showing the measured dose distribution.

TABLE 1. PLAN INFORMATION AND COMPARISON

<table>
<thead>
<tr>
<th>Beam-let size (mm²)</th>
<th>Mean gamma index (%)</th>
<th>Num. beam-lets</th>
<th>PTV coverage (%)</th>
<th>Conformity index&lt;sup&gt;a&lt;/sup&gt;</th>
<th>OAR sparing&lt;sup&gt;b&lt;/sup&gt; (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1×3</td>
<td>90.1</td>
<td>1296</td>
<td>99.8</td>
<td>1.39</td>
<td>100.0</td>
</tr>
<tr>
<td>3×3</td>
<td>96.4</td>
<td>480</td>
<td>96.4</td>
<td>1.47</td>
<td>78.0</td>
</tr>
<tr>
<td>6×6</td>
<td>95.5</td>
<td>274</td>
<td>93.7</td>
<td>1.59</td>
<td>64.6</td>
</tr>
</tbody>
</table>

<sup>a</sup> According to RTOG definition.

<sup>b</sup> Percentage of OAR volume do not receive tolerance dose.

REFERENCES


Barriers to implementation of new technology in radiation oncology: The New Zealand experience

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Aims

To address the barriers to implementation of modern clinical oncology and radiation therapy (RT) in New Zealand (NZ).

Background

NZ cancer centres have been slow to implement and utilize a number of techniques that are considered components of routine radiation oncology practice. These include PET scanning for cancer staging and RT planning, IMRT, 3-D and 4-D treatment planning, HDR brachytherapy and stereotactic treatments.

Methods

Knowledge of the sector and involvement in national committees provided insight into the current situation regarding RT in NZ.

Results

Barriers to implementation were multifactorial and included:

- **Modest health expenditure.** NZ has a modest GDP per capita (~US$22K) and health expenditure per capita (~US$2K) compared with many other developed countries. This limits the capacity for expenditure on all health areas, including oncology.

- **Disease pattern with characteristics of developed and developing countries.** The increasing proportion of indigenous (16%) and Pacific (7%) peoples with deprived socioeconomic circumstance in the NZ population requires high expenditure for infectious disease, the metabolic syndrome (diabetes, cardiovascular disease and obesity), and other determinants of health.

- **Devolved responsibility for health care.** Health care in NZ is largely devolved from the central government to 21 District Health Boards (DHBs) that manage health services for their local populations. Cancer may not be a priority, especially for the majority of DBHs (15) that do not have radiation oncology facilities.

- **Reduced consultation.** Clinicians have been in advisory roles and not in senior decision roles.

- **Fragile workforce.** The global market for health professionals presents a problem for maintenance of a stable workforce in radiation oncology. Adequacy of the workforce is
required for both routine treatment and for development and implementation of new technology. Recruitment and retention issues must be addressed.

- **Funding of national cancer plan.** The NZ Cancer Control Strategy, launched in 2003, struggles to achieve desired milestones, due to limited funding.

- **Rudimentary process for prioritization and horizon scanning.** Development of these key aspects is contemplated, with recognition of the difficulties, including methods of assessment, applicability to the NZ health system and funding implications.

- **Data deficiencies.** Lack of prospective data collection and outcome measures for oncology both regionally and nationally has reduced the ability to present arguments for improved facilities and targeting of poorly performing areas.

- **Legislative requirement to reduce health inequalities.** The NZ legislation is founded on recognition of the indigenous peoples of NZ (Maori). The national health plan identifies cancer as one of 13 health priorities. Thus, competition for available funding is intense.

**Discussion**

NZ is a small country (population: 4 million) with a GDP per capita that sits at the lower end of OECD countries. There are significant ethnic minorities which are over-represented in poor socio-economic status and carry disease burdens characteristic of developing countries.

Acknowledgement of the issues listed above is occurring and is being addressed slowly. The impact of these factors on provision of radiation oncology services and progress towards implementation of modern radiation oncology services will be discussed, using examples. It is hoped that the NZ experience may be of benefit to other countries.
Cost implication of usage of cobalt teletherapy machine versus linear accelerator in a developing country

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This is part of a prospective study in the (only) two tertiary health establishments A and B (in Northern Nigeria), possessing cobalt-60 machine and linear accelerator, respectively, and serving a population of about 70 million people.

**Aim**

(i) To highlight the usage of cobalt teletherapy and linear accelerator megavoltage machines in the treatment of common cancers in Northern Nigeria between 1 January 2004 and 31 December 2007 in both tertiary health establishments.

(ii) To compare cost benefit, downtime in the use of these armamentaria in low-resource institutions.

<table>
<thead>
<tr>
<th></th>
<th>Cobalt-60</th>
<th>LINAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients treated</td>
<td>1232</td>
<td>2832</td>
</tr>
<tr>
<td>M:F</td>
<td>1:2</td>
<td>1:2</td>
</tr>
<tr>
<td>Population: Adult</td>
<td>1196 (97.1%)</td>
<td>2778 (98.1%)</td>
</tr>
<tr>
<td></td>
<td>36 (2.9%)</td>
<td>54 (1.9%)</td>
</tr>
<tr>
<td>Tumours treated:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix</td>
<td>430 (34.9%)</td>
<td>651 (23%)</td>
</tr>
<tr>
<td>Breast</td>
<td>238 (19.3%)</td>
<td>850 (30%)</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>223 (18.1%)</td>
<td>107 (3.8%)</td>
</tr>
<tr>
<td>Soft tissue/bones</td>
<td>72 (5.8%)</td>
<td>408 (14.4%)</td>
</tr>
<tr>
<td>Prostate</td>
<td>23 (1.9%)</td>
<td>142 (5%)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>22 (1.8%)</td>
<td>93 (3.3%)</td>
</tr>
<tr>
<td>Urogenital/bladder</td>
<td>21 (1.7%)</td>
<td>34 (1.2%)</td>
</tr>
<tr>
<td>Brain</td>
<td>12 (1%)</td>
<td>62 (2.2%)</td>
</tr>
<tr>
<td>Skin</td>
<td>6 (0.5%)</td>
<td>85 (3%)</td>
</tr>
<tr>
<td>Advanced cases</td>
<td>77%</td>
<td>71%</td>
</tr>
<tr>
<td>Cost of treatment per fraction</td>
<td>$6.6</td>
<td>$8.3</td>
</tr>
<tr>
<td>Total number of machine</td>
<td>19</td>
<td>151</td>
</tr>
<tr>
<td>downtime (frequency)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital stay (outpatient)</td>
<td>3.5 weeks</td>
<td>18 weeks</td>
</tr>
</tbody>
</table>
Crude overall duration of treatment interruption was longer on linear aAccelerator than on cobalt teletherapy machine.\((P\) values to be discussed).\)

Cost implication of machine downturn (2004–2007) for cobalt machine was $793 while for Linac, $49,586.8 (2004–2006); 2007: upgrading of linear accelerator, $283,549 (@ $1=N121 NGR). Causes of downtime will be highlighted at the presentation.

**Conclusion**

Cobalt megavoltage teletherapy machine is more cost effective than linear accelerator for patients and Institutions in low resource regions. There is no much difference in cost of treatment between the two, downtime, however is more with linear accelerator. Advanced cases comprising the bulk of patient load can be treated with cobalt as well as linear accelerator.
Pretreatment verification of dose calculation and delivery by means of measurements with PLEXITOM® phantom

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The dependent check of MU calculations and dose delivery is an important part of QA system. The dose delivered during radiation therapy is usually monitored by means of in vivo dosimetry. The disadvantage of this method is its low sensitivity and specificity. Only errors larger than 5% may be detected. There is a relatively large number of false positive results. Therefore, better methods of dose delivery monitoring are sought for.

Purpose

To validate a pre-treatment method of dose calculation and dose deliver verification based on measurements with metaplex PTW phantom.

Material and methods

The PTW acrylic phantom PLEXITOM® was used for pre-treatment measurement of doses delivered to patients treated with external beams. Measurements were made with a 0.125 cm³ flexichamber and UNIDOS electrometer. The phantom allows for measurements at depths from 0.1 cm to 12.2 cm with 0.1 cm step. The size of the phantom was 19 cm × 11.5 cm. The position of the chamber in one plane is set remotely from the operating room. If required the depth of measurement was enlarged by placing on the top of the phantom additional water equivalent plates.

Since April 2008, for each patient treated in our hospital for each treatment field, the dose at radiological depth of dose prescription point was measured with the PTW phantom. The source-detector distance was always equal to source-prescription point distance. If a prescription point is layed out of central plane, the geometry of measurement was established by appropriate shift of treatment couch. Before starting the measurements the output factor in the reference conditions was measured (10 cm square field, 10 cm depth, and SDD 90 cm). All results made during this day were multiplied by the ratio of expected OF and actual measured output factor. The pressure and temperature were checked several times during measurements and, if needed, the appropriate correction factor was applied. To measure the prescribed dose for single field, the treatment field was loaded from R&V system (Lantis). All measurements were always made at zero gantry position.

For each patient: 1) the result for each single field was compared with the dose calculated with the treatment planning systems (XiO CMS), 2) the sum of doses measured for all fields was compared with the prescribed dose.

In this work results for patients treated in the H&N, thorax and pelvis region and for the Inverse Hockey Stick Technique for off-central points are presented. Our action level for
deviations was 3%. If a difference greater than 3% was noticed the case was analysed and possible causes were searched.

Results and discussion

The uncertainty of the dose measurement was estimated at 1.5% (two standard deviation).

TABLE 1. RESULTS OF PRE-TREATMENT MEASUREMENTS

<table>
<thead>
<tr>
<th></th>
<th>H&amp;N</th>
<th>Thorax</th>
<th>Pelvis</th>
<th>IHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>23</td>
<td>12</td>
<td>28</td>
<td>32</td>
</tr>
<tr>
<td>Number of fields</td>
<td>57</td>
<td>43</td>
<td>93</td>
<td>32</td>
</tr>
<tr>
<td>(measurements)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (%)</td>
<td>0.66</td>
<td>1.13</td>
<td>-0.41</td>
<td>-1.66</td>
</tr>
<tr>
<td>Sd of mean (%)</td>
<td>0.24</td>
<td>0.22</td>
<td>0.14</td>
<td>0.21</td>
</tr>
<tr>
<td>Number of deviation&gt;3%</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Deviation from expected dose range (%)</td>
<td>-3.6–6.4</td>
<td>-1.9–4</td>
<td>-2.6–3.6</td>
<td>-4.1–0.7</td>
</tr>
</tbody>
</table>

There was no case for which the action level was exceeded for the sum of doses measured for single fields. The results and analysis of results for which the action level was exceeded revealed that there was no systematic error made in preparation of irradiation.

In the H&N location for one field the difference was 3.6% but for the sum of doses delivered from all fields the deviation was only 0.5%. For four patients in the thorax region the deviations were greater than 3%. In two cases the physical depths differed from radiological depths substantially. From these patients only for one patient that the sum of doses delivered from all fields differed from expected dose of more than 2%. For the pelvis region only for two of 93 measurements that the results deviated by more than 3% from expected values. Also for IHS technique only for two fields the deviations were greater than 3%.

In each location the mean value calculated over results obtained for all patients differed significantly from zero. The largest mean difference was obtained for the IHS technique which probably reflects the fact that measurements were not performed in full scatter conditions. Full scatter conditions could not be obtained due to a very long photon field applied in the IHS technique. The average time spent on measurement for one field was about six minutes.

Conclusions

Pre-treatment measurement of doses at radiological depth can be regarded as a powerful tool for improving safety of treatment delivery. The PLEXITOM® phantom is a very useful tool for pre-treatment measurements. Some changes of phantom design would make it more convenient for dose delivery verification.
TLD audits in non-reference conditions in radiotherapy centres in Poland

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The Secondary Standard Dosimetry Laboratory (SSDL) of the Medical Physics Department of the Centre of Oncology in Warsaw became a member, in 1988, of the IAEA/WHO international network of SSDLs. The SSDL has been carrying out external postal TLD audits in teletherapy centres in Poland since 1991. Regular yearly audit runs have been carried out in reference conditions. Yearly audit runs have been extended to non-reference conditions since 2003. The results of selected runs are presented.

Materials and methods

A TLD system consists of Fimel PCL3 TLD automatic reader, Niewiadomski & Company LiF: Mg,Ti powder, IAEA holders, IAEA waterproof capsules, Unidos E with ion chamber type PTW 30013, water phantom: MT-150T (Med Tec) and Co-60 unit - Theratron 780 E (Theratronics).

Pilot studies were performed in order to test the methodology for dosimetry measurements and the documentation for the practical operation of the audit system in a variety of non-reference conditions: on-axis, off-axis (symmetric and asymmetric fields) and for fields formed by MLC.

After successful pilot runs in selected centres, a nationwide run of the on-axis, off-axis measurements for symmetric open and wedged fields and for fields formed by MLC has been performed. TLD runs for on axis measurements in non-reference conditions were performed in Co-60 beams, in X ray beams and in electron beams. The participants determined the doses with their treatment planning systems. The TLD capsules were irradiated at 10 cm and 5 cm (or 20 cm) depth for open fields (8×8 cm², 10×10 cm², 10×20 cm²) and wedged field (10×10 cm²) in Co-60 and X ray beams. In electron beams the TLD capsules were irradiated at a depth of d_max for 6×6 cm² and 10×10 cm² fields.

TLD runs for off-axis measurements in non-reference conditions were performed in X ray beams. The participants determined the doses with their treatment planning systems. The TLD capsules were irradiated at 10 cm depth for symmetric open and wedge fields (20×20 cm², +/- 5 cm off-axis).

TLD runs for fields formed by MLC were performed in X ray beams. The participants determined the doses with their treatment planning systems. The TLD capsules were irradiated at 10 cm depth for six MLC fields: reference, small, circular, inverted Y, irregular and irregular with wedge.

Results

The results of the audit in non-reference conditions for on-axis measurements are in the majority of cases within the 3.5% tolerance limit, which is usually used for reference conditions.

The nationwide audit, off-axis symmetric fields and the fields formed by MLC (Figs 1–3) show that it is possible to keep the dose determination within the 5% limit by implementing correct methodology and carefully carried out measurements and calculations of doses.
J. Rostkowska, et al.

**FIG. 1.** Non-reference conditions on-axis.

**FIG. 2.** Non-reference conditions, off-axis, symmetric field.

**FIG. 3.** Non-reference conditions, on-axis, fields formed by MLC.

**Conclusion**

The methodology and results of the audit permit to introduce and maintain the audit programme in non-reference conditions, for on-axis and off-axis measurements, at the national level.
Quality assurance programme implementation for computerized treatment planning systems


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In radiotherapy patient treatment procedures involve different steps: one is the dose calculation distribution performed by a treatment planning system (TPS). The quality control (QC) application procedures are essential to avoid the risk of overdosage of normal tissue and underdosage of tumour. In practice, TPS commissioning involves numerous tasks such as the generation of reliable set of dosimetric reference data and the effective methodology application. This work represents our experience in QA implementation programme for precise Plan (vs R2.15) TPS. The necessary tests to implement the QA programme were established and performed, in accordance with the IAEA technical reports series IAEA TRS-430 and the AAPM Task Group 53.

Data were obtained from five linear accelerators (4 GE Saturne and 1 Elekta Precise). Monitor unit accuracy calculations were performed under the following conditions: with a water phantom in the TPS clinical workspace. Reference points were entered, along the central axis on the central slice, for different depths. For each field size, energy and SSD (100 cm) were normalized separately to the reference depth using individual prescriptions and 100 cGy for each delivering.

In the TPS, profiles were computed in a phantom to a field 30×30 SSD (90 cm), and depth dose curves also obtained in the same phantom but for a field of 10×10 in size SSD (100). The obtained curves were compared with experimental data acquired under the same conditions.

Non-dosimetric verified the hardware, network systems integration, data transfer, and software parameters such as printer, digitizer, CT, block cutting system and the Mosaïq R&V system.

The results obtained are consistent with the specifications of the manufacturer. For dosimetric tests, the absolute dose was measured for simple geometries, such as square and rectangular field. Results were analysed by the use of confidence limit as proposed by Venselaar, et al. Criteria of acceptability had been applied also for the comparison between the values of MU calculated manually and MU generated by TPS.

Quality assurance programme tested accuracy and constancy through several hardware and software upgrades to our TPS. These tests are outlined for precise plan TPS but can be generalized to any TPS currently in use.
REFERENCES


Implementation of linac quality control for IMRT technique

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Despite the fact that “step and shoot” IMRT technique is similar to conformal therapy, additional procedure is needed, particularly linac testing during practical introduction. Dose control at small monitor units (MU) amount was included in the programme. Dose delivery linearity control was carried out up to 1 MU. Radiation field uniformity and symmetry were studied at first, second of dose delivery. Control was performed for minimal, average and maximal dose rate and for low and high X ray energies of Elekta Precise Dig. Dose delivery maximal error was 2\% for 18 MeV under 1 MU and dose rate 449 MU/min. Radiation field uniformity and symmetry for different MLC positions and MU were studied using 2-channel dosimeter with diamond detector. The short resolution time of the diamond detectors allowed to measure the dose profiles for very small exposure (up to 1MU). The field shape was not changed in range 1–500 MU.

The use of small fields during IMRT needs accuracy of leaf positioning up to submillimeter. Leave position symmetry was checked up by standard figured tests when single leaf deflections were observed.

Nine 2 cm adjacent strips segments IMRT plan was used for quantitative assessment of leaf position accuracy. These segments were also investigated in static mode with dose field analyser. The measurements have shown the shape of penumbra does not change with moving away the centre of field, the leaves position error does not exceed 1 mm at the central area and 1,5–2 mm at the edge of field. The last is important only for up to 2 cm size fields with screened central area. Such fields are used rarely in clinical practice. Leaves position adjustment can be performed with accuracy up to submillimeter for whole field size but this should be reasoned out because of the high labour output ratio.

Radiation transmission through the leaves and leakage between adjacent leaves do not exceed 3–4\% of dose from the large amount of segment delivered together.

One of the tasks of IMRT QC we observed was that TPS algorithm takes properly into account the transmission through the leaves. Analysing algorithm and comparing two TPS profiles under leaves only and both under leaves and diaphragm, we made sure dose calculation is done correctly.

Leaf transmission constituted 3\% that coincided with Linac characteristics. Another important problem was to assess radiation leakages between adjacent leaves. We used radiographic films to evaluate them. Visual estimate did not show substantial leakages. To perform quantitative assessment we needed a densitometer.
Testing of treatment planning system in aspect of transitioning from 3-D to IMRT

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IMRT planning supposes us to use as large amount of fields and field segments with complex shapes and segments with screened isocentre. This involves certain demands to the treatment planning system (TPS) dose calculation algorithm and brings us to a necessity of additional control. While introducing IMRT into practice we encountered some problems.

In our Center we have the linear accelerator Elekta Precise Digital with 1 cm at isocentre MLC, TPS Precise Plan with facility to create IMRT plans, and standard dosimetric equipment: water and solid water phantoms, Keithly dosimeter with ionization chamber and a set of radiographic films.

With the advent of the ability to create sophisticated dose distributions, requirements on accuracy of target and definition of critical structures increased. To combine the CT, MRI, PET, etc. data one needs special fusion programmes. Such programmes can be delivered by a TPS vendor or sold separately. In addition to the dose to point prescription dose-volume constrictions for target and critical structures appeared. They are described by so-called cost function. Dose in a point of beam intersection may differ from dose in point of prescription. For example, ICRU 2008 recommends prescribing dose to a volume rather them to a point. This mismachining may need special attitude, perhaps specific forms of delivered dose registration. We have created a set of tests to check parameters of TPS important for IMRT. Fields with narrow fragments are often used in IMRT planning. Collimator scattering contribution increases in this case. The difference between absolute dose calculations and measurements was no more than 4%.

The next problem concerned the TPS ability to calculate dose distribution from screened isocentre fields correctly. This is because dose distribution is usually calculated relative to isocentre dose, which in this case is negligibly small and consequently uncertain. We verified that TPS calculation agreed well with measurement. The difference was less than 1% in simple geometries and up to 5% in complex geometries with heterogeneity.

To apply an IMRT plan to a patient, one needs to verify it beforehand. As a patient-specific test we chose to perform absolute dose measurements in several critical points for single multisegment field and total dose measurements in water phantom in vertical and horizontal mode for all beams.

Good agreement of calculation and measurements led us to transit from 2-D to 3-D conformal radiotherapy and to begin introducing IMRT in our clinical practice. To use IMRT in clinical practice more extensively, we need to work out a patient-specific QA protocol. In spite of the absence of required equipment and software for this QA we consider the use of IMRT in clinical practice possible because we made a basic set of tests.
Practical aspects of radiochromic films implementation for clinical QA

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The aim of this work was the efficient QC routine development and implementation to widen the dosimetrical and clinical techniques range under conditions of the dosimetric equipment set limitations.

EBT and RTQA GafChromic® films types were used. The EPSON Perfection 3200 Photo flatbed scanner was used for film digitizing and primary optical density information readout.

All dosimetrical measurements were made at 6 MV photon field of SL75-5 (Phillips) linac. The clinical dosimeter Unidos (PTW) was used for the absolute dosimetrical calibration.

To estimate the measurement system properties as well as define the optimal dosimetric information readout parameters, the preliminary measurements series were conducted. The influence of time factor, external conditions and scanning parameters to the film’s properties behaviour were investigated.

The optimal scanning conditions were defined (150 dpi, 24 bit). The red channel was chosen for relevant optical density readout. The influence of multiple scanning was found and estimated. The optical density change was up to 1.8% after 25 serial scanning and up to 2.8% after 50 ones.

The significant optical density change after irradiation was discovered during the observation period. The uniform increase of the optical density amounted to 3% regarding the initial calibration, meaning in two months after the exposition.

The insignificant inter-serial dependence between five investigated packs of films was found. The noticeable sensitivity to visible light was observed for RTQA GafChromic® films.

After the measurement system has been developed and characterized, the calibration curves for both film types were plotted using the absolute measurements data received at the reference conditions. Field sizes, needed number of points for calibration curves building were optimized. The dosimetrical data readout technique based on calibration curve was developed. The technique validation at non-reference conditions was made.

Since EBT GafChromic® films were initially planned to be used as the tool for the absolute dosimetry, additional tests were conducted to check the fringe effects influence and to find any limitations of the minimal film sizes. Because not noticeable effects were found, the film square of 3×3cm² size was chosen as optimal for the reliable dosimetrical measurements and convenient usage and handling.
The developed dosimetric technique based on EBT GafChromic® films usage was implemented for measurement of the surface dose, the doses at small fields and at the build-up region as well as for in vivo dosimetry purposes.

The developed routine based on the RTQA GafChromic® films usage allowed improvement of the machine QC as well as gave the new opportunities for the patient QC.

The film scanning and data processing time were estimated. The scanning time with the chosen scanning parameters averaged two minutes for any type of films. The data processing time for EBT GafChromic® film is about two minutes for reliable absolute dose measurement. The RTQA GafChromic® film processing time (for precise field alignment for example) averages about 15 minutes. The 15 points calibration curve plotted process needed to be repeated for each new film pack takes 2.5 man-hours independently of the film model. The irradiation process itself at linac takes about 1 hour and 20 minutes from this time and can be easily included in the monthly QC schedule.

The techniques based on the radiochromic films like EBT GafChromic® and RTQA GafChromic® are economically efficient, allows expansion of significant dosimetrical and clinical techniques range and QA improvement, and can be quite easily introduced clinically.
Transition of 2-D to 3-D craniospinal irradiation and resulting quality improvement: An IAEA/RCA RAS/6/048 project of Singapore

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IAEA/Regional Cooperative Agreement (RCA) project RAS/6/048 is a project to apply 3-D high precision radiotherapy for predominant cancers in the Asia-Pacific RCA member countries. Individual RCA member countries identify their specific needs and work towards implementing 3-D conformal planning projects.

Singapore has sophisticated 3-D conformal planning expertise but a few cancer indications are still planned conventionally using historical 2-D techniques. Up till January 2007 craniospinal irradiation (CSI) in National Cancer Center Singapore (NCCS) has been done in two phases and planned using partial 2-D 3-D radiotherapy treatment techniques. In the old standard CSI method, patients are conventionally simulated (2-D) for phase I treatment to brain and spine, and halfway through radiotherapy treatment patients will undergo CT simulation for 3-D planning only for phase II treatment of the brain alone. There are several disadvantages to this old standard CSI technique and a project to develop a new optimized fully 3-D process of CSI technique has been undertaken.

We investigated a process of developing, implementing and evaluating an optimized fully 3-D radiotherapy treatment planning for CSI in NCCS. Patients requiring CSI are CT scanned before the start of radiotherapy treatment for 3-D treatment planning of both phases I and II instead of midway through radiotherapy treatment by the old standard technique. Target organ of brain and spine as well as critical normal organ like eyes, optic nerves, lens, optic chiasm, pituitary, brainstem, middle ears, spinal cord, lungs and heart are outlined on Eclipse radiotherapy planning computer. Radiotherapy fields are optimized by using virtual simulation, a field-in-field spinal boost, dynamic multileaf collimation (MLC) wedge compensation and matching of spine and brain fields during both phases of treatment. The dose plan is verified by established quality assurance protocols by our physicists before treatment starts and during radiotherapy with weekly check films. Radiotherapy treatment plans between both methods were then compared and evaluated by several criteria [1].

There is better dose coverage of spine with the optimized 3-D planning using field in field boost compared with the single unoptimized spinal field in the old CSI technique. The prescribed 23.4 Gy isodose conforms to the spine curvature in the 3-D method (Fig. 1).

Accurate dose calculations with DVHs are available for both spine and brain when CT scanning is done from phase I. Using the old CSI method, only DVH for the phase II brain is available. There is a decrease in middle ear doses when oblique fields are applied using virtual simulation visualization during phase II of 3-D planning. In the old CSI method, the fields will be parallel, opposed fields with consequent higher dose delivered to bilateral ears (Fig. 2).

An analysis of workflow was done. In the old partial 2-D 3-D CSI method, the patient will require three visits for radiotherapy planning: conventional simulation of phase I of spine and brain, and then CT sim and plan verification of phase II to brain alone. In the new fully 3-D CSI process, only two radiotherapy planning visits are required for CT sim and plan verification. The CT data are used for radiotherapy planning of both phases.
It is cost effective and sustainable on a long term basis to the patient and department because there is no increase in procedure treatment costs to the patient and even a decrease in the number of patient visits by using the new 3-D planning from phase I compared to the old partial 2-D 3-D CSI techniques. There is a more accurate dose estimation and, consequently, an improved quality of follow-up can be done. Virtual simulation of treatment fields enables more precise positioning and matching of various fields, reducing error and uncertainty. The new optimized fully 3-D radiotherapy treatment planning for CSI enabled more accurate dose coverage, more precise dose estimation, and better internal ear dose sparing.

FIG. 1. Sagittal view showing comparing incomplete coverage of spine (green contour) by 23.4 Gy isodose (red) using a single field by old standard CSI method (left) and complete coverage new fully 3-D optimized CSI method (right).

FIG. 2. Lateral opposing fields of old CSI method will irradiate bilateral middle ears (brown and light blue) (left) but is spared using optimized 3-D technique involving posterior oblique fields.

REFERENCE

Tissue equivalent absorption in combined wax and rubber layers using 1.25 MeV gamma ray

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During radiotherapy treatment to cancer patients, three dimensional compensators are often used to provide corrections for missing tissue and/or tissue inhomogeneities encountered by photon beam. To design and construct compensators, it is necessary to evaluate how the beam quality changes with different materials placed in the path of the photon beam [1–3].

Different locally available materials were placed in the path of 1.25 MeV. Gamma radiation and absorption were measured along the central axis at 80 cm SSD using a Farmer type thimble ionization chamber of 1.6 cm outer diameter. A standard field size of 10×10 cm\textsuperscript{2} was used. Water depth of 10 cm was chosen to represent a normal tumour depth to cover a variety of deeply seated tumour that may require tissue compensators. Among the materials used, it was found that the absorption of wax (0.93gcm\textsuperscript{-2}) and rubber (1.15gcm\textsuperscript{-2}) would be above and below the absorption curve of distilled water. Therefore, we concluded that a combination of these materials could ideally be used as tissue equivalent materials.

Different combination of wax and rubber plates were kept together to act as a single plate. The graph of percentage transmission verses thickness of the combined material was plotted and compared with that of the distilled water. The following combinations of rubber-wax were tested: Rubber – 1.0 cm and Wax – 0.5 cm (R1.0 W0.5); R1.0 W1.0; R1.0 W1.5; R1.1 W1.5. The transmission curve for different combinations were found to be close to the absorption curve of distilled water. However the combination R1.0 W0.5 was found to exactly overlap the curve of distilled water. Hence it could be inferred that this particular rubber-wax combination will function as tissue equivalent material. Therefore this combination could be used to construct missing tissue compensators.

\hspace{1cm}

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{percentage_transmission.png}
\caption{Percentage of transmission of wax (1.5 cm), rubber (1 cm) and distilled water.}
\end{figure}
FIG. 2. Percentage of transmission of combined material of wax and rubber.

REFERENCES


Doses to patients from photoneutrons emitted in a medical linear accelerator

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The goal of the present study was to estimate the equivalent doses from photoneutrons produced in a medical linear accelerators. Measurements of such doses from neutrons are difficult to perform with the standard nuclear instrumentation, due to the high fluence rate of photons with respect to neutrons and the pulsed radiation field. Therefore a computer code allowing a suitable simulation of the entire process of photoneutron generation and transport across the accelerator head represents a useful tool to evaluate the undesired neutron leakage dose at the patient. The Monte Carlo (MC) code Geant4 has been used to achieve the goal of this study.

The ambient dose-equivalent from photoneutron contamination arising from a Clinac 2100C was calculated using Geant4 code, as a function of the radiation field size. The number of initial histories was 3000 million for the $40 \times 40 \text{ cm}^2$, 2500 million for the $10 \times 10 \text{ cm}^2$ and 1000 million for the $1 \times 1 \text{ cm}^2$ field size. The ambient dose-equivalent was calculated using the fluence to ambient dose-equivalent conversion factors presented by Ferrari and Pelliccioni 1998 [1].

Neutron history files were generated, from our geometry detector, which contained the parameters of number, position, direction, energy and track length for those neutrons generated from photon interactions. The neutron histories from the point of interest were analysed by OriginPro ver7.5 SR0 software.

The results of neutron yields in the components of the head (target, flattening filter, primary collimator and jaws) with $1 \times 1 \text{ cm}^2$ field size are shown in Fig. 1. The results of neutron yields are in good agreement with previously published data [2, 3]. It is clear that the maximum neutron yield was found in the jaws, and the increment of neutron number was proportional with energy.

The fluence was estimated at 1 m from the target as the neutron yield divided by area of the detector. The ambient dose equivalence using $1 \times 1 \text{ cm}^2$ field size, at isocentre and X ray modes of 20, 18, 15 and 10 MV, was found to be 1.79, 1.60, 0.62, and 0.02 mSv.Gy$^{-1}$.
respectively. The mean energies of neutrons were 0.48, 0.44, 0.40, and 0.16 MeV at X ray modes 20, 18, 15, and 10 MV, respectively.

Fig. 2 shows the ambient dose equivalent and fluence of neutrons per unit of area per Gy against the radiation field size at the isocentre plane. It is evident that as the size of the radiation beam increases, so does the photoneutron fluence, with the difference between the smallest and the largest field size being in the order of 23.5±1.5%. Since the large amount of neutron yield was found in the jaws, this suggests that the photoneutron production of other linac head components above the movable collimators share the dose increment. Thus, as the field size increases, more and more photoneutrons are able to reach the isocentre.

FIG. 1. Geant4-calculated neutron yields in the Varian Clinac 2100C head (1 x 1 cm$^2$ field size).

FIG. 2. (a) Ambient dose equivalent (mSv/Gy) and (b) the neutron fluence $\Phi$ (cm$^{-2}$.Gy$^{-1}$) against the radiation field size at the isocentre plane calculated with the Geant4 code.
REFERENCES


A method for testing the Linac jaw position of adjacent fields using the EPID

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Purpose

Standard treatment planning techniques sometimes require a field junction across the planning target volume to achieve an optimal dose distribution of the target and organs at risk. To avoid underdosing, the accuracy of the jaw position during beam delivery is of great importance. A regular test of the jaw position of adjacent fields should be included in the Linac QA. In our clinic the tolerance is ±1mm, and we generally use an overlap of 1 mm when planning adjacent fields, with respect to uncertainties in the jaw positions. The test is traditionally performed with film and analysed by visual inspection. The purpose of this work is to develop an easy-to-use method of testing the Linac jaw position using the EPID.

Method

Images of up to four adjacent fields are consecutively taken with the EPID, by changing the jaw positions and/or rotating the collimator. Thereby, each quadrant of the EPID is irradiated with an asymmetric field (no overlap). In-house software for analysing the Dicom images is developed using MATLAB. The images are merged into one image using the software. One (any) field is then moved vertically or horizontally relative to the other fields using the arrow keys, until a line profile across the junction is flat. This is considered the perfect junction. The amount of displacement is displayed. The validity of the method is confirmed by simultaneously irradiating the EPID and Gafchromic film, with the film positioned at the isocentre level. The film is visually analysed.

Results

The comparison shows that the EPID and the Gafchromic film give comparable results when measuring the overlap/gap at field junctions. The method for analysing the EPID images is objective and gives a numerical value of the discrepancy. Analysing four field junctions (four EPID images) requires a total time of about two minutes. The time required at the treatment machine is approximately the same for the EPID as for film alone.

Conclusions

The EPID is a good substitute for film for testing the Linac jaw position of adjacent fields. The proposed method is fast, easy to use, and gives an objective and reliable value, which makes it suitable for regular QA.
FIG. 2. User interface of the MATLAB tool.
Superficial dose distribution in breast for tangential photon beams, clinical examples

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Purpose/objective

The accuracy of the dose prediction in the superficial (0–2 cm) region of the breast is of great importance for evaluation of late skin toxicity and estimation of target coverage. Tangential beams and curved surface pose a challenge for dose calculation algorithms due to lack of electron equilibrium and incomplete scatter conditions in the region close to the breast/air surface. Measurements and calculations have been performed in a previous work in the case of cylindrical solid water phantom irradiated by one or by two opposed tangential beams. The objective of this study is to investigate the superficial dose distribution in breasts by using patient CT data.

Material and methods

Tangential 6 MV open beams of varying size and angle of incidence are applied to a number of patient geometries. Treatment planning calculations are performed for a Varian 600C accelerator using Eclipse 8.1 pencil beam and AAA algorithms. Monte Carlo calculations are carried out by implementing a BEAMnrc model of the accelerator head. The MC calculations have been verified against TLD and film measurements in the case of a cylindrical solid water phantom [1]. The code ctcreate from the Monte Carlo package has been used to create a phantom from patient CT scans with voxels not larger than 2.5×2.5×5 mm. Eclipse and Monte Carlo 2-D dose distributions are compared in Mathworks as well as in RIT113 software.

Results

According to the MC calculations, the lateral superficial part of the breast receives full dose beyond 2 mm without added bolus material. The build-up region is larger where the beams enter. The quantitative result depends on the form of the breast. AAA calculations are in good agreement with MC data beyond the first 3–5 mm. Fig. 1 shows isodose curves for one tangential field obtained by MC, and the corresponding gamma analysis of AAA results. There is a tendency for AAA to underestimate the dose at the lateral regions. Larger deviations are observed for the pencil beam algorithm.

Conclusions

The lateral superficial part of the breast receives full dose beyond 2 mm without added bolus material. The behaviour of the calculation algorithms as found in the phantom case [1] can not always be directly translated into the case of a real patient geometry. Quantitative agreement between MC and AAA calculations depends on the breast shape. AAA has superior accuracy to pencil beam.
FIG. 1. Isodose curves for a single open tangential field obtained by MC (left), and gamma analysis of AAA with MC data as a reference (right), dose difference 3%, DTA 3 mm. The colour display indicates the gamma value.

REFERENCE

Use of an amorphous silicon electronic portal imaging device for fast and accurate MLC leaf position verification

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Typically, the success of an intensity modulated radiation therapy (IMRT) treatment relies on the positioning accuracy of the multileaf collimator (MLC) leaves for both step-and-shoot and sliding window techniques.

At Siriraj Hospital, MLC leaf position verification was initially done with film when performing a visual spot-check for leaf alignment and ionization chamber method. If to quantify leaf position deviations of 0.5 mm, the results of film measurements are difficult to interpret and quantify. It should be scanned and analysed using a film dosimetry programme, which is time consuming. The ionization chamber method can measure the reproducibility of a leaf gap accurately, but offers the possibility to perform this check for one leaf pair and one point at a time only. To overcome the limitations of these methods, a fast and accurate method for weekly leaf verification has been developed to determine the accuracy of MLC positioning accuracy, using the amorphous silicon based electronic portal imaging device (EPID).

All measurements were performed on a Varian Clinac 23EX linac equipped with a Millennium MLC-120 multileaf collimator (Varian Medical System, Palo Alto, CA). A Portal Vision aS500 EPID (Varian Medical System, Palo Alto, CA) was used to acquire portal images in this study. We irradiated a Kodak X-Omat V film and the EPID with a source to detector distance (SDD) of 100 and 140 cm. respectively, using the modified Memorial-Sloan-Kettering strip test field producing a pattern of five 1 mm bands sliding gap and 2 cm apart. All EPID images were acquired at an SDD of 140 cm using a 6 MV photon beam running at a dose rate of 300 MU min⁻¹ for gantry angle of 0°, 90° and 270°.

We also simulated mechanical problems that may occur during a DMLC treatment at certain positions by introducing known leaf position errors of 0.2, 0.5 and 1 mm at central axis and near the field edge. Each simulated error was introduced in one leaf pair only. Then we tested whether this can be resolved visually and digitally using film with buildup 2 mm. and EPID and compared the performance of these two methods. In this study, we investigated the practicality of using an EPID as an alternative to film for routine DMLC QA in our institution.

The results showed good agreement with film, while giving easier visual inspection than the film without being scanned. It can be concluded that an amorphous silicon based electronic portal image device is a good alternative to radiographic film for the routine MLC QA and also to overcome the problem of film processors that are being removed from our institution’s service.

We will implement this EPID QA tool to be used as a quick morning check of the calibration and the performance of the MLC as well as to check MLC position accuracy on a weekly basis. By using the EPID, leaf position verification can easily be performed for different
gantry angles for both the short and long term reproducibility in leaf position. The short term reproducibility defines possible variations in leaf positions during a given treatment session by assessing from repeated deliveries of the DMLC field and EPID image acquisition with interval times less than a minute. While the long term reproducibility describes the variations in the leaf position over a period of several months.
Applications of statistical process control to radiotherapy quality control

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The control chart was introduced in radiotherapy quality assurance (QA) as a modern QA tool to separate the systematic error from random error [1]. In this study, control charts were applied to QA checks of output and flatness/symmetry.

The output and flatness/symmetry verification of 6 and 10 MV photon beams delivered by a Varian Clinac 21EX linear accelerator were undertaken with RBA-3 dose constancy check. It consists of five parallel plate chambers, one on the central axis and the other four on the radial and lateral planes at 8 cm from the centre. The data were collected during January to September, 2008. Fifty monitor units were delivered with 20×20 cm\(^2\) field size at 100 cm SSD. A control chart consists of three basic components: a central line as mean value, two horizontal lines of the upper control limit (UCL) and lower control limit (LCL), and the data points. Output constancy check is the individual data, so the individual (X)/moving range (mR) charts were selected. The average and limits for output are calculated using [2].

\[ UCL_x = \bar{X} + 3 \frac{\bar{mR}}{d_2}, \quad CL_x = \bar{X}, \quad LCL_x = \bar{X} - 3 \frac{\bar{mR}}{d_2} \]  

(1)

The moving range and their limits for output are calculated from:

\[ UCL_{mR} = \bar{mR}(1 + 3 \frac{d_3}{d_2}), \quad CL_{mR} = \bar{mR}, \quad UCL_{mR} = \bar{mR}(1 - 3 \frac{d_3}{d_2}) \]  

(2)

The mR is the absolute value of the delta between two consecutive data (\(mR_i = |X_i - X_{i-1}|\)). The constants \(d_2\) and \(d_3\) depend on \(n\) value, where \(n\) is the number of values in the subgroup. In this case, \(n=2\), so \(d_2\) is 1.128 and \(d_3\) is 0.8525 [1].

For the flatness/symmetry check, there are subgroups of size \(n=4\), so we selected the average (X-bar)/range(R) charts. The average and limits for flatness/symmetry are calculated from:

\[ UCL_X = \bar{X} + 3 \frac{\bar{R}}{d_2 \sqrt{n}}, \quad CL_X = \bar{X}, \quad UCL_X = \bar{X} - 3 \frac{\bar{R}}{d_2 \sqrt{n}} \]  

(3)

The range and their limits for flatness/symmetry are calculated from (2) but change \(\bar{mR}\) to \(\bar{R}\), where \(R\) is the range of the value in each group (\(R_i = X_{\text{max}} - X_{\text{min}}\)). The constants \(d_2\) and \(d_3\) depend on subgroup size \(n\), so \(d_2\) is 2.059 and \(d_3\) is 0.8798 [1]. If the calculated range is negative value, we use zero because range is not less than zero.
The results of the control charts for both output and symmetry/flatness for 6 and 10 MV are shown in Fig. 1.

**FIG. 1.** Results of A 6 MV, B 10 MV for (a) output average chart, (b) output range chart, (c) flatness/symmetry average chart, and (d) flatness/symmetry range chart.
The first ten points in the open circle of each chart were used to calculate the control chart limit. For the interpretation of the results, if there are any data points outside the limit, it meant that the point contains a systematic error. All of the points in the output charts in Fig. 1 A.(a,b) and B.(a,b) were under control but there were some points located outside the limit for flatness/symmetry, Fig. 1 A.(c,d) and B.(c). It was clear to say that systematic error had occurred. It might be due to non-leveling of detectors or inaccurate optical distance indicator reading. When the correct conditions were set, all of the data were in action threshold again.

Using control charts enabled us to identify systematic error and correction that can be made in routine QA check.

REFERENCES

Comparison of dose distributions of Novalis Brainlab treatment planning system, Monte Carlo (BEAMnrc and DOSRZnrc) and in vivo dosimetric measurement methods

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This presentation discusses the comparison of dose distributions of Novalis Brainlab treatment planning system, Monte Carlo (BEAMnrc and DOSRZnrc ) and in vivo dosimetric measurement methods. For a prostate located tumour, dose volume histograms and dose distributions are calculated with Novalis TPS and Monte Carlo. Both of these computerized values are compared with in vivo dosimetric measurement methods for a rando phantom. The degree of matching of the calculated values (Monte Carlo and Novalis TPS), whether TPS results are calculated precisely or not for nonhomogen volumes, and commercial TPS’s divergence from sensitivity are discussed in detail.

The aim of this study is to compare the dose distribution results of prostate located tumours obtained from iPlan(TPS of Novalis Brainlab) treatment planning system with the results of BEAMnrc, DOSRZnrc calculations and film, thermoluminance dosimetry (TLD) measurements and ensuring the quality control of the treatment planning system.

The film and TLD dosimeters used in the measurement were calibrated at the beginning of the study. The linear accelerator part of the Novalis Brainlab was modelled and simulated in BEAMnrc Monte Carlo programme and its results (i.e. flatness, percent depth dose distributions) were checked by using the water phantom measurements. Then, the Alderson rando phantom was digitally imaged by using a computerized tomography and the images were transferred to both the TPS(iPlan) and the DOSRZnrc Monte Carlo programme. The treatment plans were computed at the pelvis region of rando phantom for defined target volume with intensity modulated radiotherapy (IMRT) technique. The measurement points for target and critical organ doses were defined at the TPS and DOSRZnrc. The doses for defined points were measured in the rando phantom by using TLDs and films at the treatment machine (Novalis Brainlab).

All treatment fields (IMRT technique was used) of rando phantom were controlled by taking images from electronic portal imaging device before each dosimetric measurement.
Evaluation of radiation dose for stereotactic radiosurgery systems in Korea

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Since stereotactic radiosurgery (SRS) delivers high radiation doses to localized lesions, it requires quality control (QC) for accurate dosimetry. However there is some discrepancy of dose verification of each institution, standardization of QA equipment and dosimetry is needed to achieve accurate dose delivery. In this study, we designed a standard dosimetry model and evaluated an accuracy of stereotactic radiosurgery equipment, CyberKnife and Gammaknife within Korea.

To design a standard dosimetry model, we performed status survey for CyberKnife and GammaKnife machines installed in medical institutions at first. Machine installations, treatments and equipment for dosimetry were surveyed. And we determined standard condition for the evaluation of radiation dose precision of each SRS institution [1]. To do intercomparison of dose accuracy of all CyberKnife and GammaKnife machines under operation in Korea, as of December 2007, we visited each institution and then directly measured radiation dose based on the standard condition of dose determination.

For CyberKnife, as a standard dosimeter, we used 0.6 cc ionization chamber and electrometer by PTW. As a standard phantom, PTW water phantom made of acrylic wall have been used in every three sites and they have referred to N\textsubscript{k} based on IAEA TRS-277 and TRS-398 protocol as a standard radiation dosimetry protocol [2, 3].

For GammaKnife, 0.125cc ionization chamber and electrometer by PTW was used for standard dosimeter. In every three sites operating CyberKnife, the results showed a good agreement with an error of ±1.0%. According to the field check result of eleven sites operating GammaKnife, there is an agreement with an error ±2.0% in six sites. However, between two sites, there is a considerably big discrepancy with an error of ±3.0%.

According to the site evaluation result of the radiation dose from stereotactic radiosurgery equipment, it is considered that dose measurement standardization is satisfactory enough to be accepted because the protocols of AAPM and IAEA are in common use in most medical institutions in Korea. Especially because CyberKnife is relatively newly developed, the manufacturer, Accuray company, had distributed a self-made QC/QA programme based on recommendations relating the dosimetry protocols of AAPM or ICRU. These programmes have been considered very reliable by many users. However, there is about ±3% relative error in some institutions. It is considered that this error is caused by the use of unverified thermometer or barometer, the absence of systematic dose evaluation protocol by a sophisticated medical physicist or proper detector for small field measurement besides the recommended dosimeter by manufactures. In the future, the enforcement of periodic QA
project on the dose in SRS is regarded to be necessary at a level of society and government for the purpose of improving precision and guaranteeing reliability in SRS equipment dose evaluation by output measurement and inter-comparison with SRS institutions.

TABLE 1. INTERCOMPARISON RESULTS OF OUTPUT DOSE ACCURACY OF THREE CYBERKNIFE INSTITUTIONS IN KOREA

<table>
<thead>
<tr>
<th>Institute</th>
<th>Measurement</th>
<th>Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>X Hospital</td>
<td>1.002E-02 Gy/M.U</td>
<td>+0.2%</td>
</tr>
<tr>
<td>Y Hospital</td>
<td>1.002E-02 Gy/M.U</td>
<td>-0.3%</td>
</tr>
<tr>
<td>Z Hospital</td>
<td>1.009E-02 Gy/M.U</td>
<td>+0.9%</td>
</tr>
</tbody>
</table>

TABLE 2. INTERCOMPARISON RESULTS OF OUTPUT DOSE ACCURACY OF ELEVEN GAMMAKNIFE INSTITUTIONS IN KOREA

<table>
<thead>
<tr>
<th>Institute</th>
<th>Nk</th>
<th>ND,W</th>
<th>Setting</th>
<th>Error(Nk)</th>
<th>Error(ND,W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Hospital</td>
<td>1.926</td>
<td>1.927</td>
<td>1.922</td>
<td>-0.2%</td>
<td></td>
</tr>
<tr>
<td>B Hospital</td>
<td>3.147</td>
<td>3.148</td>
<td>3.166</td>
<td>+0.60%</td>
<td>+0.57%</td>
</tr>
<tr>
<td>C Hospital</td>
<td>3.183</td>
<td>3.184</td>
<td>3.10</td>
<td>-2.6%</td>
<td>-2.63%</td>
</tr>
<tr>
<td>D Hospital</td>
<td>2.463</td>
<td>2.464</td>
<td>2.525</td>
<td>+2.51%</td>
<td>+2.47%</td>
</tr>
<tr>
<td>E Hospital</td>
<td>2.378</td>
<td>2.379</td>
<td>2.376</td>
<td>-0.08%</td>
<td>-0.12%</td>
</tr>
<tr>
<td>F Hospital</td>
<td>2.429</td>
<td>2.430</td>
<td>2.451</td>
<td>+0.9%</td>
<td>+0.86%</td>
</tr>
<tr>
<td>G Hospital</td>
<td>2.374</td>
<td>2.375</td>
<td>2.46</td>
<td>+3.62%</td>
<td>+3.57%</td>
</tr>
<tr>
<td>H Hospital</td>
<td>2.363</td>
<td>2.366</td>
<td>2.42</td>
<td>+2.42%</td>
<td>+2.28%</td>
</tr>
<tr>
<td>I Hospital</td>
<td>1.874</td>
<td>1.877</td>
<td>1.94</td>
<td>+3.52%</td>
<td>+3.35%</td>
</tr>
</tbody>
</table>

REFERENCES


Radionuclide study of sentinel lymph nodes in patients with breast cancer

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Background

The problem of dissemination of breast cancer into lymph nodes is essential not only for survival but also for choice of tactics and volume of treatment. According to the conception of sentinel lymph nodes (SLN), their investigation is performed with the aim of identification of first draining nodes correspondingly to nodes of primary tumour. Specific feature of SLN is enlargement of first lymph node and visualization of afferent lymph vessel.

Aim

The aim was to study the status of sentinel lymph nodes during their intraoperation detection using manual gamma Europrobe (Canberra Packard).

Materials and methods

Twenty breast cancer patients were examined using lymphoscintigraphy in combination with intraoperation detection of SLN. $^{99m}$Tc$^m$-nanocole infused peritumouraly and intracutaneously (10 MBk/kg body weight) in 0.2–0.3 mL of water was used for the investigation.

The next step of the study was lymphoscintigraphy using OFECT “E CAM” (Siemens). Early and late images (20 minutes and 2 hours after $^{99m}$Tc$^m$-nanocole administration, respectively) were obtained. And 24 hours later, SLN intraoperation detection was performed by manual gamma-probe.

Results

In accordance with the obtained data it was revealed that in 17 of 20 patients lymph nodes of axillar pool on the side of the lesion were visualized. In two patients lymph nodes were detected on contralateral side. In 14 patients with visualized lymph nodes histological examination confirmed SLN. Eleven (11) patients appeared to be affected by metastases; in the remains, no malignancies.

Conclusion

Examination of SLN using manual gamma-probe can be used for the estimation of metastases spread pathways and of the rate of malignant injury of lymph nodes in breast cancer patients. The usage of lymphoscintigraphy in combination with gamma detection and following biopsy of SLN ia perspective direction in the development of organ-saving surgical interventions in breast cancer.
Analysis of dose uniformity in total body irradiation for paediatric patients

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Total body irradiation (TBI) is a technique widely applied in paediatric patients. Dose gradient has to be known in order to decide the use of bolus and/or compensators for getting as much dose uniformity as possible. Dosimetry of this particular technique has to take into account different aspects like a great source-surface distance, a field much greater than patient dimensions, diameter variation along the patient, dose rate variation, in-patient inhomogeneities. In this paper we analyse the measurements carried out at the Children’s Hospital “Professor Dr. Juan P. Garrahan”, Buenos Aires where a new linear accelerator with an MLC has been installed in 2006.

All measurements were carried out with a 6 MV Varian linear accelerator, CLINAC 23 EX-S with the gantry at 90° for lateral irradiation with two opposed fields of 124 cm×24 cm, and a collimator angle of 45° for having the field diagonal as the length of the field. An automatic water phantom together with plastic ones (polystyrene and water equivalent) were positioned over the special treatment table for TBI at a distance of 310 cm from the source. Cylindrical ionization Farmer-type of 0.6 cm³ and 0.2 cm³, as well as plate-parallel chambers were used in conjunction with Farmer and Ionex electrometers. Depth doses were measured in water with and without interposing an acrylic plate positioned at two different distances from the surface in order to visualize changes in build-up near surface. As the results showed a high dose at surface when using acrylic plates, it was decided not to use any plate. Diagonal profiles for the whole field were also measured in order to get flatness value at long distances. Aluminium was the material chosen for compensating variable patient thickness and the attenuation coefficient measured for different field sizes. Entrance and exit doses had been compared with doses at the middle of the phantom for different diameters.

For a very wide field, at a distance which is three times the nominal distance for this linac, the maximum dose shifts from 1.5 cm to 1 cm depth and, in agreement with bibliography, the inverse square law does not accomplish for this technique. Considering the skin dose obtained with this shifting, it was decided not to add any acrylic plate to avoid overdose to skin patient. Attenuation coefficient for Al and 6 MV varied slightly with field size for broad beams, and a unique value of 0.11 cm⁻¹ was adopted for aluminium. In order to be able to determine, after treatment, the dose at the middle plane of the patient, a factor K was calculated from entrance and exit dose measurements.

The Radiotherapy Department of the Paediatric Hospital of Buenos Aires, after having done approximately 50 TBIs since 1994 (most of them with a ⁶⁰Co unit and some patients with an 10 MV linac), began in 2008 with TBI for children with the 6 MV linac considering that a dose uniformity within ±10% can be achieved with appropriate compensators and flattening filter.
M.L. Mairal, et al.

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First steps in 3-D radiotherapy in Bolivia with cobalt-60

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Since 1970, the Radiotherapy Department of Hospital Obrero Nº1 in La Paz, has been using a standard 2-D radiotherapy technique for our patients.

In 2006, and through an IAEA donation, the cobalt-60 source has been replaced and the department has acquired a 3-D treatment planning system (CMS). In 1997, a general consensus document was made by the DYNARAD/BIOMED group. Following these guidelines we have initiated 3-D conformal radiotherapy in our centre [1].

From April 2008 we started to use the shaping of the radiation beam initially for the treatment of palliative patients while our protocol for curative 3-D was being drafted.

Our main objective has been to start shaping the radiation beam with the available materials in our department, to reduce the side effects of treatment without affecting the clinical outcome.

Our process starts in the CT-scanner room at the Imaging Department, with the acquisition of a CT scan in treatment position (Fig. 1.a). The images are then transferred to the TPS through a CD, and delineation of GTV, CTV and PTV and the organs at risk is done [2]. We continue the process with the selection of the beams entrance and we input shielding in the treatment planning system. Once the plan is found suitable for clinical prescription (Fig. 1.b) and dose-volume histograms (DVH) have been evaluated, we proceed to printing, cutting and preparing the blocks for shielding. The blocks are made with lead pearls (Figs 1.c and 1.d).

This process has been carried out as described above in 20 patients. All patients have achieved the expected outcome and the acute toxicity has been lower in about 23% of the cases than in the group that was not treated using the beam shaping technique.

We are aiming at extending this technique to all our patients. This will eventually result in a better tolerated treatment, without affecting the expected outcomes in terms of disease control.

Before the initiation of treatment, a verification portal film is taken at the cobalt machine (Fig. 1.e) and once this verification film is approved by the radiation oncologist, we start the treatment with a cobalt machine, Theratron 780.

REFERENCES


FIG. 1. Preparation process for 3-D conformal radiotherapy with cobalt-60.
Clinical usage of a novel verification system for intensity modulated radiation therapy

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Intensity modulated radiation therapy (IMRT) requires a high level of patient specific treatment verification, as pointed out, e.g. in the German national standard DIN 6875-3, in which plan-related dose verification is recommended [1]. This contribution presents first results obtained with the novel verification system COMPASS (IBA Dosimetry, Schwarzenbruck, Germany) for head and neck plans.

In our department (Radioonkologie Moerkensstrasse, Hamburg, Germany) the dose distributions are not only measured, but also verified by an independent calculation with a second treatment planning system. In COMPASS, both these functionalities of patient-specific QA are combined in one system. The measurements are carried out using the 2-D pixel ion chamber array MatriXX together with a gantry fixture device (IBA Dosimetry).

COMPASS requires a comissioning similar to the one of a TPS, i.e. acquisition of dosimetric base data of 6MV photon beam (ONCOR Impression, Siemens) with a water phantom. The validation of COMPASS comprises the comparison of output factors, depth dose curves and profiles against base data, using square fields. The influence of defective beam delivery was simulated by introducing discrepancies in the plan settings (photon energy, MLC and collimator positioning). Data were analysed using the gamma method, where voxels with $\gamma>1$ ($\Delta d=3\text{mm}$, $\Delta D=3\%$) were taken into account and with the dose difference tool in COMPASS. The usage of COMPASS in clinical practice was analysed using four head and neck cases. For comparison of obtained dose distributions, the TPS KonRad (Siemens) was used.

It could be shown that the output factors, depth dose curves and profiles, which were computed in COMPASS using the DICOM RT-PLAN input or which were reconstructed based on MatriXX measurements were in good agreement with the base data.

The introduced displacement of a single leaf was already detectable for 1 mm discrepancy. Photon energy changes were detectable only for field sizes $>10\times10\text{cm}^2$. The comparison of computed and measurement-based reconstructed 3-D dose distributions with the initially planned ones resulted in an agreement of better than 2% average dose in most cases. The slope of DVH curves from the TPS and from COMPASS is also in good agreement.
Differences were noticed specially in areas adjacent to air cavities. This is caused by the different algorithms used in TPS (pencil beam) and COMPASS (collapsed cone/super-position) [2].

Discrepancies were noticeable as well in the low dose area as in organs at risk close to the gradient towards high dose area. Fig. 1 shows the gamma map for $\gamma>1$ in the transversal plane for a seven field head & neck plan.

**FIG. 1. Map of gamma values $\gamma>1$.** Left: Planning CT and ROIs without dose. Right: Difference between dose calculated with TPS KonRad against COMPASS measurement. Disagreement is visible in low-dose areas (yellow arrow) and in the vicinity of air cavities (green arrow). The blue arrow shows a disagreement caused by random misalignment of the MLC within its specification.

**Summary and conclusion**

The investigations have shown that the COMPASS reconstruction for 6 MV photon beam is in good agreement with the base data. Misalignment of a single leaf was detectable down to 1 mm. Analysis of four head and neck cases resulted in good agreement between average doses and DVHs. COMPASS allows to reduce the time needed for dosimetric pre-treatment verification of an IMRT plan and documentation of the results from 3.5 hours with conventional technique to one hour using COMPASS.

**REFERENCES**


Verification of LGP prediction in gamma knife in presence of inhomogeneities using PAGAT polymer gel dosimeter

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**Background and purpose:** Polymer gel dosimetry is still the only dosimetry method for directly measuring three-dimensional dose distributions. MRI Polymer gel dosimeters are tissue equivalent and can act as a phantom material.

In this study for verification of LGP (Leksell Gamma Plan) predictions, obtained isodose maps and DVHs with PAGAT polymer gel dosimeter are compared with those calculated by LGP system for single-shot irradiations of 8 and 18 mm collimators of gamma knife (GK) unit in homogeneous and inhomogeneous phantoms.

Stereotactic gamma knife (GK) radiosurgery plays an important role in managing small intracranial brain lesions of volume typically less than 25 cm$^3$ [1, 2]. The efficiency of the technique is based on the high precision delivery of a therapeutic radiation dose to the target employing a steep dose gradient in all three dimensions, which facilitates restriction of the dose to the surrounding normal tissues within the accepted tolerance levels.

**Method and materials:** A custom-built 16 cm diameter spherical Plexiglas head phantom was used in this study. Inside the phantom, there is a cubic cutout for insertion of gel phantoms and another cutout for inserting the inhomogeneities (air and PTFE [Poly-tetra-fluoro-ethylene], i.e. bone equivalent material with density of 2.2 gm/cm$^3$). The phantoms were scanned with a Siemens clinical 1.5 T MRI scanner. The multiple spin-echo sequence with 32 echoes was used for the MRI scans.

In this study PAGAT polymer gel dosimeter was fabricated according to composition proposed by Venning, et al, [3] who noted using MRI, the formulation to give the maximum change in the transverse relaxation rate $R_2$ was determined to be 4.5% $N,N'$–methylene-bis-acrylamide (bis), 4.5% acrylamide (AA), 5% gelatine, 5 mM THPC, 0.01 mM hydroquinone (HQ) and 86% H2O. For fabricating the gel dosimeter, another proposed method [4, 5] was used.

The parameters of the sequence were, as follows: TR 5900 ms, TE 20–640 ms, slice thickness 1 mm, field of view (FOV) 128 mm, Percent Phase FOV 75%, matrix size 256×192, pixel size 0.5×0.5 mm$^2$, and one acquisition. In total 17 slices were scanned through the volume of phantoms. The $R_2$ were computed using modified radiotherapy gel dosimetry image processing software coded in MatLab [6].

The obtained $R_2$ matrix on scanned planes of cubic gel phantoms were subsequently converted into a relative dose matrix normalized to the maximum prescribed dose of 40 Gy.

**Results and discussion:** Fig. 1 shows the comparative differential DVHs between LGP prediction and both homogeneous and inhomogeneous gel phantoms within high isodose levels (>40%) in irradiation with single-shot of 18 mm collimator of GK unit.
The differences between the DVHs of measurement and LGP prediction in the homogeneous phantom within some isodose intervals exceed the acceptance criterion (i.e. within 80–90% and 90–100% relative isodose levels reach 7.81% and 13.32%, respectively). However, the average difference between MC simulation and measurement is 5.96%, which is a little more than the acceptance criterion (5%). These differences may be due to measurement uncertainties in gel dosimetry.

The biggest differences between homogeneous and inhomogeneous phantoms using measurement were observed within 80–90% and 90–100% isodose intervals between PTFE inserted phantom and the other two, which reach 15.04% and 21.33% in comparison with homogeneous and 20.51% and 30.98% in comparison with air inserted phantoms, respectively, that in both cases exceed the acceptance criterion (5%).

Another important difference is seen between homogeneous and air inserted phantoms within 90–100% isodose interval, which is 9.65%.

Fig. 2 (a–d) shows the 2-D dose distributions on axial plane of homogeneous and inhomogeneous phantoms in irradiation with 18 and 8 mm collimators of GK unit.

The results of measurement in homogeneous and inhomogeneous phantoms showed that presence of inhomogeneities in head phantom can cause spatial uncertainty higher than ±2 mm and dose uncertainty higher than 7%.

Regarding acceptance criteria for conformal radiation therapy, it is important to avoid delivering less than 93% of prescription dose to larger than 1% of the target or more than 110% of the prescription dose to greater than 20% of the target [7].

The results showed that in some situations (e.g. presence of both air and PTFE within phantom) the mentioned criterion may not be guarantied, i.e. dose difference exceeds 7%, that is, less than 93% of prescription dose may be delivered to the target.

Conclusion: The presence of inhomogeneities can cause dose differences that are not in accordance with accuracy in treatment with GK radiosurgery and can cause considerable errors in dose calculation within high isodose levels with respect to LGP prediction which assumes the target is a homogeneous material.
FIG. 2. 2-D dose distribution in axial plane in irradiation with 18 mm (a, b) and 8 mm (c, d) collimators of GK unit obtained using PAGAT Polymer gel dosimeter. Dashed lines are isodose lines in air inserted phantoms and full lines are isodose lines in homogeneous (a and c) or PTFE inserted phantoms (b and d).

REFERENCES


Production of a new type of low-cost high-density concrete for shielding megavoltage radiotherapy bunkers

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The use of high density concrete in megavoltage radiotherapy rooms decreases the required thickness (and hence the occupied space) of a concrete barrier but normally at a higher cost. A method for production of an economic high density concrete with appropriate engineering properties would be very useful.

Galena (PbS) mineral was used in this study to produce a high density concrete. Galena can be found in many parts of Iran as well as some other countries. The Galena mineral used had a density of 7400 kg/m\(^3\). The concrete samples had a density of 4800 kg/m\(^3\) compared to that of ordinary concrete (2 350 kg/m\(^3\)) or barite high density concrete (up to 3 500 kg/m\(^3\)).

To measure the gamma radiation attenuation of the Galena concrete samples, they were exposed to a narrow beam of gamma rays emitted from a cobalt-60 radiotherapy unit. The measured half value layer (HVL) thickness of the Galena concrete samples for cobalt-60 gamma rays was much less than that of ordinary concrete (2.6 cm compared to 6.0 cm).

To test their compression strengths, two types of concrete mixes were produced. The water-to-concrete ratios of the reference and Galena concrete mixes were 0.53 and 0.25, respectively. The Galena concrete samples showed a significantly higher compression strength (500 kg/cm\(^2\) compared to 300 kg/cm\(^2\)).

A comparison of shielding and engineering properties of Galena concrete samples to those of a few other types of concrete is presented in Table 1.

<table>
<thead>
<tr>
<th>Type of concrete</th>
<th>Density (kg/m(^3))</th>
<th>HVL for 1.25 MeV Gamma Radiation (cm)</th>
<th>Compression Strength (kg/m(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary</td>
<td>2500</td>
<td>5.25–6.2</td>
<td>300</td>
</tr>
<tr>
<td>Barite [1]</td>
<td>3180–3550</td>
<td>3.6–4.0</td>
<td>140–394</td>
</tr>
<tr>
<td>Galena</td>
<td>4200–4600</td>
<td>2.56</td>
<td>500</td>
</tr>
</tbody>
</table>

*NI: not indicated by the authors.*
The Galena concrete samples made in our laboratories show good shielding/engineering properties in comparison with other reported samples made by using high density materials other than depleted uranium. Considering the possible hazards of depleted uranium, it may be claimed that the Galena concrete can be a substitute non-radioactive shield for applications such as shielding megavoltage radiotherapy rooms. It also costs less than the other high density concretes.

Based on these results, Galena concrete may be a suitable option where high density concrete is required for the shielding of megavoltage radiotherapy rooms at centres with limited resources. We are also in the process of producing a suitable concrete for both megavoltage photon and neutron shielding.

**BIBLIOGRAPHY**


CT-based intracavitary brachytherapy for gynaecologic tumours: First experience

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Nowadays different techniques for cervix cancer intracavitary therapy are used. Brachytherapy could be given with different dose rates (LDR, HDR, and PDR). Treatment planning is based on orthogonal radiographs and the treated volume is adapted to the PTV as much as possible. The doses are calculated at different points for the organs at risk and PTV (ICRU points). There has been noticed and increased interest in implementing image-guided brachytherapy to define better the structures of interest and assess the radiation dose distribution in tumours and surrounding normal tissues. CT is used for a better definition of the target and normal organ volumes and to calculate the dose to critical structures. Imaging information is used to optimize source placement to better achieve desired dose constraints. Improved dissymmetry for intracavitary gynecologic implants has shown increased maximum doses to normal organs than traditionally been reported [1].

The use of modern imaging techniques as CT provides further improvement for in cervix cancer intracavitary therapy. These techniques require organ counting on the images taken after the application and prior to irradiation. The purpose of this study is to compare radiography-based TP with CT-based TP for cervix cancer [2].

Methods

Afterloading system with HDR Iridium 192 was used for brachytherapy and individual 3-D plan calculated for each fraction. Spiral computed tomography “Somaton AR.STAR” Siemens was recently installed in our Institute of Oncology for CT-based treatment planning for intracavitary brachytherapy.

Fourteen (14) patients with cervical cancer were treated in 2007–2008 with CT compatible HDR intracavitary applicators and underwent post-implant pelvic CT scans with applicators in place. CT images were transferred to the ABACUS 3.1 treatment planning system. The gross tumour volume (GTV) and organ at risk were digitized. Dwell positions were identified and registered in the uterine tandem and colpostats for each patient.

All patients were treated with 5–7 Gy per fraction to point A using CT scans based planning. By performing the CT scanning useful information was obtained, such as assessment of cervical diameter, thickness of the rectovaginal septum, location of the tandem in the uterus. CT is also invaluable in defining the thickness of the uterine walls and distances to the rectosigmoid and bladder closest to the intrauterine applicator. This can help determine when dose specification should be changed to reduce the risk for late complications.
Conclusion

Individual treatment planning of brachytherapy was done on the basis of CT scans. Point doses have underestimated normal tissue doses, and cross-sectional imaging has added very useful information.

A good logistic performance and interdisciplinary approach including physicians, physicists and radiotherapy technologists is essential in order to reduce the time for planning and increase the quality of the treatment.

REFERENCES

Results of practical implementation of film dosimetry for routine verification of IMRT plans

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More than 200 IMRT plans were verified using CarPet phantom (ESTRO Quasimodo project) [1]. The plans, mainly for head/neck and pelvic regions, were generated using Eclipse (Varian, Paolo Alto, USA) treatment planning system. Field settings and numbers of monitor units were copied from the patient plan to the phantom CT images and the dose distributions were recalculated. In order to measure the dose distribution Kodak EDR2 films were placed inside the phantom. The phantom with the films was irradiated using all fields of the plan for recording total absolute dose distribution. The plans were delivered using 6 MV or 15 MV photon beams of Clinac2300 C/D (Varian, Paolo Alto, USA) linear accelerator. A calibration film was irradiated using programmed dynamic multileaf collimator (dMLC) in order to read the absolute dose distribution from the measuring films. The calibration film and the irradiated measuring films as well as the non irradiated film were processed the day after irradiation with Compact 45 (Protec, Oberstenfeld, Germany) film processor. After processing, the films were digitized using VXR-16 Dosimetry Pro scanner (Vidar, Herndon, USA). Digital images were obtained with 16-bit depth greyscale and 72 dpi resolution.

The calibration curve derived from the images of the calibration and the background films was created using FilmCal (PTW Freiburg) software. For each individual plan the calibration curve as well as the images of the measuring films and the calculated dose distribution were imported into IMRTCompare in-house developed verification software. The digital images were converted into 2-D dose maps and compared against the calculated dose distributions.

In the evaluation of the verification results the gamma concept was used [2]. Two methods of calculation of the gamma factor were implemented in the software: Depuydt [3] and in-house developed (INH). The 3 mm in spatial domain and 3% of the planned isocentre dose was taken as parameters for the gamma evaluation.

Only the rectangular region embedding the 80% isodose of the planned dose distribution was evaluated. The number of points from the selected region with gamma factor <1 was recorded for each plan. Histograms presenting the number of plans for the given number of points with \( \gamma >1 \) are shown in Figs 1 and 2 for both algorithms. The acceptance criterion was set as 95% of points for which \( \gamma >1 \).

For the calculation algorithm proposed by Depuydt, about 75% of evaluated plans were accepted for irradiation. For the INH algorithm about 60% of cases would pass the verification. The fraction of accepted plans remained stable over the time for both algorithms.
FIG. 1. Histogram of results of verifications for Depuydt implementation of the gamma evaluation. On the horizontal axis fraction of points passing $\gamma > 1$ criterion.

FIG. 2. Histogram of results of verifications for INH implementation of the gamma evaluation. On the horizontal axis fraction of points passing $\gamma > 1$ criterion.

Different software or different calculation algorithm may change the results of verification. Therefore, the acceptance criteria should be evaluated individually for each laboratory, depending on the equipment used. The fact that some cases fail the verification shows that there is still a need for a pretreatment dosimetric verification for each individual IMRT plan.

REFERENCES

What is an appropriate radiotherapy technology? A Pretoria Academic Hospital perspective

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The opportunity to design a new radiation oncology facility only presents itself once in a professional lifetime (if you’re lucky).

The new Pretoria Academic Hospital evolved over a period of more than ten years of planning. Since there were no clear guidelines or budget presented during the acquisition of equipment we posed the question: what is appropriate?

The factors determining appropriateness will be discussed and the various options tested against these. The recent experience of our facility with new equipment will be used as the basis for the arguments.

Although there were national and regional plans available for oncology services, we were left in limbo with regard to budgets, expected service levels and timeframes. Our department drew up a plan loosely based on the replacement of current technology with the equivalent new technology and rough estimates of expected patient numbers. We opted for a high tech approach.

The next hurdle was to work within the tender system to draw up appropriate specifications and to manage the acquisition process. A sophisticated evaluation was done based on cost of ownership over a seven year period. The lessons learned from this experience will be shared.

Commissioning of equipment and new techniques presented a huge challenge since it had to be performed with available resources while normal patient treatment had to be maintained. The whole philosophy of the department changed and we dragged a number of personnel kicking and screaming into the 21st century. As of today IMRT and SRS have become a routine part of life and IGRT capabilities are being developed.

The experience in our department has shown how a high tech approach can be implemented successfully in a developing world setting to improve productivity and personnel morale. However, the needs and expectations vary between centres and our findings will be extrapolated to different scenarios.

The answer to this question is neither clear cut nor static and in this ever evolving world of ours we can simply present a snapshot in time.

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Purpose

To show the implementation of a QA Clinical Programme in RT in IRCLCC using complementary ISO 9001:2000 norms, Guidelines of IAEA-TECDOC-1040 and QUATRO checklist (integrated).

Epidemiology

In Uruguay, a quarter of all deaths per year are caused by cancer. Life span is 75 years. The adjusted mortality rate of cancer (2002) in 100 000 inhabitants is 107.7 for women (No. 21 worldwide) and 191.2 for men (No. 13 worldwide). In Uruguay (2005) 595 cases of invasive uterine cancer (carcinoma in situ excluded) are diagnosed per year.

Material and methods

ISO 9000 family norms, IAEA-TECDOC-1040, QUATRO checklists, Uruguayan guidelines for the application of Unit ISO 9001:2008 in press. Quality Manual of IRCLCC was used. We analysed the information registered in relation to the Strategic Plan for RT service in HPR, Documented process, audits 2006–2007, technical cooperation projects with the IAEA, government and university. This was done in the framework of the NATional CANcer PROgram (PRONACAN) created in 2005. It is a programme aimed mainly to reduce mortality and incidence of cancer in the country by means of the coordination of activities and resources (Article 2, Executive Power Decree, 27.06.05).

Results

The Quality Assurance Committee was working weekly. Priorities were defined. Statistics showed that the total number of patients (seen and treated per year, in relation to the diseases, geographic distribution, anatomic site, stages, procedures performed and performance of service). All patient treatments were decided in specialized rounds four times a week (ateneos). Determination of obligatory requirements for EBRT and brachytherapy treatments. National guidelines treatment protocols were approved by the university and the government. QUATRO audit checklists were introduced as guidelines in each patient’s file.

Two internal audits were implemented in December 2006 and 20007. In 2006 (March), only 30% of adherence to the requirements. 2006 (December), 60% adherence. 2007 (December), 85% of adherence.

Project for replacement of equipment, Ministry of Public Health/Hospital Pereira Rossell: 1) URU/6/019, a high dose rate (HDR) remote afterloading programme for cervix cancer,
2) New linear accelerator 2 photon and 5 electron energies, HH:RR:5. New radiation therapy physicians and six technologists, three nurses with university degree or academic studies were included in the staff.

Conclusions

The complement of different tools of ISO 9001:2000 norms, IAEA-TECDOC-1040 and QUATRO checklist as guidelines was feasible and useful for the implementation of a QA programme in IRCLCC.

Audits were used as endpoints for evaluation and motivation of the staff. Adherence to the requirements has been approved year after year.
Regulating emerging technologies

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The presentation is designed for individuals who are involved in therapeutic administration of radioactive material and the implementation of the radiation safety programme.

The United States Nuclear Regulatory Commission (NRC) has regulatory authority over the medical use of by-product material and the radiation from by-product material. The presentation will address how the NRC regulates new medical uses (i.e. emerging technologies) used in radiation oncology that are too new to be covered in the current regulations. NRC’s process that allows licensees to get approved for these emerging technologies until regulations are promulgated for the new modalities will be described.

The presentation will also cover NRC’s reporting requirements for medical events and other radiation safety-related incidents. Some examples of errors that have occurred for these new NRC-regulated activities will be provided. The root causes in these events will be identified to prevent similar additional incidents from occurring in other facilities performing the same type of therapy.
Effectiveness of IVD as a tool for QA in radiotherapy

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Radiation therapy has proved to be very effective when it comes to the treatment of cancer but also very dangerous if quality assurance and control are not observed properly. In vivo dosimetry (IVD) is a very effective and indispensable non-invasive method of assuring that errors in treatment are discovered early during treatment. While diodes have their advantages over TLDs this paper will focus mainly on diodes.

The survey conducted showed that, for properly calibrated diodes, error in positioning of shielding blocks or error in calculation can be detected using diodes for both small and large fields as well as for asymmetric fields with half beam blocking. Diode positioning methods on the patient also affects the accuracy of the obtained results and can affect quality delivered to the patient. For tumours in motion the diodes offers no reasonable advantage in QA.

Direct reading of the dose delivered to the patient makes it possible for the investigations to be conducted immediately after the treatment with the patient still in the treatment position for the possible causes of the errors. Since the diodes are placed on the patient’s skin and not in the centre of the tumour (point of interest in clinic) the given dose was the one considered as a reference thus the diode reading is directly related to the dose delivered to the patient. Measurements were done on patients receiving radiation therapy for both open and wedged fields and was found that the deviation of the calculated ‘given dose’ (dose maximum) and the measured dose was within 3% for most of the open fields and it increased slightly for wedged fields using the Isorad diode for 6–12 MV, notable increases are observed with increase in wedge angle.

Comprehensive quality assurance in terms of treatment delivery has been achieved by the use of IVD, hence the recommendation of doing in vivo dosimetry on every patient undergoing photon and electron teletherapy within the first three treatments at most. Even with the growing confidence in the use of diodes for QA/QC purposes the fact remains that treatment should not be changed based solely on the findings of IVD.

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University based IMRT implementation in Chile

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Objective

The introduction of IMRT in third world countries has been slow. The objective of the study is to evaluate the implementation of IMRT in Chile and its impact on the current daily practice.

Material and methods

Historical review of the steps taken for the implementation of IMRT was done. Review of the treatment diagnosis for patients treated with IMRT from April 2002, when the first IMRT patient was treated at PUC, to June 2008 was done. Data on IMRT QA for all treatments delivered had been collected prospectively and reviewed. Analysis of treatment results and complications is underway for each specific diagnosis and the preliminary results on IMRT for prostate cancer is presented.

Results

A requirement prior to the implementation of an IMRT was to have a 3-D CRT programme. The 3-D CRT programme was routine practice at PUC since 1996, five years before the initiation of IMRT. After making a decision to have an IMRT programme, the first step was to have international IMRT training for both the physician and the physicist. Later, equipment selection was performed and purchase was done. Further training was taken for the selected equipment, including practical training. Inverse planning was done initially on CADPLAN and later on Eclipse software. Sliding window technique was selected for treatment delivery. Extensive commissioning of all the IMRT components was done. A QA programme for IMRT was established [1]. The IMRT treatment QA component for each patient included ion chamber measurements for dose verification and film QA for each individual field delivered and for the entire dose distribution. Film dosimetry analysis was done with the RIT software. An independent software, MUIcheck, was used to verify the machine monitor units obtained from the treatment planning computer.

During the period of the study 702 patients have been treated with IMRT at the PUC Cancer Center. The patients’ median age at the start of IMRT was 64 years (4–86) of whom 66% were male and 34% female. IMRT treatment was delivered to the following sites: prostate 30%, head & neck 30%, abdomen and pelvis 20%, brain 10%, others 10%. IMRT indications have increased steadily over time and, today, represents approximately 30% of all treatments delivered.

A total of 1051 inverse plans were generated including PTV1 and PTV2, for primary and boost delivery. The QA results with the comparison of the computer generated treatment planning dose and ion chamber measurements for all plans is shown in Fig. 1. The comparison showed that most results are within $\pm 3\%$ between calculated and measured doses.
Analysis of treatment results by diagnosis is underway. For prostate cancer, definitive treatment with IMRT has resulted in an overall survival of 85% and biochemical disease-free survival according to the M.D. Anderson risk groups: 100% for low risk, 83% for intermediate and 58% for high risk. Late treatment complications grade 3 or 4, according to the LENT/SOMMA scale, occurred in the bladder in 6% of the patients and in the rectum in 2% of the patients.

Conclusions

- IMRT can be implemented effectively in developing countries.
- 3-D CRT experience is essential before starting an IMRT programme.
- IMRT training is indispensable prior to starting the programme.
- Extensive treatment QA is necessary for safe treatment delivery.
- Our IMRT treatment results compare satisfactorily with the reports in the literature [2].
- The percentage of patients treated with IMRT has increased continuously over time.

FIG. 1. Ion chamber verification – IMRT.

REFERENCES


Pre-clinical commissioning of plans with an aperture based IMRT treatment planning system

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Essential milestones according to international recommendations [1] for the transition from three dimensional conformal radiotherapy (3-D CRT) to intensity modulated radiation therapy (IMRT) in clinical practice has been fulfilled in the main physics, QA and dosimetric aspects at the Department of Radiotherapy of the National institute of Oncology and Radiobiology (INOR), Havana, Cuba.

Previous to implementing IMRT, a pre-clinical procedure was developed in order to commission the treatment planning techniques on real patients and validate the rationale of this transition from the dosimetric and radiobiological perspective.

The comparison was based on a group of patients eligible for IMRT, who were actually treated with 3-D CRT. IMRT plans were designed and virtually applied to the same patients, simulating the eventual IMRT treatment. Dose prescription and fractionation were also equivalent in both techniques, for radiobiological comparison purposes. The results should allow evaluating the rationale of IMRT plans in terms of reduced complication rates and/or possibility of dose escalation to the PTV.

Based on CT scan sets of prospective and retrospective 3-D CRT patients, dosimetric and radiobiological quality indeces of the plans were defined, using the results of dose volume histograms (DVH) of targets and organs at risk.

Ten patients were included in the study. The 3-D CRT and IMRT plans were obtained with Elekta’s PrecisePlan® RTPS and the computed DVHs were used for dosimetric qualitative comparison of each patient’s plan pair, as shown in the example, Fig. 1.

![FIG. 1. Comparison of DVHs for a selected H\&N patient. OARs considered were spinal cord and st. brain.](image-url)
M. Nápoles, et al.

For radiobiological estimation of potential treatment outputs, the DVHs were used as input to compute the equivalent uniform dose (EUD) of targets and organs at risk (OAR), as well as for determination of tumour control probability (TCP) and normal tissue complication probability (NTCP) in each plan. The software Albireo Target version 4.0.1.2008 [2] was employed for this purpose, which is based on both Poisson’s and Lyman’s models for TCP and NTCP, respectively. For comparison purposes, up to two OARs were considered in each patient, regarded as of major clinical impact in the treatment outcome. These parameters were compared between 3-D CRT and IMRT plans, as shown on Table 1.

TABLE 1. COMPARATIVE RESULTS OF TREATMENT PARAMETERS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Relative deviation (%)</th>
<th>Tumour</th>
<th>OARs</th>
</tr>
</thead>
<tbody>
<tr>
<td>arit. mean of ΔEUD</td>
<td>-6.7</td>
<td>-</td>
<td>-39.7</td>
</tr>
<tr>
<td>arit. mean of ΔTCP</td>
<td>0.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>arit. mean of ΔNTCP</td>
<td>-</td>
<td>-</td>
<td>-97.6</td>
</tr>
</tbody>
</table>

Values represent the relative variation of each parameter from 3-D CRT to IMRT plans, averaged for all patients included; positive values indicate increments, while negative values are decrements of the parameters.

EUD-based and TCP/NTCP-based objective functions were studied in order to establish a radiobiological figure of merit for the transition to IMRT.

Both objective functions for IMRT plans were significantly higher than that of the corresponding 3-D CRT plan, which was fundamentally due to the reduction of EUD of OARs and NTCP, when IMRT plans were performed properly, as shown on Table 1. EUD-based objective functions are very sensitive to selected organ penalties; nevertheless, in all cases the results indicated a rational advantage of the IMRT plan. Further studies are in progress to establish more evidence-based parameters. Similar results were observed for TCP/NTCP-based objective functions.

As a collateral result of this research, the staff involved in treatment planning process (radiation oncologists, medical physicists and dosimetrist) have developed skills in using the treatment planning system and independent verification tools.

This pre-clinical experience is expected to create the basis for further clinical implementation of randomized studies that demonstrate the superiority of the IMRT versus 3-D CRT in our environment.

REFERENCES


Building of a low cost calibrated density phantom to perform quality assurance to comply with IAEA TRS-430 protocol

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IAEA TRS-430 Protocol is a useful means to effectively test a treatment planning system (TPS), especially when elaborated techniques such as 3-D radiotherapy and IMRT are used. It is known that 3-DRT and IMRT planning systems use beam modeling for calculating such treatments, tested and accepted in several ways and beam arrangements, considering that the medium density is 1.0. However, TPS may perform differently when the medium is not homogeneous, therefore dose would be over or under estimated.

It also happens that in several 3-D or IMRT actual plans have at least one heterogeneity that may affect largely the dose distribution such as beams passing through lungs, and calculations made without taking this into account will be outside the accuracy we always look after.

In order to test a TPS calculating ability whenever heterogeneities are present, we built a very low cost phantom which serves several purposes: first, find enough known densities against Hounsfield units for a given tomography machine, second, calculate the dose values predicted with the TPS when this phantom is loaded, and finally, use the same arrangement to actually measure dose in several points compared to the values predicted by the TPS. We acquired four calibrated inserts available in the market and placed them inside two PMMA slices where appropriate holes were machined for them. Between the PMMA slices we placed two slices, made from virtual water, one of them suited for a micro ion chamber, and a thin alloy slice.

FIG. 1. Calibrated inserts into the phantom (right) and a BEV of the TAC scan (left).
Materials and methods

Four calibrated inserts for key values: lung exhale, lung inhale, water and bone. Also some known material’s densities: several acrylic and virtual water slices, in order to make an arrangement for the inserts and one ion chamber. The information acquired in DICOM was loaded into the TPS, the heterogeneities were identified and given their calibrated and known values. We used our TPS (Winplt for 3-D planning and Kenos for 2-D planning, both of them of Argentinean origin and work with superposition and convolution methods). This procedure allows to evaluate the TPS performance under several conditions and, later on, irradiate the phantom in order to measure the dose given by those conditions. We are capable at the moment to assess dose by several methods: ion chamber, diode array (mapcheck) or film dosimetry.

Results

After scanning the phantom, a calibration curve for density against H.U. (Hounsfield units) was obtained and, thus, densities for other materials, such as virtual water, PMMA, and alloy were found. These densities were found to be within 5% of reported values. Foam, such as the one used for molding, has a density lower than 0.1, not useful for modeling lung density, for instance.

A dose test was performed with a virtual water phantom loaded into the TPS. 6MV and 18MV 10×10cm$^2$ beams were used in each case, and dose was calculated at 10 cm depth with a SSD=100 cm. Along with this, a virtual water phantom was set up with the same conditions and absolute dose measured with an ionization chamber. The TPS predicted irradiation times within 3% as shown below.

<table>
<thead>
<tr>
<th>Energy</th>
<th>Measured Dose (cGy)</th>
<th>UM delivered</th>
<th>UM calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MV</td>
<td>129.6</td>
<td>200</td>
<td>198.2</td>
</tr>
<tr>
<td>18MV</td>
<td>149.0</td>
<td>200</td>
<td>202.1</td>
</tr>
</tbody>
</table>

Conclusion and recommendations

A satisfactory agreement was found for the dose test for the virtual water density. This is very useful as sometimes quick measurements must be performed with plastic phantoms. We are to develop a low cost material to simulate lung, in order to test the TPS with low density conditions, and build a phantom that fully complies with TRS-430.

REFERENCES

Elaboration and commissioning of a phantom for quality control in a linac based stereotactic radio surgery system

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With the implementation of a stereotactic radio surgery system it is important to implement a quality control system to guaranty the accuracy of the given treatments.

The stereotactic radio surgery system includes a stereotactic frame adjusted to the patient’s cranium, a cone holder, collimator cones (cones 9, 12, 15, 18, 21, 24, 27 and 30 mm), mechanically adjusted and dismountable to the linac collimator system, and a fixation system for the patient’s head attached to the treatment couch and a fixation system for the couch that finally guarantees positioning within a 1 mm tolerance. All the system was adjusted to a 6 MV linac. Additionally a 3-D conformal planning system with capabilities for images fusion for CAT, MRI and digital angiography was initiated and commissioned. For this reason it was necessary to implement a system to guarantee that the image fusion was adequate and within the tolerance, the implemented system allowed simultaneously to verify the prescribed dose by the planning system and the adequate position of the isocentre.

A 15 x 18 x 18 cm³ (wide x hide x length) cubic shape phantom was built with commercial wax, with four holes to introduce different types of fiducial markers, that allowed the introduction of a ionization chamber.

An MRI was done to the wax phantom initially, then the stereotactic frame was attached to the phantom resembling a normal SRS procedure. A CAT scan and a digital angiography were done. All the images files were sent to the planning system and fusions were done to recreate an stereotactic radio surgery plannification. The planning system results were then verified and compared against the experimental dosimetry using the phantom.

FIG. 1. Phantom in CAT scan.  
FIG. 2. Phantom’s CAT scan.
In the case of image fusion control, a geometric measure of the position of fiducials and concordance with the three images was done.

To verify the position in the irradiation system, an ionization chamber PTW TN31014 (PIN POINT) type was located with a fiducial marker. The phantom was located as well following the Cartesian coordinates proportioned by the planning system. Then irradiation following the planning system parameters was done to the ionization chamber in different angles and arcs, posteriorly phantom was moved 1 mm step by step away from the isocentre, positive and negative in the three axes, until no irradiation was detected. This value was registered as the tolerance of the geometric position of the isocentre.

To verify the monitor units (MU) that were given by the planning system, a measure of the total given dose was registered with the ionization chamber following TRS-398 protocol.

Results

- The results show a satisfactory concordance between the planning system and the experimental results.
- Image fusion for CAT/MRI and angiography shows a concordance within 2 mm.
- For the results in absorbed dose, a difference below 3% was achieved (within tolerance).

Conclusion

- The above described phantom was found to be useful and was able to verify the quality of the fusion, the geometric position and the MU of the planning system.
- It was easy to build, with no significant cost.
- It can provide results that allowed the implementation of a quality control protocol for image fusion, positioning and verification of MU for our SRS system.

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**Absolute dose measurement as a verification tool for patient specific QA in IMRT**

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A method for verification of the treatment planning system (TPS) calculated absolute dose for intensity modulated radiotherapy planned cases was investigated using a semi flex ion chamber with a chamber volume of 0.125cm$^3$. We have an Elekta Synergy accelerator with dual photon (6&15 MV) energies with the capability of XVI (X ray Volume Imaging) and I view GT (portal imaging). This Accelerator is equipped with a multileaf collimator (MLC) used for IMRT and Conformal radiation. The MLC has 40 opposed leaf pairs. The leaf thickness is of 10mm and is adjoined with a backup jaw to limit the interleaf leakage.

All plans were made using the Direct Aperture Optimization (DAO). The number of beams used for delivery of treatment varied from 2 to 9 beams depending upon the site of treatments. Dose QA module in the planning system with the option of calculating dose per beam or per plan was utilized for deriving the QA plans.

Universal IMRT Phantom from PTW Freiburg was utilized for ion chamber placement. The verification was done by irradiating an IMRT verification phantom and by comparing the measured phantom values and the calculated values of the radiotherapy treatment planning system. The Universal IMRT Verification Phantom type T400201 enables to check the spatial distribution of IMRT beams using a radiographic film. The phantom is composed of two 30 cm×30 cm acrylic blocks, the depth of the film is 50 mm, and the depth of the ion chambers is 60 mm. Ion chamber was connected to integrating dosemeter to measure absolute dose values. The phantom accommodates a film of 25 cm×30 cm and up to five 0.125 cm$^3$ ion chambers type 31002/31010. The position of the film was marked by needles with respect to the phantom and the chamber orientation.

Ionization chamber used was a semi flex chamber with a chamber volume of 0.125 cm$^3$. It has a short stem for mounting and a flexible connection cable. The nominal useful energy range is from 30 kV to 50 MV photons and 6 MeV to 50 MeV electrons. The wall material is graphite with a protective acrylic cover. The guard rings are designed up to the measuring volume.

There were 72 IMRT plans generated from 31 Dec 2007–31 Aug 2008 in the department of Radiation Oncology. A per-plan module to calculate the absolute dose delivered was used due to the available phantom geometry. In the per-plan module, the gantry angles are collapsed to form a single gantry position of 0°. In all patients the clinical plans are moved to the QA module of the planning system and the beams are placed at the centre of the chamber volume. The plan was optimized to the daily dose planned and a Dose Volume Histogram (DVH) was calculated. Depending upon the segments and the placement of the same at the chamber volume, the minimum, maximum and mean dose for the chamber volume was determined with the DVH.
Inside the accelerator room the Universal IMRT Phantom was arranged with the chamber being perpendicular to the isocentre axis. The ionization chamber was placed at the central bore of the phantom. Once the plan was irradiated and the dose measured, the difference in dose measured and calculated was verified. For those plans where the differences were larger than 3%, the plans were verified to see if some of the segments were not on the chamber volume. For these plans an off axis measurement was made with the chamber placed at the adjacent chamber inserts.

An IMRT QA verification plan (absolute) performance was designed in-house to prospectively capture the patient details, calculated TPS dose(b), room temperature, atmospheric pressure on the day of measurements, chamber calibration factor [N(D,W)]; ion recombination correction factor [K(Q,QO)]; corrected room temperature and pressure [K(T,P)=(273+To/273+T)×P/Po]; measured meter reading(MR=…..nc); measured dose D(a)=N (dw)×MR×K (Q,QO)×K(TP) and the calculation of % Error per reading per patient (a-b)/b.

There were a total of 74 observations available for the % Error with a standard deviation of 1.211(Range -2.06 to +4.23), a mean value of 1.05, a median of 1.17. Only 2/72 case records had a variation of >3%.

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Intensity modulated radiation therapy for craniospinal irradiation using helical tomotherapy: Initial experience from planning to delivery


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Purpose

To establish feasibility of intensity modulated radiation therapy (IMRT) for craniospinal irradiation (CSI) using helical tomotherapy (IMRT Tomo) and report initial experience of its implementation in the clinic. A dosimetric comparison with conventional linear accelerator (IMRT LA) and three dimensional conformal radiotherapy (3-D CRT) is also reported.

Materials and methods

In the first phase, CT datasets of four previously treated patients of medulloblastoma with differing spinal lengths were used to generate 3-D CRT, IMRT LA and IMRT Tomo plans. CSI dose of 35 Gy in 21 fractions was prescribed to planning target volume (PTV). All plans were compared dosimetrically using standardized parameters.

In the second phase, three patients were treated on an ongoing prospective protocol of helical tomotherapy, with daily image-guidance using megavoltage computed tomography (MVCT). Mosfet and TLD are kept at eyes, thyroid, chest and testes during treatment for dosimetry. Doses measured will be compared with the calculated dose from Tomo planning system.

Results

The mean volume of each PTV receiving at least 95% of prescribed dose (V95%) was >98% in all plans. All plans resulted in comparable dose homogeneity index (DHI) for PTV Brain. For PTV spine, IMRT Tomo achieved highest mean DHI of 0.96 as compared to 0.91 for IMRT LA and 0.84 for 3-D CRT. The best dose conformity index (CI) was achieved by IMRT Tomo for PTV brain (0.96) and IMRT LA for PTV spine (0.83). IMRT Tomo plan was superior in terms of reduction of maximum, mean and integral doses to almost all OARs. It also reduced volume of each OAR irradiated to various dose levels, except for the lowest dose volume. The beam-on time was longer in IMRT Tomo.

During clinical implementation, practical issues that arose included challenges in whole body immobilization, areas to be imaged daily with MVCT, co-registration efficiency, intrafraction motion, and impact of differential shifts of different parts of the body, which were handled using appropriate methodology resulting in increased daily time on the machine.
Conclusion

IMRT Tomo for CSI is technically easier and dosimetrically favourable as compared to IMRT LA and 3-D CRT. In case of non-availability of tomotherapy, IMRT for CSI can be realized on conventional linear accelerator even for spinal lengths exceeding maximum allowable field sizes using appropriate intensity feathering techniques. Although time and labor intensive, challenges in successful implementation of IMRT Tomo for CSI can be circumvented provided they are preempted during the planning phase.

Acknowledgement: The authors are thankful to Dayanand Sharma for the dosimetric comparison.
**Dosimetric characteristics of 2-D ion chamber array matrix for IMRT dose verification**

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Intensity modulation radiotherapy (IMRT) planning demands stringent quality assurance and accurate dose determination for delivery of highly conformal dose to the patients. The increased complexity of clinical treatments raises the need for more accurate dose verification systems and procedures. Generally 3-D dose distributions obtained from a treatment planning system have to be verified by dosimetric methods. Mainly a comparison of two dimensional calculated and measured data in several co-planar planes are performed [1].

In principle, there are many possibilities to measure two dimensional dose distributions such as films, flat-panel electronic portal imaging devices (EPID), ion chambers and ionization chamber arrays. Radiographic and radiochromic films have good resolution but due to processing, calibration and scanning processes their handling is time consuming, hence they cannot be applied for fast real-time measurements. The flat-panel EPIDs show a good resolution and offer a possibility for real-time measurements but their calibration is complicated, as the signal has to be converted into dose. The 2-D ion chamber array system offers the real-time measurements and it can be easily connected to the PC. Good agreement in measurements between films and ionization chambers for verification of radiotherapy plans were reported by Spezi, et al. [2].

In this study, dosimetric characteristics of 2-D ion chamber array matrix (I’matriXX, Scanditronix, Wellhofer, Germany) were analysed for verification of IMRT plans.

**Materials and methods**

The ionization chamber array consists of 1020 single air-vented plane-parallel plate ion chambers arranged in 32×32 matrix. Each chamber is 4.5 mm in diameter, 5 mm in height and with sensitive volume of 0.08 cc.

A microelectronic chip reads out each of the chambers separately. The device runs with two separate counters to avoid dead time. The minimum read out time is 20 ms, which allows us to measure dynamic processes as the start-up process of the linear accelerator. The depth of effective point of measurement is located at 3.6 mm from 2-D array surface. The measurements were performed in Clinac DHX linear accelerator with 6 MV, and 18 MV photons in the solid water phantom (RW3, density 1.045 g cm\(^{-3}\)) was used with matrix for all measurements. The absolute dose was estimated using matrix and it is given by:

\[
D_{ij} = (M-B)_{ij} \times N_{DW}(^{60}Co) \times K_{uni \ ij} \times K_{TP} \times K_{user}
\]

where

- \(M_{ij}\) is matrix measured value,
- \(B_{ij}\) is matrix background value, and
- \(K_{TP}\) is correction for pressure and temperature.
S. Sathiyann, et al.

The uniformity correction factor for the detector matrix was obtained from production site [3], which is the product of uniformity calibration factor for the detector matrix and $^{60}\text{Co}$ calibration factor $[N_{\text{DW}}(^{60}\text{Co}) \times K_{\text{uni}}]$. The $K_{\text{user}}$ factor is determined for 6 MV and 18 MV photons based on the dose estimated by calibrated Farmer chamber (FC65G).

The stability, output factor, dose linearity and dose rate behaviour of the device were also studied. The IMRT fluence patterns generated from treatment planning system (TPS) like field-in-field, pyramidal and chair tests were measured with the I’matriXX and film dosimetry system. IMRT treatment plans were also verified with I’matriXX and film dosimetry.

The I’matriXX device can also be used to verify the flatness, symmetry, penumbra and field width of linear accelerator as a routine QA procedure.

**Results and discussion**

The I’matriXX device gives the absolute dose values based on the $K_{\text{user}}$ factor. The reproducibility of measurements was good. The system response to dose was found to be linear within the range of 2–500 cGy, the response of the detector was found to be independent of dose rate from 100 MU/min to 600 MU/min.

Output factor matches very well with the chamber measurements. The fluence pattern measured by the I’matriXX and film dosimetry for field-in-field, pyramidal and chair tests were found to be in good agreement with the calculated fluence. IMRT plan fluence measured by I’matriXX and film dosimetry was comparable with TPS calculated fluence. The I’matriXX device was also used for measuring flatness and symmetry of the beam for routine QA and compared with the base values.

**REFERENCES**


Inverse planning simulated annealing (IPSA) planning for 3-D image based HDR brachytherapy in cervical cancers: A dosimetric study


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Purpose

Brachytherapy forms the mainstay of treatment for both local control and toxicities in locally advanced cervical cancers. Conventional X ray based planning has been challenged in the last two decades. 3-D image based brachytherapy planning is evolving. Three dimensional treatment planning systems and inverse planning optimization for brachytherapy are becoming commercially available. The objective of this study was to compare the inverse planning algorithms with the traditional method of prescription to point A in MR image based dosimetry for HDR intracavitary in cervical cancer.

Methods and materials

The MR data set of 23 patients treated with HDR brachytherapy for cervix cancer was selected for this dosimetric study. All the intracavitary application was performed under general anesthesia and consisted of standard nucletron tandem – ovoid CT/MR compatible applicator. Fast Spin Echo T2 weighed MR scans (GE, Signa, Excite, 1.5T) in axial (true), coronal and saggital orientations was taken. The scans were taken with 3mm thickness and 0-1mm spacing. MR images were exported to contouring workstation (Oncentra V 3.0 sp1, Nucletron, Netherlands) where HR-CTV, bladder, rectum and sigmoid were contoured in accordance with GEC ESTRO GYN recommendations.

Direct reconstruction of applicators on the MR images were carried out using of multi-planner reconstruction. In some cases where ovoid channels were not visible, a simulator image of ovoid on a transparency sheet was used to guide the reconstruction of the ovoid channel. A negative offset of 7 mm was given to accurately reconstruct the first dwell position.

Two plans were generated for each patient using 3-D treatment planning system(Sunrise, Nucletron, Netherlands): standard plan consists of Fletcher loading pattern with Point A prescription and manual optimization of dwell positions was allowed to reduce doses to OAR. Inverse plan was carried out using inverse planning simulated annealing (IPSA) algorithm (Nucletron) with source loading for optimum HR-CTV coverage and constraints to minimize doses to OARs. In the standard plan, prescription of 7 Gy per fraction was normalized to Point A as compared to HR-CTV in IPSA plan. However, point A doses in IPSA plan were also documented.

The dose volume parameters recommended by GEC ESTRO GYN were evaluated for comparison: V100 (percentage of volume covering 100% of the dose), D90 (Dose to 90% of HR-CTV), D2cc and D0.1cc (minimum dose to the most exposed 2 cc and 0.1cc of bladder, rectum and sigmoid). For the high dose region V200 (volume receiving 200% of the
S. Sharma, et al.

prescription dose) was also evaluated. The goals defined for IPSA plans were as follows: HRCTV: D90=6.3 Gy, V100=90%, and a dose of ≤4.9 Gy per fraction for 2 cc of bladder, rectum and sigmoid. The data was analysed using paired sample t-test and Wilcoxon signed ranks test. The test was performed with a significance level of 5%.

Results

All 23 patients data sets were evaluated for the comparison. The volume of HR- CTV ranged from 10.4–74.2 cc with a mean of 47 cc (±18.6). Mean D90 were as follows: standard plan 6.25± 1.68 Gy and inverse plan 6.05± 0.88 Gy (p=0.333) . Mean point A dose were 7±0Gy and 6.6±1.32 Gy for standard plan and IPSA plan, respectively. Mean V100 were as follows: standard plan: 82.43±8.5% and inverse plan: 83.70±5.4% (p=0.318). Mean D2cc of bladder was 7.86±1.7 Gy, 7.10±1.6 Gy (p=.005) for standard plan and inverse plan, respectively. Mean D2cc of rectum was 3.86±0.71 Gy, 4.01±1.4 Gy (p=0.528) for standard plan and inverse plan, respectively. Mean D2cc of sigmoid was 5.50±1.5Gy and 4.84±1.3 Gy (p=0.001) standard plan and inverse plan, respectively. The mean D0.1cc of bladder, rectum and sigmoid were 11.11±2.90, 5.04±1.05 and 7.98±2.51 Gy for standard plan as compared to 9.85±2.29, 5.62±2.06 and 7.48±3.05 Gy for inverse plan. Mean V200 was 38.65 % and 41.35 % (p=0.236) for standard and inverse plans, respectively.

To summarize, in this dosimetric comparison, dose to bladder and sigmoid were reduced significantly in inverse plan as compared to standard plan without compromising HR CTV coverage. This reduction was at the expense of marginal increase in rectal doses but still within the tolerance limits.

Conclusion

PSA planning results in optimizing doses to HR-CTV and reduction in doses to bladder and sigmoid. Refinement in defining goals and challenging the standard loading patterns may further add to optimization in 3-D image based HDR brachytherapy in cervical cancers.

REFERENCE

A new biologic radiopharmaceutical for targeted therapy of breast cancer: $^{177}$Lu labelling of Mab PR81 and quality control

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Human epithelial mucin, MUC1, is commonly over-expressed in adenocarcinoma that includes more than 80% of breast cancers and represents a useful target for radioimmunoscintigraphy (RIS) and radioimmunotherapy (RIT). The PR81 is a new murine anti-MUC1 monoclonal antibody that was found to react with the membrane extracts of several human breast cancerous tissues and cell surface of many MUC1 positive cell lines. In our previous study we used this antibody, labeled with $^{99m}$Tc via HYNIC, in imaging of breast cancer in mouse model successfully as a scouting procedure.

In this study we developed an efficient method for indirect labeling of PR81 with $^{177}$Lu via DOTA as a chelator to produce a new biologic radiopharmaceutical for RIT of human breast cancer. The quality control of new therapeutic radiopharmaceutical was also performed.

Material and methods

DOTA and NHS were dissolved with dry DMSO, mixed and stirred overnight. The precipitated dicyclohexylurea was removed by filtration and washed with hot DMSO, and DMSO in the filtered solution was removed by distillation. According to different mole ratio of DOTA/PR81, DOTA-NHS was added to PR81 solution and incubated for two hours. After conjugation, DOTA was removed from DOTA-PR81 by the Sephadex G50 column and NaAc solution as elution agent. We did plenty of experiments to determine the optimal conjugation condition of DOTA with PR81. The $^{177}$Lu$_2$O$_3$ solution (10 mCi activity per 1 mg antibody) was added to DOTA-PR81 and incubated in water bath (37°C). The labeling efficiency was determined by ITLC. The amount of radiocolloids was measured by cellulose nitrate electrophoresis. In vitro stability of labeled product was determined at room temperature and in human serum by ITLC and gel filtration chromatography (FPLC) over 24 hours, respectively. The integrity of labeled MAb was checked by means of SDS-PAGE. Cell binding assay was used to test binding ability of $^{177}$Lu-DOTA-PR81 to MCF-7 cell line. Biodistribution was studied in normal BALB/c mice at four (4) and 24 hour post-injection.

Result

The labeling efficiency was $86.2\% \pm 3.2$, 30 minutes after reaction and radiocolloids was less than %2. In vitro stability was $82.6\% \pm 3.6$ and $73.4\% \pm 6.7$ at room temperature and in human serum over 24 hours, respectively. There was no significant Ab fragmentation due to labeling procedure. Both labeled and unlabeled PR81 were able to compete for binding to MCF 7
cells. Biodistribution studies in normal BALB/c mice showed that there was no significant accumulation in any organ.

**Conclusion**

The results showed that one may consider the new complex as a potential radiopharmaceutical for treatment of human breast cancer; this needs further investigation.

**REFERENCES**


4-D CT imaging technique for conformal forward planning in lung tumours
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The aim of this study is to make use of the data gained from 4-D CT imaging in modifying volume expansion and its impact on 3-D planning for lung tumours. Philips Big Bore CT scanner was used with the respiratory belt provided.

Conventionally, for lung tumours, we obtain the CT images using the free-breathing scan. The GTV is then delineated and the PTV is expanded in the following way: 2.5 cm in the superior/inferior directions and 2.0 cm elsewhere. The expansion margins take the breathing motion into account to ensure adequate coverage during treatment. With the use of 4-D CT imaging, the actual motion of the tumour can be visualized and quantified. Fig. 1 illustrates the motion of the GTV due to the lung motion for one of the cases at two breathing phases, maximum expiration, Fig. 1a, and maximum inspiration, Fig. 1b. The summation of the location of GTV in each of the breathing phase is called the maximum intensity projection, MIP, Fig. 2. 4-D CT imaging enabled us to reduce the margins of expansion to 1.5 cm in the superior/inferior direction and 1.0 cm elsewhere, while still providing adequate coverage during breathing.

The use of 4-D CT imaging leads to an increase in the GTV volume due to the fact that the MIP volume represents a larger volume, as seen in Table 1. The increase in volume is as much as 34%. However, because the actual target motion is known and the expansion margins of PTV are reduced, the PTV volume itself is reduced by more than a half. We found this to be true for the cases studied. The impact on the lung volume was also examined. The involved-lung volume was defined as the healthy ipsilateral lung tissue included in the PTV. The uninvolved lung volume was thus, the volume of the ipsilateral lung minus the involved volume. Table 1 indicates that about 8% of the lung volume has been “spared” from being included within the PTV volume. This will reflect in lower dose to the lung and an improved DVH.

To analyse the impact of using the data from 4-D CT, and the new expansion margins on the treatment planning, we calculated two isodose plans for several lung cases. For each case, one plan was done using the free-breathing CT scan and the conventional PTV expansion, while the other plan was done using 4-D CT imaging and the modified expansion. PTV coverage in both plans satisfied the following minimum criteria: At least 95% of PTV receives at least 95% of dose, and no more than 107% hot spot was acceptable. Both plans consisted of five segmented beams with forward planning technique. Our plans always make sure not to have any beams enter through the contralateral lung. Forward planning is used, with several beams having multiple MLC segments. Fig. 3 shows an isodose comparison, of one of the cases, between conventional imaging and expansion, Fig. 3a, and 4-D CT imaging and modified expansion, Fig. 3b.

Fig. 3 also shows the impact of using 4-D CT on better conformity of the plan, less hot area and reduction of the lung dose. In addition, for this case, lower dose was delivered to the
spinal cord. The dose to the lung was scored at four volume points; the mean lung dose (MLD), the dose to the 20% volume, dose to the 30% volume and dose to the 40% volume. These data were taken from the DVH information. Overall, there was a 20% reduction to the lung dose by using the MIP volume for expansion, Table 2. Table 2 reflects the data of the case shown in Fig. 3. In addition, the lung volume receiving 20% of dose, $V_{20}$, was also scored. For the same case, $V_{20}$ reduced from 210 cc down to 130 cc, a 38% reduction in lung volume receiving 20% of dose.

To summarize, the use of 4-D CT imaging technique enabled us to reduce the expansion margin for PTV, which reflected in about 50% reduction in PTV volume, while still maintaining accuracy in targeting a moving tumour. The dose to the lung was subsequently reduced. Better conformal planning and better sparing of normal tissue was achieved.

![FIG. 1a. GTV at exhalation.](image)
![FIG. 1b. GTV at inhalation](image)
![FIG. 2. MIP volume.](image)

**TABLE 1. CHANGES IN VOLUMES**

<table>
<thead>
<tr>
<th></th>
<th>Free-breathing CT</th>
<th>4-D CT</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>GTV volume, cc</td>
<td>18</td>
<td>24.2</td>
<td>+34.4</td>
</tr>
<tr>
<td>PTV</td>
<td>267</td>
<td>128</td>
<td>-52</td>
</tr>
<tr>
<td>Uninvolved lung volume, cc</td>
<td>1049</td>
<td>1130</td>
<td>+7.7</td>
</tr>
</tbody>
</table>

**TABLE 2. CHANGES IN LUNG DOSE**

<table>
<thead>
<tr>
<th>Lung volume</th>
<th>Dose 4-D CT plan</th>
<th>Dose Conv. Plan</th>
<th>% reduction in dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>40%</td>
<td>497 cGy</td>
<td>628 cGy</td>
<td>20</td>
</tr>
<tr>
<td>30%</td>
<td>640 cGy</td>
<td>793 cGy</td>
<td>19</td>
</tr>
<tr>
<td>20%</td>
<td>1300 cGy</td>
<td>1430 cGy</td>
<td>10</td>
</tr>
<tr>
<td>MLD</td>
<td>624 cGY</td>
<td>784 cGy</td>
<td>20</td>
</tr>
</tbody>
</table>
FIG. 3. The left figure shows the isodose for a conventional plan whereas the right side shows the isodose for 4-D CT plan. The comparison shows that better conformality and less hot area are achieved with 4-D CT imaging.

REFERENCES


The role of deep inspiration breath hold with active breathing control and image-guided radiation therapy for patients treated with lung cancers

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To evaluate the impact of moderate deep inspiration breath hold (mDIBH) using an active breathing control (ABC) apparatus on heart, spinal cord, liver and contra lateral lung doses and its volumes compared with free breathing (FB) with lung cancer irradiation.

One of the main benefits of the Active Breathing Co-coordinator is that it is not only useful for tumour immobilization but can also shift the normal structures out of the high dose region. Eleven lung cancer patients (three left sided and eight right sided lesions) with Stages I–III underwent standard FB and ABC \cite{1} computed topographic (CT) scans in the treatment position. This can be achieved by applying respiratory manoeuvres, such as moderate deep inspiration breath hold (mDIBH), during which the threshold volume utilized is defined as 75–80\% of the maximum aspiratory capacity. Applying mDIBH technique increases the total volume of the lungs, moving the chest wall anterior and the diaphragm inferior. All patients received radiotherapy in ABC. 4-D CT works by collecting the images in the specific phases of the respiratory cycle. Daily patient position can be corrected based on accurate 4-D data at the time of radiation delivery.

In lung cancer patients this has been shown to significantly decrease the dose to the spinal cord, due to the anterior movement of the tumour and isocentre away from the spinal cord. In addition, the increased lung volume reduces the dose received by the healthy lung tissue by moving the lung out of high dose region and decreasing the lung density. Five to seven, 6-MV photon beams with suitable gantry angles were designed according to the tumour location to conform to the PTV while sparing as much heart, spinal cord and contra lateral lung as possible. Transverse CT slices and digitally reconstructed radiographs (DRR) from the BEV were used to optimize field placement \cite{2}.

For eleven patients, treatment planning using mDIBH CT data with IMRT was then reoptimized on the free breathing data set for comparison. Dose–volume histograms for the planning target volume (PTV), heart, liver contra lateral lung and spinal cord were analysed. The studied parameters of the different plans for each patient were evaluated based on the minimum, mean and maximum difference, the range of difference, and the \textit{p} value using two-tailed paired \textit{t} test assuming two equal means. Most interesting things like changes in volumes of lungs, heart and liver were recorded.
The range of mean difference in dose (cGy) to the heart for 11 patients were 42\% (p<0.39) to -352.03 \% (p<0.1573) with ABC Technique when compared with free breathing IMRT. The volume of heart in 11 patients varied from -49.46\% to 25.31 \% (p<0.4191) in ABC compared to free breathing. In case of left lung and right lung the volume increases to 44\% and 41\% respectively. The minimum, mean and maximum difference in dose to the left lung and right lung are -175\% to -56.2 \% (p<0.0455), -65.27\% 14.83\% (p<0.1824), -21.75\% to 8.45\% (p<0.04266) and -100\% to 80\% (p<0.1918), -99.39\% to 21.6\% (p<0.0368) and -19.6\% to 21.7\% (p<0.1918), respectively. Similarly spinal cord mean dose difference was -30.94\% (p<0.041) in ABC technique and the maximum dose difference was -19.4\% (p<0.01366).

After this study on 11 patients, we can conclude that IGRT with ABC significantly reduces the mean dose to heart, contra lateral lung, spinal cord and liver compared with FB. The results were dependent on anatomy. There is no consistent data as shown in Fig. 2. ABC technique can immobilize the tumour position but there is no guarantee that it can save critical structures compared with FB. This is due to the possibility of critical structures coming into the field for more time in ABC technique. So it is always better to plan in both FB and in ABC to finalize the treatment modality.

**FIG. 1. Patient with active breath control system.**

**FIG. 2. Dose to the heart in FB and ABC.**

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Implementation of IMRT techniques in treatment of head & neck tumours

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Intensity modulated radiotherapy (IMRT) allows dose to be concentrated in the tumour volume while sparing normal tissues. However, the downside to IMRT is the potential to increase the number of radiation-induced second cancers because more fields are used, involving a bigger volume of normal tissue exposed to lower doses. It has been estimated that IMRT may double the incidence of solid cancers in long term survivors. This may be acceptable in older patients if balanced by an improvement in local tumour control and reduced toxicity.

During the trial period from 2005 to 2006, we fully treated by IMRT a group of 16 patients (9 men, of median age of 50.6, range: 36–65 years; 7 women, median age of 48.0, range 31–70 years) with brain tumour, head & neck and prostate cancer. IMRT was chosen for those cases where the target primary site location was close to the dose-limiting areas (confirmed by CT and MRI), in particular.

(1) Brain structures: meningomas (8 patients, Gr. 1–2), anaplastic astrocytomas, oligoastrocytomas and chondromas.

(2) Head & neck structures: olfactory neuroblastoma, orbital lymphoma, palatimollae tumour, and tumour orbitae.

The average dose for brain tumours was at the level $T_{Dmean} = 46.31$ Gy and $T_{Dmax} = 64.90$ Gy, respectively, with $2 \times$ IMTR boost at the level of TD 36.0 and 12.0 Gy, and $1 \times$ IMRT of prostate at the level TD 70.0 Gy. The follow-up for surviving patients treated by IMRT from the initiation of therapy is very positive. The stationary MRI findings (after three and six months) without any progress were confirmed for treated patients and only one case of the patient with local failure was presented. No ischemic cerebral symptomatology has occurred without any objective complications.

Furthermore, the patients reported subjective improvement after therapy. It is important to note that IMRT was applied only for a limited number of treatments due to higher time consumption of the delivery procedure which includes also extra time required for re-setup of the LINAC system. However, the situation will be changed very soon upon installation of an additional LINAC machine at St. Elisabeth Cancer Institute.
Session 6:
Keynote Lectures
IMAGING IN RADIOTHERAPY PLANNING
PET/CT: Is there a role in RT planning?

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Radiotherapy (RT) plays an important role in the treatment of many curable cancers. Advanced RT procedure such as intensity modulated radiotherapy (IMRT) and image guided radiotherapy (IGRT) permit to deliver higher doses to the tumour and increase normal tissue sparing. To exploit these advances, accurate patient selection and target definition is essential.

Potentialities of PET/CT in RT include: a) detection of lesions not apparent on CT or MR, such as unsuspected lymph nodes or distant metastases; b) prevention of irradiation of tissues not containing tumour, such asatelectasis; c) definition of different biologically diverse tumour subvolumes that can be irradiated with different RT doses; d) evaluation of tumour response during and after treatment; d) development of adaptive RT techniques with possible changes to target volumes during treatment course [Ling CC, 2005; Weber WA, 2006].

18F-fluorodeoxiglucose (FDG) is the most common tracer in radiation oncology [Schoder H, 2004]. However, different PET radiopharmaceuticals can be used for RT purposes. 11C-methionine is widely used for brain tumours and it has been proposed for delineating brain tumour contours [Grosu AL, 2005]. 11C-choline is indicated to restage prostate cancer [Krause BJ, 2008]. Other tracers for cell proliferation (e.g. 18F-fluorothymidine) or tumour hypoxia (e.g. 62Cu-ATSM) seem promising but are still under investigation [Chen W, 2005; Chao KS, 2001].

PET/CT imaging protocols in RT planning must be rigorous and consistently applied. Patient positioning tools (firm flat couch top, immobilization devices, laser beams), and quality control processes, especially for geometrical alignment, software for contouring and image quantification are mandatory and must be linked with the RT planning system.

The majority of published studies on RT planning involve FDG and NSCLC [Ashmalla H, 2005]. PET dramatically reduces both the inter and intra-observer variability in target definition.[Caldwell CB, 2001]. Different strategies have been proposed for target volume delineation. Visual tumour contouring is commonly used in clinical practice, but guidelines are not available. A detailed protocol should be followed, keeping as reproducible as possible the parameters influencing the contours of the tumour on PET. The limit of visual assessment is the grade of reproducibility and the inter-observer variability that can be still significant. In order to reduce such errors, automated or semi-automated methods have been proposed. SUV-based contouring consists in choosing a percentage of the maximum SUV value or an absolute SUV value as cut-off for target definition [Hong R, 2007]. However SUV measurement can be unreliable and can be limited by problems of accuracy and reproducibility [Bayne M, 2004]. Thresholding approach consists in outlining the lesion as the region encompassed by a given fixed percent intensity level relative to the maximum activity in the tumour. A threshold of 40–50% has been studied, and significant errors in the volume estimation may occur [Nestle U, 2005]. Background cut-off is another automated approach and consists in defining a cut-off with respect to the background and contouring the region
C. Messa

with intensity above the cut-off. This method is limited by the heterogeneity of the lesion and the statistical noise [Lodge MA, 2006]. Source/background algorithms have been explored in phantom studies [Daisne JF, 2003]. The availability of multiple automated methods for tumour contouring and the absence of any reliable intercomparisons make it difficult to recommend any single technique.

Several studies reported the role of PET in RT planning for specific tumour types. In NSCLC FDG-PET should be used to select patients for treatment with definitive RT. PET frequently detects unsuspected metastases (>20% of pre-PET stage III) and identifies patients with advanced locoregional disease unsuitable for radical RT therapy [Vansteenkiste J, 2004]. Inclusion of PET in staging work-up improves the apparent survival of patients treated with RT or RT and chemotherapy [MacManus MP, 2002].

PET significantly changes the target volume definition either in case of detection of unsuspected lymph nodes inducing a definition of a larger tumour volume or in case of atelectasis allowing a smaller volume of lung to be treated. In lung cancer PET can also be used to define the tumour movement: it is performed over many respiratory cycles and provides an image of the lesion representing the integral over the whole volume within which the lesion moves. 4-D PET/CT protocols are under investigation and seem to reduce the motion smearing, increase the SUV and tumour detectability, improving the accuracy in PET/CT coregistration [Nehmeh SA, 2004; Pan T, 2005].

The greatest impact of PET in head and neck cancer usually results from changes in nodal status [Schwartz DL, 2005] and/or detection of distant metastases. However, FDG-PET-based RT planning is not yet ready for routine clinical practice. PET is used to select lymphoma patients for RT and to delineate RT fields [Yahalom J, 2005]. FDG-PET is significantly more accurate than CT in both staging [Wirth A, 2002] and treatment response-assessment [Divgi C, 2005], in both Hodgkin and non-Hodgkin lymphomas. PET commonly influences RT fields in lymphoma by upstaging small nodes or by demonstrating disease in sites where low lesion/background contrast limits the efficacy of CT. PET can have a significant impact on design of involved RT fields in Hodgkin lymphoma [Hutchings M, 2007]. In esophageal carcinoma PET can improve the accuracy of RT planning [Duong CP, 2006] being more accurate than CT for nodal and distant metastases assessment [Choi JY, 2000] [Van Westreeneen HL, 2004]. A prospective trial of PET in RT planning for esophageal carcinoma [Leong T, 2006] showed that PET had a significant impact on GTV and PTV. PET often prevented geographic miss by identifying unsuspected lymph node involvement.

In conclusion, there is a strong case for the routine use of FDG-PET in RT planning for NSCLC. The use of PET for RT purposes in other malignancies should be cautiously considered, although there are still limited supporting data. At present, there are no compelling data to prove that patient outcomes are superior as a result of the use of PET in RT planning. Absolute proof of the superiority of PET-based RT would require randomized trials.
New advances in CT: Dose reduction and functional imaging

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The advent of rapid continuous CT scanning with slip-ring technology in modern day CT scanners has enabled the technique of dynamic contrast enhanced CT scanning (DCE-CT), or CT Perfusion, to study tissue hemodynamics (blood flow) and the transport of blood borne inert iodinated contrast agent into the interstitium (vascular permeability). These physiological (functional) processes are important in the diagnosis and treatment of stroke, cardiovascular disease and cancer, the three main killers in the world.

In this lecture, the focus is the application of CT Perfusion to cancer, in particular, tumour associated angiogenesis.

Tumour angiogenesis is important in neoplastic development, progression and invasion and targeting angiogenesis has led to the development of a totally new class of anticancer drugs. To study the effects of antiangiogenic and antivascular agents as well as the newer molecularly targeted cancer drugs, methods for the evaluation of angiogenesis is required. CT Perfusion functional imaging is ideally suited for measuring blood flow and vascular permeability (Figs 1 and 2) because such a study can be performed with very simple procedures and can be incorporated into the routine monitoring protocol of treatment response to angiogenesis inhibitors either in pre-clinical or clinical studies. Furthermore, the inherent quantitative nature of CT images allows more realistic tracer kinetics modelling to be applied to derive quantitative maps of blood flow, blood volume, mean transit time, and vascular permeability from a single CT Perfusion study.

One of the critical limiting factors in the adoption of CT Perfusion functional imaging is the radiation burden. In our implementation, the effective doses for a CT Perfusion brain and liver study, for example, can be as high as 5.9 and 21.3 mSv, respectively, when 4 cm of the tissue is scanned with a 64-slice CT scanner.

We investigate the use of adaptive statistical iterative reconstruction (ASIR, GE Healthcare) and a statistical image filtering technique to reduce image noise in the DCE-CT images and hence radiation dose to patients in CT Perfusion functional imaging.

In a study of four brain tumour patients, our results showed that ASIR can reduce the effective dose of a CT Perfusion brain study by four times (5.9 vs 1.5 mSv) relative to the standard technique without affecting the quality of functional maps in both grey and white matter (Fig. 3). The low effective dose made possible with the application of ASIR and statistical image filtering will increase the use of CT Perfusion functional imaging in oncologic studies.
FIG. 1. Contrast enhanced CT scan of a glioblastoma multiforme patient showing the tumour in the right parietal/occipital region. There was also extensive edema surrounding the tumour.

FIG. 2. Contrast enhanced CT (CECT) and CT Perfusion functional maps: blood flow, blood volume and vascular permeability (PS) of the same glioblastoma multiforme patient as in Fig. 1 before (top row) and one week after (bottom row) radiation treatment. The functional maps are quantitative and display blood flow and PS from 0–200 ml-min\(^{-1}\) (100g\(^{-1}\)) and 0–60 ml-min\(^{-1}\) (100g\(^{-1}\)), respectively, and blood volume from 0–10 ml (100g\(^{-1}\)) using a rainbow color scale.
FIG. 3. Functional maps from CT Perfusion functional imaging studies performed at two dose levels: 80 kVp and 200 mA (high dose) and 80 kVp and 50 mA (low dose) on a patient with a meningioma at the skull base. The first and second rows are images from the high and low dose study, respectively; while on the third row are images from the low dose study processed with ASIR and a statistical image filtering technique. While the quality of the CECT image and blood flow and blood volume map from the low dose (50 mA) study was inferior, ASIR and the statistical image filtering technique are able to restore the quality of those images to be similar to those from the high dose (200 mA) study.
Functional image-based adaptive IMRT: Dream or reality?

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Session 8a:
CURRENT TRENDS IN BRACHYTHERAPY
Current issues and trends in brachytherapy: A medical physics perspective

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Modern brachytherapy cannot be compared with the practices of the early use of $^{226}$Ra sources, with experience that commenced a century ago. Artificially produced radioactive sources such as $^{192}$Ir, $^{60}$Co, $^{125}$I and several other source types have totally replaced its use. Many other developments have followed, of which the use of afterloading devices (radiation protection) and the concepts of dosimetry “systems” (consistency in treatments) are most important. Brachytherapy relies on a few simple concepts, summarized as: dose delivery with sources close to or in the target (intracavitary, interstitial), high dose fall-off to surrounding tissues (inverse square law), and a wide choice of dose delivery regimes (choice of dose and dose rate). Its strength therefore lies in the relative sparing of normal tissue while depositing a high radiation dose directly inside the target. Often, margins (CTV=PTV) are not applied as the source and the target are interconnected (no relative movement).

Brachytherapy is often applied in combination with other modalities, often as a boost delivery technique. The present era is challenging, not only for brachytherapy. Conformal radiotherapy and IMRT, stereotactic approaches, and as a latest challenge (or threat?), particle therapy has come into the field, not to speak of the developments in medical oncology and surgery. So the competition is strong! Another observation can be made from the point of view of economics. As brachytherapy is performed with much less expensive equipment, the commercial interest in research efforts is lower than for developments in, for example, external beam therapy. Developments that took place in recent decades with brachytherapy often followed similar concepts as previously applied for external beam therapy. Due to increased speed of technological developments, however, this may no longer be the case. Companies selling dedicated brachytherapy equipment put all effort in inclusion of all modern concepts. They have quite a bit of competition themselves now and try to define their own unique selling points.

Still, the question is if such technological developments will really change the face of brachytherapy. For clinicians in the field, it is easy to produce a list of all what is happening. On one side we see the efforts of the vendors to load their equipment with other sources than the well known HDR or PDR $^{192}$Ir source types. One of the reasons is the use of lower photon emitting sources in afterloaders to have a better radiation protection ($^{169}$Yb, $^{170}$Tm) or the use of $^{131}$Cs as a replacement for $^{125}$I or $^{103}$Pd seeds. Another approach is to use a new source design with an older radionuclide, $^{60}$Co, as this would lead to a much less frequent source exchange; attractive in quite a lot of developing countries worldwide. New types of surface
applicators are designed for specific applications, e.g. to the skin (Leipzig\textsuperscript{1} applicator) or for deeper treatments into tissue, e.g. to the breast (AccuBoost). Other applicators are designed to create a better dose distribution than is possible with the original MammoSite breast balloon technique (improved skin sparing, ClearPath, Contura/SenoRx Inc). Construction plastics of many new applicators allow steam sterilization, thus avoiding the costly gaseous sterilization procedures. We see improvements in afterloading techniques, not only in the fact that treatment plans and treatment reports can now be exchanged using the hospital network and reports can be loaded into the electronic patient files. But also in the fact that a treatment plan created by a TPS from company A can be created for the afterloader of company B and vice versa (Dicom standard for brachy). Tools are developed for easy and quick treatment planning, especially in the programming phase where the applicators are reconstructed: catheter recognition, autoreconstruction, atlas of applicators, inverse treatment planning tools. And we see the first steps towards clinically acceptable improved algorithms for dose calculations, “beyond TG-43”. These steps are based on MC work and should allow to take into account shielding effects and lack of scatter due to “missing tissue” situations. Robotics is still in the early stages, but forms an area that needs our attention as it can improve consistency in needle placement and coherence between plan and realization of an implant. All these issues are high technological challenges that in some way will change the brachytherapy practices in our clinics. Still, does it really change the face of brachytherapy?

The main issues that are seen under the current trends and developments are, in contrast to this high tech stuff, rather trivial but utmost essential. We name two of them.

1. Use of imaging has for a long time been disregarded in brachytherapy. Orthogonal X ray has been the basis of reconstruction of any application, with an essential limitation: we do not know the exact size and place of the tumour as these X rays do not reveal this information. Ergo, we use points in space defined by our “systems” in order to be as much as possible consistent in our treatments of groups of patients. Very slowly we see the prospect of modern imaging with 3-D info, using ultrasound in prostate treatments and CT and MRI scanning in many other body sites. The superior tumour contrast of MR in combination with CT allows target and tumour volume definition instead of “points”. Dose can be prescribed at the tumour surface and volumetric (DVH) parameters can be used for evaluation. We need time to develop our routines, we need adaptable applicators to create more flexibility to apply dose where needed (e.g. needles added to gynae applicators). In the end, this will definitively lead to better treatments and improved results \cite{1}.

2. It is not only logical but also essential that the older ICRU recommendations 38 \cite{2} and 58 \cite{3} are rewritten to accommodate to this new approach. ICRU reports have a tremendous influence on clinical practice. Although the editors of those reports well understood the need of proper tumour coverage with brachy implants, the end results of their recommendations were by necessity very much focused on the geometry of the implant instead of the tumour to be treated. The reports recommend recording and reporting of dose to points, inspection of planar dose distributions. Recommendations to follow the implantation rules of the “systems” such as the Paris system. How to deal with 3-D information is hardly described, not surprisingly in an era where use of CT or US was far from common. Rewriting of these reports however should not lead to disregarding the essentials of the systems. For example, one of the trickiest things to do

\textsuperscript{1} Note that commercial names and products are mentioned in this abstract as examples only, without the intention of being complete or offering endorsement.
J.L.M. Venselaar and M.J. Rivard

is to allow large contiguous volumes of high dose in an implant as a result of an inverse planning outcome based on the outer contours of a surface dose prescription.

These two points are of course closely interrelated. But these issues will make the difference in future brachytherapy practices, more than any of the above listed technological improvements. A new ICRU 38 revision committee has started. It seems to be a matter of time to start a new ICRU 58 revision committee.

REFERENCES


Potential and limitations of image-guided brachytherapy in cervical cancer

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New directions in prostate brachytherapy

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Excellent long term tumour control can be achieved with brachytherapy, and this approach is considered a standard treatment intervention associated with comparable outcomes to prostatectomy and external beam radiotherapy for patients with clinically localized disease. In general, for patients with low risk disease, seed implantation alone (i.e. monotherapy) achieves high rates of biochemical tumour control and cause-specific survival outcomes. For those with intermediate risk and selected high risk disease, a combination of brachytherapy (low dose rate permanent interstitial implantation, or high dose rate brachytherapy via after-loading catheters) with external beam radiotherapy is commonly used.

Significant improvements over the years have been made in treatment planning and the technical delivery for prostate brachytherapy. What can we expect of this treatment intervention in the years ahead? In which areas do we expect improvements? This review will assess our current understanding of LDR and HDR brachytherapy and highlight anticipated future directions for this treatment intervention in the management of localized prostate cancer.

Enhanced image guided approaches low dose rate seed implantation

During the last 15–20 years there have been significant improvements in the technical aspects of delivery of prostate brachytherapy which have made the procedure more precise and effected a consistently more reliable form of delivering a high dose of radiation to the prostate gland. Transperineal ultrasound guided approaches have facilitated image guided placement of the seeds and are attributed with improved long term outcomes and reduced treatment related complications. More recently, intra-operative planning is used that relies on three dimensional anatomic reconstruction of the prostate in real time and incorporation of similar inverse planning and sophisticated optimization algorithms used for IMRT to rapidly create a plan in the operating room. These approaches have further improved accuracy and consistency of the dose delivery to the target with a concomitant reduction of dose to the urethra and rectum. Notwithstanding these improvements, current approaches are not able to precisely identify the deposited seed coordinate for every seed implanted within the prostate gland. This is due to limitations of visualization of individual seeds on ultrasound due to hemorrhage artifact and suboptimal resolution of currently available ultrasound systems. As a result it is estimated that 15–20% of prostate implants performed by experienced practitioners will yield suboptimal coverage of the prostate gland with the prescription doses or slightly higher than anticipated doses to the rectum or urethra. Several approaches are currently being refined using intraoperative imaging to give the operator the precise coordinates of deposited seeds in an ongoing fashion during the actual implant procedure. Such approaches are anticipated to substantially enhance the accuracy of the implant and further reduce the dose to normal tissues.

Prostate brachytherapy as an effective tool for achieving dose escalation

The two most commonly used radioisotopes for permanent seed brachytherapy are iodine-125 and palladium-103. Preliminary results of a randomized prospective trial have not shown to date any significant toxicity or tumour control differences between these isotopes. Cesium-131 has a half life of 9.7 days and delivers 90% of the prescribed dose to the prostate in 33 days compared to 58 days for palladium and 204 days for iodine-125. Whether there are ultimately any differences

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in tumour control outcomes or long term morbidity between any of the isotopes is unknown at this time. Nevertheless it appears that brachytherapy may represent one of the most potent tools available to the radiation oncologist to achieve effective escalation of the radiation dose. Based on several published randomized trials and long term outcomes of single institution studies, the delivery of a high radiation dose is critical in the management of intermediate risk and selected high risk prostate cancer patients.

Combination of brachytherapy and external beam radiotherapy is generally considered a more suitable treatment option than implantation alone for patients with higher risk disease. The combined approach effectively delivers an escalated dose of radiation which has been estimated to have a biologic equivalent that well exceeds 100 Gy equivalent of external beam radiation. Combination approaches have been delivered in various ways and treatment schemes. In general, 45 to 50 Gy of EBRT is delivered using conventional or conformal-based techniques to the prostate and periprostatic tissues. If a low-dose-rate boost is used, the brachytherapy prescription dose is 90 Gy for $^{103}$Pd implants and 110 Gy for $^{125}$I implants. In the absence of clinical trials comparing HDR brachytherapy boosts versus low-dose-rate boosts, or the optimal sequence of therapy (brachytherapy boost preceding EBRT or vice versa), or the preferred isotope to be used for combined modality therapy, there is no definitive evidence demonstrating the superiority of a particular treatment strategy over another. Nevertheless, the combined modality approaches appear to be associated with superior tumour control outcomes compared to external beam radiotherapy with nadir PSA levels of <0.5 ng/ml often achieved reflecting effective prostatic tissue ablation.

A phase III trial, RTOG 0232, has recently been activated that compares permanent source brachytherapy as monotherapy to the combination of external beam treatment followed by brachytherapy for patients with intermediate risk prostate cancer. The primary endpoint of this study is survival outcome, and secondary endpoints include PSA relapse-free survival, distant metastases-free survival, and quality of life endpoints. Eligibility criteria for this study include: clinical stage T1c-T2b, Gleason <7 with PSA 10-20 ng/mL or Gleason 7 with a PSA <10 ng/mL. The AUA voiding symptom score should be $\leq$15 and prostate volume <60 grams.

HDR brachytherapy offers several potential advantages over other techniques. Taking advantage of an afterloading approach, the radiation oncologist and physicist can more easily optimize the delivery of radiation therapy to the prostate and reduce the potential for under-dosage (“cold spots”). Further, this technique reduces radiation exposure to the radiation oncologist and others involved in the procedure compared with permanent interstitial implantation. Finally, HDR brachytherapy boosts may be radiobiologically more efficacious in terms of tumour cell kill for patients with increased tumour bulk or adverse prognostic features compared with low-dose-rate boosts such as $^{125}$I or $^{103}$Pd. Current approaches are employing HDR monotherapy for intermediate risk patients, avoiding the need for supplemental external beam radiotherapy. The five year outcomes of such approaches are promising and appear to be comparable to the outcome of other treatment interventions.

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A prospective randomized study comparing three-fraction regimen of HDR brachytherapy for cancer of uterine cervix stages IIB and IIIB

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Purpose

Cancer of uterine cervix is one of the leading malignancies affecting South African female population. In recent years, High dose rate (HDR) brachytherapy in combination with external beam radiotherapy (EBRT) has been popular in the management of uterine cervix. Various fractionations regimens of HDR are used in different centres. This randomized prospective study reports the treatment results and incidence of bladder and rectal complication following radical treatment of carcinoma of cervix with standard EBRT and 2, 3, 4 fractions of HDR brachytherapy.

Method and material

Sixty-six patients with biopsy proven stage IIB and stage IIIB cancer of cervix were recruited. All patients were treated radically and received EBRT 50 Gy in 25 fractions at 2 Gy per fraction. Almost all patients received concomitant cisplatin 80 mg/m², three times weekly. Patients were then randomized into one of the three-fractionation regimens of HDR: 6.5 Gy×4; 8 Gy×3; and 9 Gy×2. Each HDR application was evaluated separately. AP and lateral radiographies were taken. ICRU rectum, bladder, and PSW reference points were identified. Using the linear quadratic formula, the biologically effective dose to the tumour using an α/β ratio of ten (Gy₁₀) was calculated to point A in order to determine a dose response relationship for local control. The biologically effective dose (BED) to organs at risk was calculated using an α/β ratio of three (Gy₃), and this was used to assess the complication rate of the treatment. Patients were assessed by SOMA Lent toxicity criteria during the course of treatments, at six weeks and finally at six months when Pap smears were performed to assess local control.

Result

Sixty-six patients were entered in this study. Fifty-nine of them completed chemoradiotherapy, and attended both six weeks and six months of follow up and evaluation. The mean age of the patients was 51.6 years and the mean duration of the treatment was 47.2 days. Of the 59 patients who completed treatment and had six months follow-up, 29 patients were stage IIB and 30 were stage IIIB. The overall complete response rate for the whole group was 88%. The response rate was 90% in Arm I, 85.7% in Arm II, and 88.8% in Arm III, which was not statistically significant (p=0.463). The following prognostic factors were analysed to assess their influence on local control and found to be not significant: stage (IIB vs. IIIB)(p=0.995), age above and below 50 years (p=0.532), treatment duration (p=0.6608), and number of fields used (p=0.603). The adverse effects of radiation-induced toxicity depended on age group (p=0.01), number of fields (p=0.001), and BED Gy₃ dose to organ at risk were statistically significant (P=0.001). The rectal, grades 3 and 4 radiation induced toxicity were
observed to increase when the BED Gy\textsuperscript{3} dose was above 105 Gy\textsuperscript{3}. Similarly, bladder grade 3 and grade 4 toxicity rates were increased with BED Gy\textsuperscript{3} dose of 120 Gy\textsuperscript{3} (p=0.001).

**Conclusion**

Limiting the number of HDR brachytherapy application from three or four to two fractions has the potential benefit of improved patient compliance. Two HDR applications of 9 Gy each is most cost effective and resource sparing to the institution compared to 3 or 4 insertions. In a country with limited resources, decreasing the waiting list and avoiding cost of hospitalization can be achieved by using two fractions of HDR.

The study proved that 9 Gy\texttimes{}2 fx HDR brachytherapy with concomitant chemo-radiotherapy was equally effective in local control and treatment related complication compared to other two fractionation regimens during the six month follow-up.

**REFERENCE**


Session 8b:
HOW TO SET UP A QA PROGRAMME
Current trends in QA for radiotherapy

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This opening presentation of the session will discuss the use of risk management tools from the industry applied to the process of radiation therapy. Creating and managing a system based on these principles together with analysis of risks and hazards using tools from well known high security areas, e.g. aviation and nuclear power stations will be presented.

The creation starts by identifying the process and its main outcome and, for this, one may use a process tree model. Eventual sub-processes have to be identified too. When the process tree has been created it will be easier to systematically identify major hazards during normal and abnormal activities as well as assess their likelihood and severity. This can, for example, be facilitated with the failure mode and effect analysis (FMEA) method to identify the processes/sub-processes/steps that are more error prone, assigning risks and consequences in each step.

![Diagram of a simplified process tree for external radiotherapy. Each of the sub-processes should be further analysed for a complete tree.](image)

During the FMEA, which is a proactive method, the following questions have to be answered for every step in each sub-process:

a) what could possibly go wrong (potential failure mode)?
b) how could that happen, i.e. what are the causes that result in a failure mode?  
c) what effects would this failure mode produce (potential effects of failure)?

The purpose is to estimate consequences of a single failure of components/steps for the whole system/process. It is also possible to add actions to take and assign responsibilities to individuals/groups in the radiation therapy team.

FMEA is a systematic method to detect failure modes of parts of systems; however, it is only identifying single failure modes, not the combination of them. For the latter, other methods may be applied. The failure modes are usually put together in a table as well as the assigned probability for the failure to occur (“O”), the severity of the effects (“S”), and the probability
that the failure will be undetected (“D”). A risk priority number (RPN) is defined as the product of these three numbers. In this way one may identify the processes or steps that have to get the highest attention in the process of improving the radiotherapy process.

In the industrial world, consensus exists for the scales or quantification of these numbers. There have been efforts to implement them in the medical society, but whether or not these are applicable for radiotherapy is still under evaluation.

Having a feedback system for adverse event and potential incidents, e.g. the ESTRO endorsed Radiation Oncology Safety Information System (ROsis) — http://www.rosis.info — will facilitate the identification of the failure modes in the involved processes. Quantification of the RPN variables will also be accomplished by using incident reporting and feedback systems.

The approach of FMEA can also be used to develop and implement preventive actions and to assign responsible persons to carry out these actions. The ROSIS project has discussed this as one approach to include in a risk management system for radiotherapy. The following table is an example from this group.

**TABLE 1. AN EXAMPLE OF A FMEA ANALYSIS OF SETTING UP THE PATIENT AND DELIVER A TREATMENT AT THE INCORRECT POSITION. A LOT MORE FAILURE MODES CAN BE IDENTIFIED IN A COMPLETE ANALYSIS**

<table>
<thead>
<tr>
<th>Potential failure mode</th>
<th>Potential cause(s) of failure</th>
<th>Potential effect(s) of failure</th>
<th>O</th>
<th>S</th>
<th>D</th>
<th>RPN</th>
<th>Proposed action(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incorrect isocentre</td>
<td>Shift between reference point and isocentre not present in R/V system</td>
<td>Dose delivered to wrong volume, PTV under-dosed and/or OAR overdosed during all fractions</td>
<td>4$^1$</td>
<td>10$^2$</td>
<td>3$^3$</td>
<td>120</td>
<td>Second check of all parameters, review methods</td>
</tr>
<tr>
<td>Shift specified incorrectly in set-up instructions</td>
<td>See above</td>
<td>6$^4$</td>
<td>10</td>
<td>5$^5$</td>
<td>300</td>
<td>Training and second check of all parameters, review methods</td>
<td></td>
</tr>
<tr>
<td>Shift specified correctly but made incorrectly</td>
<td>See above</td>
<td>Dose delivered to wrong volume, PTV under-dosed and/or OAR overdosed during one fraction</td>
<td>4</td>
<td>6$^4$</td>
<td>3</td>
<td>72</td>
<td>Training, verify table position</td>
</tr>
<tr>
<td>Staff omitted to make shift</td>
<td>See above</td>
<td>2</td>
<td>6</td>
<td>10</td>
<td>120</td>
<td>Training, verify table position</td>
<td></td>
</tr>
</tbody>
</table>

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1 The value was chosen based on the assumption that this does not happen too often. Suggestion is that the data are missing once per 2,000 cases. In Lund we have about 2,600 patients annually and it seems to be an accurate number that these data get missing not more than once a year.

2 If this will be undetected throughout the full treatment the ranking of 10 may be adequate.

3 This number is incredibly hard to set since it depends very much on the clinical environment. If, for example, it is possible to acquire the patient position (treatment position) by a simple action by the therapist this can be added to the set-up and the patient will be treated “correctly” at each fraction. On the other hand since the data are missing one may step back in the process to get the correct data. Based on the latter process a low number is assigned.

4 This probably occurs much more often than the above case.

5 The delectability is definitely lower in this case compared to the first failure situation.

6 Having a lower severity for this failure mode seems appropriate since there are chances to detect this at the succeeding treatment sessions.
Looking at the analysis one realizes that the failure mode resulting in the highest RPN should be of primary concern, which in this case is the second failure mode with the wrong parameters entered into the R/V system.

An intimately related process is the Root Cause Analysis, which has for a number of years been used when an adverse event has occurred (e.g. methods like this have been promoted by the Swedish National Board of Health and Welfare). FMEA and RCA cannot be separated. FMEA seeks to know the effects of each of all possible causal failure modes. On the other hand, RCA seeks to know the causal set of each of all possible effects. Thus these methods are complementary and are therefore also the inverse of each other. The underlying assumptions are that for every effect there must be a set of causes and for every set of causes there must be some effect. FMEA is the temporal mirror of RCA reflected in the “now” moment. FMEA looks forward in time and RCA looks backwards.

Another important topic to consider is the identification of control variables (measures) of each of the sub-process. By observing at the right time what happens in a process that lead to a change, the quality responsible physicist or any member of the team responsible for the process/sub-process can troubleshoot the root cause of the variation that has crept into the process and correct the problem. Statistical process control (SPC) indicates when an action should be taken in a process, but it also indicates when an action is not required. An example is when one wishes to keep the output (absorbed dose per monitor unit) of an accelerator constant and one performs measurements at a regular interval. If one does not understand SPC concepts (the output varies in time) one might adjust the dosimetry circuits each time a deviation is detected. This type of action could be harmful and possibly generate even more variation in output. The SPC technique would account for the “normal” variation in output and better indicate when a corrective action should be taken.

The methods and approaches adopted from the non-radiotherapy world such as those discussed here will have a potential of facilitating the development and creation of systematic QA programmes that balances patient safety and quality versus available resources.
Developing a quality assurance programme for cooperative group clinical trials

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Unlike many other medical specialties, radiation therapy is extremely quantitative and objective, and consequently lends itself better than most to measurement. This provides radiation oncologists and physicists the ability to measure the quality and quantity of the therapy (radiation dose) as well as the outcome. This has allowed radiation oncologists to determine the importance of accuracy in radiation treatment delivery. However, balancing the need for accuracy with the demand for resources for a quality assurance (QA) programme is difficult.

To maintain the required accuracy in dose delivery, the entire radiation therapy process must be covered by a comprehensive QA programme. It is recognized that there is a need to evaluate the influence of different factors affecting the accuracy of radiation dose delivery and to define the actions necessary to maintain treatment uncertainties at acceptable levels.

Radiation therapy clinical trials also must be subjected to rigorous QA procedures to ensure that the results of the trials are meaningful. The Radiological Physics Center (RPC) was established in the late 1960s as a resource in radiation dosimetry and physics for cooperative clinical trial groups and the radiation therapy facilities that deliver radiation treatment to patients entered into cooperative group protocols. The primary responsibility of the RPC is to assure the National Cancer Institute (NCI) and the cooperative groups that participating institutions have adequate QA procedures and no major systematic dosimetry discrepancies, so that they can be expected to deliver radiation treatments that are clinically comparable to those delivered by other institutions in the cooperative groups. To accomplish this, the RPC monitors the basic machine output and brachytherapy source strengths, the dosimetry data utilized by the institutions, the calculation algorithms used for treatment planning, and the institutions’ QA procedures. The methods of monitoring include on-site dosimetry reviews by an RPC physicist and a variety of remote auditing tools.

The remote auditing tools include (a) mailed dosimeters (TLD) evaluated on a periodic basis to verify output calibration; (b) questionnaires to document changes in personnel, equipment, and dosimetry practices; (c) comparisons of dosimetry data with RPC “standard data” to verify the compatibility and acceptability of dosimetry data; (d) evaluation of reference cases and actual patient calculations to verify the validity of treatment planning algorithms, the consistency of their application, and compliance with protocols; (e) review of the institutions’ written QA procedures and records; and (f) mailable anthropomorphic phantoms to verify tumour dose delivery for special treatment techniques.

Chart reviews conducted by the RPC include rapid review of patient treatment plans prior to treatment, timely review of charts during the conduct of a trial, and retrospective review of patients following their treatment. The results of the reviews are provided to the study chairs, the cooperative groups, and when appropriate and constructive, to the institution.
Patient treatment audits also are essential components of the RPC’s credentialing programmes. Several cooperative groups have determined that the technologies used in certain clinical trials are sufficiently advanced to warrant credentialing of institutions that wish to participate in these trials. The credentialing procedures range in complexity from a simple registration process, to the completion of knowledge assessment questionnaires, to the performance of treatment planning benchmarks, and in certain situations, to the planning and irradiation of anthropomorphic phantoms.

The RPC maintains a database of participating institutions that includes the results of RPC on-site measurements made at these facilities. The database contains measured data describing depth dose, output factors, wedge factors, and other dosimetry parameters from photon and electron beams of several thousand radiation therapy machines. The database includes five or more consistent data sets for 82 photon beams from 48 models of accelerators. Review of these data suggests that machines of the same make, model and energy have very similar characteristics (standard deviations of ≤1%). The RPC has identified “standard data” (field size dependence, depth dose and off-axis factors) for the majority of the 82 photon beams. The RPC “standard data” are updated periodically as more measurements are made during on-site dosimetry review visits. The database has been “mined” on a number of occasions to enable the RPC to characterize parameters that are consistent from one machine to another. The RPC is presently engaged in characterizing the radiation beams in the “standard data” database using Monte Carlo calculation techniques. Preliminary investigations have shown that depth dose data and output factors can be modeled successfully using Monte Carlo techniques for several models of linear accelerator.

The RPC works with all of the NCI-sponsored cooperative groups, either directly or in collaboration with the Advanced Technology Consortium (ATC), a consortium of four QA offices funded by the NCI.
How to set up a quality assurance programme

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Proper and safe delivery of radiotherapy treatment services requires the implementation of an appropriate system of quality assurance (QA) to ensure that every procedure involved is in order and the equipment used performs according to specified quality standard. To be effective, the QA programme should be comprehensive, multidisciplinary and fully compatible with the equipment technology and treatment techniques used and designed to address the identified risks and hazards. General guidelines for implementation of comprehensive QA programmes in radiotherapy have been published by a number of institutions, e.g. AAPM Report 46. However, local standards and site-specific risks and hazards should be identified and considered when developing a QA programme. In addition, when new treatments such as three dimensional conformal radiotherapy (3-D CRT) are introduced, a corresponding redevelopment and upgrade of the existing QC protocols and procedures is necessary in order to ensure quality treatments. The key elements for successful implementation of a QA programme include (a) a well defined and documented QA organization structure with clearly defined roles and responsibility for the individual elements/teams in the system, (b) full support and commitment of the head of department and hospital management for implementing such a QA system, and (c) all the staff involved, frontline staff in particular, must be supportive of the programme and appreciate the importance and values of QA.

This presentation is based on our experience in setting up a multidisciplinary QA system in support of implementation of IMRT and other 3-D CRT treatment modalities.

The radiotherapy QA system in our institution is managed by the Radiotherapy QA Committee which is part of the Departmental Quality and Risk Management Committee. The latter in turn is part of the Hospital Quality and Risk Management Committee. Under the management of the RT QA Committee are a number of process-specific QA teams, each responsible for a defined range of responsibilities. The organization structure and generic key responsibilities of each structure element of the RT QA system are given in Fig. 1. The RT QA Committee is chaired by the head of radiation oncology, with the head of medical physics, head of radiation therapist, and a senior nursing staff as members. Membership of the process-specific QA teams is summarized in Table 1. Other relevant duty staff are co-opted to the QA teams to help in the preparation and updating of the QC protocols and worksheets as and when necessary.

Medical physicists play a key role in radiotherapy QA. They serve in the Physics QA Team and in a number of other QA teams. The Physics QA programme covers equipment facilities, dosimetry, treatment planning and dose calculation and physical aspect of RT treatments. The programme focuses on both equipment (and software) performance and processes and procedures performed by staff. In the case of equipment performance which is mainly a quality issue, an equipment-specific QA programme was designed for each key radiotherapy and physics equipment covering procurement (specification and selection), acceptance testing,
commissioning, and periodic QC. Similarly, a procedural QA was developed for each key physics and clinical (physical aspect) process, which included validation of the commissioning and integrity of a 3-D treatment planning computer system, QC of IMRT treatment plans and dose calculation, QC of treatment delivery and dosimetry. Both quality and procedural QC are equally important. The former is essential for ensuring service quality while the latter aims at reducing risk and preventing accidents due to human errors. The QC protocols should be under constant review and redevelopment to cater for new development of radiotherapy technologies and techniques. As a result of the increasing complexity of the radiation therapy process, new and more specialized QC procedures had to be developed as part of the clinical implementation process. This in turn would also require new QA equipment.

As part of the QA programme, the RT service/products are subject to both internal and external audits. An internal audit team has been established to review the appropriateness of the QA system and QC protocols and monitor the level of compliance with such protocols and the integrity of the records and documentations. An external audit mechanism has also been established to audit some key service processes and products. One of the audits conducted was the credentialling of our IMRT treatment planning and dose calculation by the US RTOG QA mechanism arranged through participation in its multi-centre clinical trials. Another external audit established was the annual audit of all the treatment equipment dosimetry calibration by the US Radiological Physics Centre.

FIG. 1. Organization structure of the radiotherapy QA system.

<table>
<thead>
<tr>
<th>TABLE 1. QA TEAMS</th>
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<tr>
<td>QA teams</td>
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<tr>
<td>Clinical management process, protocols, guidelines</td>
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<tr>
<td>Medical Physics</td>
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<tr>
<td>Patient data &amp; documentation</td>
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<tr>
<td>Treatment delivery- external beam</td>
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<tr>
<td>Treatment delivery- brachytherapy</td>
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<tr>
<td>Treatment planning and simulation</td>
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Radiotherapy is a multidisciplinary specialty, using complex equipment and procedures for assessment, planning and delivery of treatment. It requires careful and accurate application. The success of radiotherapy in terms of the probability of local control of the tumour depends upon an adequately high dose of radiation being delivered to the intended target volume, the latter being selected to provide adequate coverage of the tumour volume and any relevant surrounding margins. At the same time, the limiting factor in radiotherapy treatment is the probability of complications (i.e. radiation-induced morbidity) in the normal tissues close to the high dose regions. Such complications normally occur after a latency period and may develop progressively throughout the rest of the patient’s life (late effects).

Both of these aspects — tumour control and normal tissue complications — make strong demands on the accuracy and precision of the treatment delivered to the patient. This in turn leads to strong demands on quality assurance and quality control on all of the steps, processes and equipment contributing to this. In particular, because of the potential for long term irreversible damage and because of the delay in its possible onset, there has traditionally been an emphasis on using quality assurance in radiotherapy to prevent or minimize such damage and also on establishing careful long term follow-up. Thus quality assurance approaches have long been recognized as important and have been widely applied, but until recently they have been limited in concept to quality control of the more physical and technical aspects of the treatment process.

It is now widely appreciated that the concept of Quality Assurance in Radiotherapy is broader than a restricted definition of technical maintenance and quality control of equipment and treatment delivery and instead that it should encompass a comprehensive approach to all activities in the radiotherapy department, from the moment patients enters it until the moment they leave, and also continuing into the follow-up period. The comprehensive approach is favoured because it is recognized that partial organization of only some of the key steps in the radiotherapy process is not sufficient to guarantee to patients — and to society — that each individual will receive the best available treatment of his/her disease.

The principles and structure of a comprehensive radiotherapy quality system have been summarized in the report Quality Assurance in Radiotherapy (QART) of the Quality Assurance Committee of the European Society for Therapeutic Radiobiology and Oncology (ESTRO). Preparation of the report was supported by “Europe against Cancer”, an initiative of the European Union, which funded the discussion meetings of representatives of the National Societies of Radiotherapy, of Medical Physics and of Radiography from up to 25 countries (from EU, EFTA, Central Europe and the Mediterranean). This has ensured that from the outset, although the project has been administratively managed by ESTRO, it has been run in concert with the National Societies. The final version of the report was formally
endorsed by all participating National Societies¹ before its publication in Radiotherapy and Oncology.

The practical implementation of these principles at the departmental level, however, can prove to be difficult in the absence of appropriate guidance. The National Societies and ESTRO therefore decided to seek additional support from “Europe against Cancer”, in order to develop a fuller manual providing local quality project managers with an ad hoc methodology. The present report is the result of this initiative. It contains practical guidelines on the methodology, covering considerations of documentation, procedures and personnel, and it is illustrated by numerous examples.

¹ Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Israel, Italy, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom.
Session 9:

*Keynote Lectures*

**TRAINING, EDUCATION AND STAFFING:**
**GETTING READY FOR NEW TECHNOLOGIES**
Training and educating the medical specialist: The CanMEDS model

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Building human resources is essential to economic and social development. Whatever the stage of their development, each developing country has tried to address this fundamental issue by improving their higher education system in order to train qualified professionals in medical fields. In that perspective, an alternative to the traditional model is needed. This talk reviews CanMEDS (Canadian Medical Education Directions for Specialists) as a potential model for training and education of medical specialists. This model has addressed the concepts of “educational competency”, “outcome-based education” as the foundation of CanMEDS programme. This programme highlights the multidimensional profile and role of a medical specialist who has been educated through that model, i.e. the medical expert, professional, communicator, collaborator, manager, health advocate, and the scholar.

For each of these roles, the learning outcomes and the evaluation methods to measure them will be described. On the curriculum perspective this educational framework raises the following basic questions: What to teach? Who to teach? How to teach? How to evaluate?

BIBLIOGRAPHY


“He who can does. He who cannot, teaches.” A blueprint for the partnership between professional educators and medical education

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George Bernard Shaw’s infamous aphorism about the teaching profession has plagued this profession for nearly a century and continues to be remarkably enduring. The power of this quote reinforces the fact that fiction is not ideologically neutral and that in many cases, fiction both reflects and conveys certain sets of sociocultural values, beliefs and attitudes of society. The ideological and historical implications of this particular philosophy of the teaching profession not only contributes to the low status of teaching but also cultivates the belief that no formal training is needed to teach in any discipline.

Within the medical field, however, there has been a long held consensus that the broader functions of medical education are not so easy to learn from someone untrained in educational methods such as expertise in curriculum development, teaching methods and assessment. Recognizing not only the pressures and time constraints of academic physicians but also the lack of recognition assigned to teaching as an important professional activity, such renowned individuals as Flexner and Billroth have repeatedly indicated that there is a role for professional educators in medicine. As early as 1876, German surgeon Billroth voiced his concern about medical pedagogy and noted that the importance of form and method must not be underestimated. Since the early 1800s, there has been a call to strengthen existing medical pedagogy and to discover and implement new techniques which could serve more usefully within the already existing structures [1]. In academic hospitals where research outstrips teaching in importance, Flexner believed that research was not an end in its own right; he believed that research was important because it led to better teaching and ultimately, better patient care [2].

To incorporate professional educators within medicine education must be based upon the notion of reciprocity: “We are enriched by our reciprocate differences” (Paul Valery). A culture of reciprocity encourages educators to not simply spread new orthodoxy about the curriculum but to “strengthen pedagogy already good, to salvage techniques which could serve more usefully, and to point out principles and practices that have not yet found their way widely into medical schools” [3]. Professional educators can fulfil the role of exploring the culture of medicine by translating educational discourse into the discourse, climate and characteristics of the medical setting. As a professional educator who has been involved in radiology education, it has become important to move beyond traditional educational boundaries and to work together with the imaging physicians, residents and scientist in order
to create and nourish a shared vision of educational scholarship. Moving beyond traditional disciplinary boundaries “offers us opportunities to communicate with colleagues in differing fields with eyes that lead to discovery patterns — patterns that cannot always be seen through traditional disciplinary lenses” [4].

An anthropological search indicates that, within the medical world, there is evidence that the role of the professional educator has been recognized and that George Bernard Shaw’s demeaning image of the teacher has not been embraced. Pioneering professional educators within various medical departments throughout the world have shared their stories, struggles and successes. However, despite the evidence that these educators have played a role within medical education, the partnership between medicine and education remains, for the most part, at the pioneering stage. A critical analysis of how the partnership between professional educators and the medical world has evolved, an overview of the the issues encountered and the challenges that remain may offer a blueprint for medical departments and medical agencies to design and cultivate a partnership between professional educators and medical education.

REFERENCES

Cultivating a capacity for phronetic action to address the needs of diverse learners

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What does it mean to move knowledge about teaching into the global medical education community in ways that demonstrate complex understandings of diversity?

How might phronesis offer a unifying and essential habit of the mind that guides the work of medical educators in today’s global context?

The impetus to increase diversity in medical imaging programmes or build and maintain competent and sustainable human resources in outreach settings for ethical reasons must include a parallel commitment to develop professionals and programmes adequately prepared and supported to meet the learning needs encountered in the diverse context.

Drawing on the Aristotelean concept of phronesis, a context-dependent way of being in which one exhibits practical wisdom and ethics, the presenter will explore ways of cultivating capacity that may lead to phronetic action to address the needs of diverse learners.
Educating radiation therapists in developing countries

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The radiation oncology service in the developing world is inadequate and in many countries absent. Radiation therapists practising within a fully functional and integrated team contribute to a quality service. However, education is the key to unlock this potential.

Unless positive steps are taken, the gap between state of the art radiation oncology and the available service in a low or medium income context will widen relentlessly. Patients diagnosed with cancer are increasing, and early detection combined with appropriate treatment will lead to cure for many. In advanced diseases many will be relieved of intense suffering through the contribution that radiation oncology makes to palliative care. Hence, to effectively address the burden of cancer we need to take advantage of the developments with insight.

The first step towards a quality service is documenting available services and education or training programmes. Awareness of what the developed world presents as the standard in radiation oncology is necessary. It is also important to explore an appropriate response for low income countries to these developments. Technology developments are many but not all advances will serve the health care needs of the country in question. Very costly advances that translate into a benefit for very few people should not be adopted in favour of expenditure to help many.

Brief mention of the complex discussion of a shift from largely palliative treatment to a model that promotes prevention and cure is justified to frame the need for more extensive RTT education. Firstly there is enormous human benefit from a health care system that facilitates wellness and early detection of disease through a structure that promotes health education and good diagnosis at a wide network of community clinics close to where people live. This same infrastructure can also effectively manage long term post-treatment follow-up. There is also economic soundness in a health service that promotes effective healthcare that extends the life expectancy of many people.

RTT education

Appropriate education programmes for RTTs will establish these professionals for a role in the development of radiation oncology [1]. The role must include some level of contribution to treatment preparation and the safe and accurate delivery of radiation treatment with competence to care for the patients. Role extension beyond this is inevitable and existent but the detail will vary according to the needs.

The standard model is RTT training following diagnostic radiography. This is suitable but costs more and burdens the radiology service. The alternative of a first qualification is now common. A programme designed specifically for RTTs but not divorced from diagnostic radiography can offer the benefits of optimum utilization of the existing infrastructure but
with direct entry to radiation oncology. The IAEA syllabus for RTT education and training is a framework for both options [2].

The aim is to develop professionals with entry-level competence to practise. This needs appropriate cognitive knowledge to support practice and generic skills to enable life long learning in a changing environment. The system involves careful planning of a participatory learning environment where learning activities enable and encourage students to reach the learning outcomes [3] for the needs of the environment and that speak to development [1].

A curriculum must be designed by selecting teaching and learning activities to guide and support students to achieve the outcomes [3]. An integrated curriculum with workplace and classroom activities enables learning for acquisition, integration and transfer of cognitive knowledge, clinical competence and generic skills [1]. Alignment is essential and assessment methods must involve ‘doing’ so that students demonstrate achievement of the learning outcomes [3].

The outcomes may be met through an external provider but sustainability is more likely through the introduction of a local programme. This would include an external contribution as needed and appropriate.

Conclusion

The developing world needs to rapidly expand radiation oncology services. In planning for this the implementation of appropriate education programmes for RTTs is essential. These programmes are best offered through collaboration of higher education and health care institutions, with a conferred qualification that acknowledges the expertise and knowledge needed for practice. The RTT must be equipped to enter a complex workplace. To be successful they need learning that integrates knowledge, understanding, skills and clinical competence. They also need the opportunity to engage with an environment that develops values, attitudes and behaviours for practice as a member of an integrated health care team. RTTs must be educated for a vision of development if we want to optimally utilize the resources available, seek cost effective options for progress and offer the best to cancer patients. Once a country implements a local programme a model to utilize fellowships to supplement the local education of RTTs and build capacity of educator/trainer and student is recommended. This will spread the available resources across the greatest number of individuals and enhance the gain to the country.

REFERENCES

Training, education and staffing: Getting ready for new technologies

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In my presentation, the following items are raised and discussed.

1. The problems we are now facing with education, training and staffing of radiation oncologists, physicists and radiological technologists, especially with training of medical physicists are: (a) In what way can we develop a structured programme and employ it to our standardization of methodology of training? (b) What is the border between the baseline and advanced level? (c) What is the method of exchanging common credits between training facilities and exchange of excellent trainers? (d) How to maximize cost performance of training of medical physicists? (e) What are the instruments/machines/systems to be commonly used and shared to be used between training facilities? Double investment for expensive implementation should be avoided. (f) What is the most appropriate staffing, namely optimized mix of proper staff between radiation oncologists, medical physicists and radiological technologists? What is the appropriate number of staff per patient?

2. What is the priority of new technologies to be adopted? Highly advanced modalities such as heavy particle therapy, IGRT, PET-CT, etc. are attractive, but cost/performance such as effectiveness, efficiency and efficacy should be taken into consideration. Is the result of medical technology assessment available before adoption?

3. In what way can we make most of the IAEA? Can IAEA resolve compatibility between aiming at highly advanced technology and breaking down to comprehensive appropriate technologies? Vertical ascent to top ranked technologies or horizontal spread of bottom line layer? It is easy to say both of them should be attained. The IAEA must be relevant. For instance, a system of education/training of trainers of medical physics in Japan is now being organized through the AAPM and ACMP in USA, although the IAEA has many top ranked text books and training programmes such as TECDOCs, RCA, technical cooperation projects, etc.

4. What is the ultimate mission of qualified medical physicists? Technology is technology, and nothing more than technology. On the other hand, physics is a basic natural science, and it is also our attitude toward nature from the standpoint of human mental activities. A patient who is suffering from cancer wants to recognize the meaning of his/her life, and wants to die with true understanding of life which is based on understanding of nature by physics. Physicists have to mentally influence patients who are under cancer treatment.

5. Education and training of medical physicists in AFOMP countries [1]: AFOMP was founded in July 2000 during the World Congress in Chicago. AFOMP ETC (Education and Training Committee) and PDC (Professional Development Committee) were founded in 2001. Until the end of 2008, 12 meetings such as the Joint Symposium with IOMP, workshops and training courses were held. The main targets of AFOMP ETC are (a) To provide a common definition of a qualified medical physicist, (b) To identify the current status of medical physicists and (4) To draft regionally harmonized standards.
K. Inamura

A survey in the member countries of AFOMP was carried out during 2004 and 2005. Extracted features are: (a) difficulties in defining a qualified medical physicist, (b) diversity in level and quality of medical physicists among AFOMP countries, (c) few clinical training courses in provincial cities or less developed countries, (d) high workload of physicists with more than 500 patients per year per physicist, as indicated in a new report from BIJJ (Biomedical Imaging and Intervention Journal) [2], (e) there is less than one ROMP (radiation oncology medical physicists) per two oncologists on average, (f) one megavoltage treatment unit per medical physicist, (g) a structured clinical training programme is essential, (g) the number of patients per physicist varies more significantly (250 to 800), (h) Medical physicists share a common work environment and face similar challenges independent of the country they are working in, (i) this forms the foundation for effective communication in larger organizations such as AFOMP, (j) AFOMP has an important role to play by defining professional responsibilities and educational standard, and also by bringing physicists together and organizing conferences and workshops.

6. The action plans we are now engaged in are: (a) AFOMP activity based on financial support from AFOMP dues collected from AFOMP member countries, corporate membership and grants from IOMP must be continuously received, (b) Education and clinical training courses/workshops are to be held in both big cities and in provincial cities where there are no medical physicists.

7. Cooperation between AFOMP and the IAEA are: (a) to review, examine and endorse the technical documents (TECDOCs) published by IAEA, (b) to taget top level training tools and trainers based on a structured programme, (c) to develop tools and portfolios for completion of core competencies, (d) Under an IAEA/RCA project RAS/6/038, “Strengthening Medical Physics”, an implementation guide and an application form were sent to each of the member countries in 2007, and the applications were due at the end of 2008.

8. Struggles in AFOMP countries and proposed solutions are: As an example of struggles in AFOMP countries, Japan, has a difficult situation: (a) There is no medical physics training system although they have academic education system of high standard. In spite of this, they have so many training sites of radiological technologists numbering more than 60. (b) Contradiction and friction exist between both systems of education/training, namely radiological technologist versus medical physicist. One of the proposed solutions is the implementation of the IAEA/RCA training programme for radiation oncology medical physicists. This structured programme is a kind of standardized methodology to develop a country’s own training programme. Adoption of it is the fastest and most effective method for Japan to build up its own clinical training programme.

Work value measurement should be done by time study and evaluation of results of radiotherapy. Value added quality of life should be sought.

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IAEA support for education and training of staff in radiation oncology

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The objective of the IAEA Programme in Human Health is to enhance the capabilities in Member States to address needs related to the prevention, diagnosis and treatment of health problems through the application of nuclear techniques. This paper will address the main IAEA activities in support of education and training of staff working in radiation oncology.

Education and training of radiation oncologists and therapy radiographers

Capacity building for Member States should be addressed as an integrated package reflecting the levels of needs for each Member State or region. In this context attention should be paid to the appropriate use of needs analysis methodology developed by the IAEA Education and Training Support Group (ETSG).

One of the IAEA’s goals in its programme in radiation medicine is to enhance the capabilities of Member States to address major health problems by providing targeted education and training. For example, in 2008 the IAEA and the European Society for Therapeutic Radiology and Oncology (ESTRO) conducted a pilot training course on best practices in radiation oncology. Selected groups from eight European countries received instruction on how to create their own ‘Train the Trainers’ courses for radiation therapy technologists (RTTs) in their respective countries.

The shortage of medical specialists for cancer treatment in developing countries was the driving force behind a new distance learning course launched in 2008 entitled Applied Sciences in Oncology (http://rpop.iaea.org/RPoP/RPoP/Content/index.htm). Intended for radiation oncologists, RTTs, medical physicists and radiation biologists, this distance learning course can be used as self guided or tutored programme as a complement for the training in their countries through formal educational programmes.

The syllabi for the training of radiation oncology nurses, technicians and radiation oncologists have been produced to help Member States establish training programmes in these fields. A syllabus in radiation biology is under preparation.

Within the IAEA Technical Cooperation (TC) Programme, more than ten national and regional training courses are organized annually to implement evidence based approaches in radiation oncology. Currently there are ten active coordinated research projects (CRPs) in radiation oncology and one in radiation biology. These adapted research projects also serve the purpose of training in good clinical practice; some of the CRPs include a Ph.D. training programme.

Education and training of medical physicists

There is a shortage of clinical medical physicists especially in developing nations. In recent years, the increasing complexity of both treatment and diagnostic radiation equipment, higher expectations for good health care and implementation of more stringent radiation safety
standards and accreditation requirements have exacerbated the already critical shortage of fully competent medical physicists in the developing nations. For example, in Africa there is a need for additional 250 clinical physicists and, in Latin America 450 would be needed to effectively implement the quality assurance programmes required in radiation oncology alone.

The assistance provided by the IAEA in the transfer of technology includes a large human resource component that deals with training. This is evidenced, for example, by the fact that during 2006–2007 30 national and regional training courses were conducted in medical radiation physics (Fig. 1), which complimented technology transfers or facility upgrades. Follow-up communication with the course participants is now underway, and is being compiled in an effort to assess the impact such courses have had. In addition to this training component, the IAEA has engaged in the development of syllabi and handbooks for teachers and students to assist Member States in setting up indigenous education programmes in medical physics. The first such handbook was dedicated to radiotherapy physics and was published in 2005. To support the implementation of the handbook for the training of medical physicists, relevant educational material has been made available in PowerPoint presentation format and, along with the handbook, is available for free download from the IAEA website.

Spurred by the success of this project, two similar handbooks on medical physics in diagnostic radiology and nuclear medicine physics are in preparation.

A new Interregional TC Project on “Strengthening medical physics in radiation medicine” (INT/6/054) has recently been approved and will be implemented during 2009–2012. This project will offer a unique opportunity to respond to the growing need for an internationally accepted definition of the role of a clinical medical physicist, initiate activities that support the harmonization of educational and clinical training material, and also promote the recognition of medical physics as a profession worldwide. This new IAEA initiative is supported by the professional societies. As of January 2009, a new interregional TC project aiming at strengthening medical physics in radiation medicine has been initiated. This new project will be implemented in collaboration with international organizations (WHO, PAHO) and relevant professional societies. The shortage of clinically qualified medical physicists, insufficient training (especially clinical training) and lack of professional recognition were identified as the main problems to be addressed through this project. The project duration is five years (2009–2013) and will be implemented as an interregional project through the IAEA TC Programme. The project activities will consist mostly of coordination and working meetings. Two medical physicists from IAEA Member States will be selected as counterparts from each region (Africa, Asia and the Pacific, Europe and Latin America), and professional societies are expected to be represented at these meetings.

**FIG. 1. IAEA’s national and regional training courses in medical radiation physics, 2006–2007.**
Session 12:
IMRT/IGRT/ADAPTED RT:
CLINICAL CHALLENGE AND EVIDENCE
Overview of IMRT in head & neck cancer

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IMRT: Current state of the evidence

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IMRT offers substantial theoretical advantages in radiation dose distributions that, if they can be realized in clinical practice, may allow us to reduce the volume of normal tissues irradiated in the vicinity of the clinical target volume (CTV), in other words decrease the planning target volume so that it approximates the CTV. Realizing it in clinical practice, however, is proving rather difficult because

- physicians are often unable to delineate the correct size, shape and position of the CTV,

- the size, shape and position of the CTV often changes between fractions of radiotherapy and even during a fraction,

- treatment planning for IMRT is plagued by “cold” and “hot” spots within the CTV,

- treating accurately even a static phantom by IMRT has proven to be remarkably difficult.

For all these reasons it can not be assumed at present that IMRT helps cancer patients live either longer or with a better quality of life, or even that the outcomes after IMRT are as good as those seen after ‘conventional’ radiotherapy; the risk of ‘geographic miss’ is quite high with IMRT. Prospective studies must be undertaken to determine whether the outcomes are better or worse after IMRT than conventional irradiation.

Table 1 shows the tumour control and adverse effects after ‘conventional’ radiation therapy for many cancers commonly treated by radiotherapy (the scoring systems used did vary among the various papers; Gr=Grade). There clearly is a great deal of room for improvement in many cases. At present, however, there is no evidence from any high quality studies that IMRT helps those patients live either longer or with a better quality of life. Two small, randomized trials in early stage nasopharyngeal carcinoma showed that parotid-sparing IMRT may preserve parotid salivary flow better than conventional radiotherapy; its impact on the patients’ quality of life was less certain however and impact on tumour control as yet unknown. Two randomized trials in patients with breast cancer purportedly showed a benefit from ‘IMRT’ over conventional radiotherapy. However, the techniques employed did not rise to the level of IMRT (dose-sculpting); they only decreased the dose inhomogeneity within the breast — a laudable objective but achievable long before IMRT and practised in many institutions for decades.

In summary, IMRT is well worth studying in prospective clinical trials but should be used very sparingly in practice outside of those trials.
<table>
<thead>
<tr>
<th>Type of cancer (references)</th>
<th>Treatment (besides conventional irradiation)</th>
<th>Outcome: Tumour control</th>
<th>Outcome: Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma (13)</td>
<td>Temozolomide</td>
<td>Median survival 14.6 months. Death in 73.5% by 2 years.</td>
<td>Gr 3–4 non-hematological toxicity in 31% (most common: fatigue and other constitutional symptoms, rashes and other dermatological effects, infection, effects on vision, nausea, vomiting).</td>
</tr>
<tr>
<td>Head &amp; neck: locally advanced, unresectable (15)</td>
<td>Cetuximab</td>
<td>Median survival 49 months. Death in 45% by 3 years. Local failures in 53% by 3 years. Distant metastases in 17% by 3 years.</td>
<td>Gr 3–5 mucosal toxicity in 56%. Gr 3–5 dysphagia in 26%. Gr 3–5 dermatitis in 23%. Gr 3–5 weight loss in 11%.</td>
</tr>
<tr>
<td>Head &amp; neck: locally advanced, resected (16)</td>
<td>Cisplatin</td>
<td>Median survival 48 months. Local failures in 16%. Distant metastases in 20%.</td>
<td>Gr 4–5 non-hematological toxicity in 27% (most common: mucositis, pharyngeal/esophageal toxicity, nausea, vomiting, skin toxicity).</td>
</tr>
<tr>
<td>Larynx: locally advanced (18)</td>
<td>Cisplatin</td>
<td>Death in 26% by 2 years. Laryngectomy in 12% by 2 years. Distant metastases in 8% by 2 years.</td>
<td>Acute gr 3–4 non-hematological toxicity in 77% (most common: mucositis, pharyngitis/esophagitis, laryngitis). Dysphagia persisted at 2 years in 15%.</td>
</tr>
<tr>
<td>Nasopharynx (19)</td>
<td>Chemotherapy</td>
<td>Death in 24% by 3 years. Local failures in 14%. Distant metastases in 15%.</td>
<td>Gr 3 or worse toxicity in 76% (most common: stomatitis, nausea, vomiting, hearing loss, weight loss).</td>
</tr>
<tr>
<td>Lung: non-small cell, locally advanced (22)</td>
<td>Continuous hyperfractionated accelerated radiation therapy</td>
<td>Median survival 16.5 months. Death in 71% by 2 years. Local failures in 77%. Distant metastases in 52%.</td>
<td>Symptomatic acute pneumonitis in 10%. Severe dysphagia persisted at 2 years in 7%.</td>
</tr>
<tr>
<td>Lung: non-small cell, locally advanced (23, 24)</td>
<td>Chemotherapy before irradiation</td>
<td>Median survival 13.2 months. Death in 68% by 2 years. Local failures in 59%. Distant metastases in 39%.</td>
<td>Acute gr 3–5 toxicity in 52%. Late gr 3–5 toxicity in 3%.</td>
</tr>
<tr>
<td>Type of cancer (references)</td>
<td>Treatment (besides conventional irradiation)</td>
<td>Outcome: Tumour control</td>
<td>Outcome: Adverse effects</td>
</tr>
<tr>
<td>-----------------------------</td>
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</tr>
<tr>
<td>Lung: Small cell, limited disease (26)</td>
<td>Chemotherapy</td>
<td>Median survival 23 months. Death in 74% by 5 years. Local failures in 36%. Distant metastases in 6% (in addition to local failure).</td>
<td>Acute gr 3–5 esophagitis in 32%. Other common non-hematological toxicity: infection, fever, vomiting, pulmonary effects, weight loss.</td>
</tr>
<tr>
<td>Esophagus (27)</td>
<td>Chemotherapy</td>
<td>Median survival 18 months. Death in 60% by 2 years. Local failures in 55%. Distant metastases in 16%.</td>
<td>Acute gr 3–5 toxicity in 71% (treatment-related death due to infection in 2%). Late gr 3–5 toxicity in 37% (esophageal stricture, perforation, bleeding).</td>
</tr>
<tr>
<td>Breast: Early, post-lumpectomy (28)</td>
<td>Tamoxifen</td>
<td>Death in 7% by 5 years (2.5% due to breast cancer). Local failures in 3.5% by 8 years. Distant metastases in 4.5%.</td>
<td>Gr 3 fatigue in 1%. Gr 3 skin erythema in 1%.</td>
</tr>
<tr>
<td>Breast: Post-mastectomy (31)</td>
<td>Chemotherapy</td>
<td>Death in 53% by 20 years. Local failures in 13% by 20 years. Distant metastases in 52%.</td>
<td>Fatal cardiac toxicity in 1% at 20 years. Arm edema in 6%. Symptomatic pneumonitis in 0.6%.</td>
</tr>
<tr>
<td>Pancreas: Resected (32)</td>
<td>Chemotherapy</td>
<td>Median survival 17 months. Death in 80% by 5 years. Local failures in 23%. Regional failures in 7%. Distant metastases in 75%.</td>
<td>Gr 3 or worse non-hematological toxicity in 58% (most common: diarrhea, stomatitis, nausea, vomiting).</td>
</tr>
<tr>
<td>Prostate: Early (33)</td>
<td>Brachytherapy</td>
<td>Death in 3% by 5 years (none due to prostate cancer). Distant metastases in 1%.</td>
<td>Acute gr 3 GU bleeding/toxicity in 8%. Late gr 3 urinary obstruction/retention in 2%. Moderate/severe erectile dysfunction in 9%.</td>
</tr>
<tr>
<td>Prostate: Post-prostatectomy (34)</td>
<td></td>
<td>Median survival 15 years. PSA relapse in 50% by 10 years. Distant metastases in 50% by 15 years.</td>
<td>Toxicity in 24% (most common: urethral stricture in 18%, urinary incontinence in 6.5%, rectal complications in 3%).</td>
</tr>
<tr>
<td>Type of cancer (references)</td>
<td>Treatment (besides conventional irradiation)</td>
<td>Outcome: Tumour control</td>
<td>Outcome: Adverse effects</td>
</tr>
<tr>
<td>-----------------------------</td>
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</tr>
<tr>
<td><strong>Prostate: Locally advanced, intermediate risk (35, 36)</strong></td>
<td>Androgen deprivation</td>
<td>Death in 12% by 5 years (none due to prostate cancer).</td>
<td>Gr 3 erectile dysfunction in 26%. Gr 3 urinary bleeding/incontinence in 4%. Gr 3 diarrhea/rectal bleeding in 4%.</td>
</tr>
<tr>
<td><strong>Prostate: Locally advanced, high risk (37-39)</strong></td>
<td>Androgen deprivation</td>
<td>Death in 22% by 5 years (6% due to prostate cancer). Local failures in 2%. Distant metastases in 10%.</td>
<td>Fatal urinary stricture in 1%. Gr 3 toxicity in 2.7% (urinary stricture/toxicity or small bowel obstruction). Gr 2 toxicity in 19% (most common: cystitis, hematuria, incontinence, proctitis, leg edema). Erectile dysfunction in 68%.</td>
</tr>
<tr>
<td><strong>Cervix (42)</strong></td>
<td>Chemotherapy</td>
<td>Death in 27% by 5 years. Local failures in 19%. Distant metastases in 14%.</td>
<td>Acute gr 3–5 non-hematological toxicity in 11%. (most common: nausea, vomiting, diarrhea). Late gr 3–4 toxicity in 12% (most common: bowel and urinary effects).</td>
</tr>
<tr>
<td><strong>Endometrium: Post-hysterectomy (43)</strong></td>
<td></td>
<td>Death in 19% by 5 years (9% due to endometrial cancer). Local failures in 4%.</td>
<td>Gr 3–4 toxicity in 2% (most common: bowel obstruction). Gr 2 toxicity in 6%. Gr 1 toxicity in 16%.</td>
</tr>
<tr>
<td><strong>Rectum: Locally advanced (44)</strong></td>
<td>Chemotherapy</td>
<td>Death in 24% by 5 years. Local failures in 6%. Distant metastases in 36%. Abdominoperineal resection necessary in 17%.</td>
<td>Acute gr 3–4 non-hematological toxicity in 27% (most common: diarrhea, skin toxicity). Long term gr 3–4 toxicity in 14% (most common: diarrhea, bowel obstruction, anastomotic stricture, bladder problems).</td>
</tr>
<tr>
<td><strong>Anal canal (45)</strong></td>
<td>Chemotherapy</td>
<td>Death in 25% by 5 years. Colostomy necessary in 10% by 5 years. Distant metastases in 15%.</td>
<td>Acute gr 3 or worse non-hematological toxicity in 74% (most common: skin, GI toxicity). Long term gr 3 or worse toxicity in 11% (most common: effects on the bowel, skin, subcutaneous tissues).</td>
</tr>
</tbody>
</table>
Prescribing, recording, and reporting – ICRU considerations and recommendations for IMRT

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The advent of intensity modulated radiation therapy (IMRT) is rapidly changing the field of external treatment of cancer by ionizing radiation. Specifically, IMRT allows a dramatic improvement in the confinement of energy depositions to a completely arbitrary three dimensional region with substantial reductions to energy deposition in non-targeted regions. Avoidance of critical organs at risk, that is the delivery of non-toxic levels of energy depositions to such regions, the targeted region can experience escalated levels of radiation. The advantage for curative treatment and even palliative treatment are readily apparent. Historical evidence always indicates improved tumour control and decreased toxicity whenever such increases in the ratio of treatment volume to non-treated volume absorbed dose occurs. This is exactly the basis for using the improved physical dose distribution of energetic protons and light ions such as carbon.

For indirectly ionizing beams such as energetic bremsstrahlung beams, IMRT is accomplished most commonly by the iso-centric delivery of numerous variable intensity highly non-uniform small beams — beamlets — in a CT like fan beam geometry. Radiation treatment planning then is quite demanding and is performed in 3-D and in an optimized iterative manner based on equivalent 3-D imaging of the volume to be treated. Such advancements introduce new demands on traditional prescribing, recording, and reporting of treatments.

IMRT requires the use of accurate guidelines for the selection and delineation of the various target volumes on a volumetric basis. In addition, various imaging modalities (including functional imaging) may be used for planning not only before the start of treatment, but also during treatment to adapt the dose distribution. The concepts of gross tumour volume (GTV) and clinical target volume (CTV) have been crucial conceptually, but recommendations for outlining were needed for a practical implementation on a daily basis.

The IMRT planning process uses an optimizer, which expresses the radiation oncologist’s treatment goals. The committee has designated the set of optimizer parameters the “planning aims” to differentiate from the usual meaning of “prescription”. Multiple recent publications have pointed out that the choice for planning target volume (PTV) margin should be based on clinical QA measurements and place more emphasis on systematic uncertainties as they have more impact on the accuracy of dose delivered to the patient as compared to random uncertainties. Unlike 3-D CRT, IMRT does not deliver dose to all of the target volume at one time. IMRT delivered to moving organs may allow hot and cold spots to develop in the CTV.
even though a generous PTV margin has been drawn. IMRT has gained prominence because it allows a lower dose to neighboring sensitive normal tissues even though it may result in less dose homogeneity to the tumour.

Paramount is the movement from a single point in the target volume being the fundamental specification. In fact, a volume-based specification of absorbed dose is needed. This is most easily accomplished by employing the concept of dose-volume histograms in the context of absorbed dose at different levels delivered to certain proportions of the treated volume. By a logical and careful choice of these reporting parameters, the connection with the previously used ICRU reference point is maintained. Such a result is fundamental to making the connection between IMRT therapies and prior work, allowing the decades of clinical experience to be interpreted in the context of the new modality of IMRT.

Also tightly related to treatment specification is the inherent issue of dose inhomogeneity. IMRT treatment delivery at any instant is inherently inhomogeneous. Only when the full treatment in 3-D is complete is the absorbed dose in the treatment volume reasonably uniform. Moreover, the convolution of numerous small beamlets results in very steep doses gradients around the target volume — a blessing for tissue sparing; a challenge for target volume specification and beam deliver. However, these features place significant demands on all aspects of quality assurance from the acquisition of appropriate 3-D imaging (perhaps even 4-D imaging time information), complete understanding of the full properties of the beamlet delivery, the dose optimization process, and the treatment verification. All of these aspects are then coupled to the clinical situation, the clinical experience and the goals of the situation at hand.

The aforementioned issues and related topics are the subject of the current ICRU Report on IMRT.
Session 13a:
RADIOTHERAPY IN PAEDIATRIC ONCOLOGY
How to improve paediatric radiation oncology in Latin America

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Childhood cancers represent 2–3% of all malignant tumours and they need to be separated from adult cancers by the differences in primary sites, histological pattern and biological clinical behaviour. Although the incidence has stabilized over the past few years, approximately 260,000 new cases are diagnosed each year in the world among patients who are 19 years or younger. In developed countries paediatric cancer is the second cause of death between 0–14 years (Little, 1999) and actually the same tendency is observed in Latin America, probably due to the improvement actions against other childhood diseases. In Brazil (2005), which is with young population (38% of the population is under 19 years), cancer is the No. 1 cause of death by disease in the paediatric population (8% of all deaths). Within few variations, the same condition may be extrapolated to other Latin American countries. Treatment of childhood cancer is often regarded as one of the great successes of contemporary medicine. About three of four children with cancer could be cured with modern multidisciplinary treatment. Many reasons may point to this success: improvement on early diagnosis, more effective chemotherapy, rational use of surgery, access to a specialized treatment centre and technological facilities, more participation on collaborative protocols, best supportive care reducing the collateral effects of treatment, follow-up of treated patients and the development of programme care for the survivors. Radiotherapy has had an important role in the therapeutic approach and cure, as part of the multidisciplinary care. Unfortunately, it has also been associated with adverse late effects on growth and development, endocrine function, gastrointestinal dysfunction, musculoskeletal hypoplasia, cardiac dysfunction and second malignancies. Radiation therapy in children is a special activity with many particularities:

1. Patient collaboration depends on age. A young child may need daily anesthesia and the radiotherapy service must have adequate infrastructure to offer this.
2. Immobilization systems need to be improved to guarantee safe radiation administration.
3. Improve on simulation, lead blocks construction (mould-room technique) and dose distribution studies are mandatory to offer well defined fields, avoiding the normal tissues.
4. Parents frequently have false information about radiation therapy and they are very worried about its late effects. A clear talk with the family is even necessary to avoid doubts and to improve the relationship with the therapeutic team.
5. The radiation oncologist needs to be integrated to the therapeutic group and familiarized with the protocols rules.
6. Nurses and radiation technologists must be prepared to treat children. Patience is necessary and a smile is fundamental.

The most challenging issue in radiotherapy for childhood tumours is minimizing the late effects of therapy among survivors. Many strategies may be used to achieve this objective: to avoid radiation on therapeutic protocols, to reduce the radiation dose and to improve the use of the new technologies. The tendency to avoid or to reduce radiation dose is observed in

313
many childhood tumours, but a final dose over 40 Gy is yet necessary in many situations.

Historically, radiotherapy fields are defined in two dimensional plain radiographs based on anatomic landmarks. To account for localization uncertainties, generous margins around the tumour are used in treatment planning. For children, this type of procedure includes a large amount of normal tissue on radiation fields, with great probability to produce late effects. With advances on anatomic and functional imaging, as well as high speed computing capability, three dimensional visualization of tumours has dramatically reduced localization uncertainties. Three dimensional conformal radiotherapy (3-D RTC) may be considered the standard radiation technique and the minimal condition for radiation therapy in childhood. Multiple radiation fields may be used to converge on the target and deliver radiation doses that conform to the target’s geometric shape. Fields are chosen to provide the optimal radiation to the tumour while minimizing dose to the normal structures. The DVH generation from 3-D planning permits to know-how is the received dose by the normal tissues. This programme offers better information about radio-chemotherapy interaction, with the adoption of changes on clinical approach and measures to improve the therapeutic ratio.

Knowledge of dose distribution to the normal tissues is particularly important in children, helping to define actions to prepare the future of the cured patient. The late effects observed on survivors are dependent of 2-D techniques, from an era where the dose received by the normal tissues was not well defined. Currently, 3-D CRT is the mainstay of radiotherapy. To improve this technique is urgent for paediatric radiotherapy in Latin America. Other techniques as IMRT, stereotactic radiotherapy and photon beam therapy are also becoming more widely available with increasing utilization on paediatric radiotherapy. Many questions involve this use and we need to be critical about the real advantages of these exciting new developments in radiotherapy field. IMRT, for example, has the advantage to improve the dose distribution on the target against the disadvantage to increase the volume of low dose received by the normal tissues. The development possibility of more second primary cancer on survivors is a debate point for experts. The clinical experiences are on the initial phase and mature results are necessary to consolidate these techniques in routine practice.

Until definitive results, **3-D CRT is considered the minimal technical requirement for radiation therapy in children and efforts may be done to improve it in Latin American countries.** This is a job for all: a) for radiation oncologists, improving the knowledge about the possibilities of radiation therapy in children, the participation on collaborative protocols and integration on a multidisciplinary specialized team; b) for the institutions promoting better conditions to children cancer care and the minimal facilities to paediatric radiation therapy incorporating new linear accelerators and 3-D TPS on radiotherapy services; c) for the national and international scientific organizations and associations making easier the access to the information, to the therapeutic protocols and the guidelines for treatment of children cancer, offering refreshers courses and permanent programme of actualization and continued education.

It is mandatory to incorporate 3-D technology in clinical practice to develop QA programme and to share experiences between the many institutions and entities, improving participation of the many cases involved in this setting.

All of these are very important, but a new mentality about paediatric radiation therapy in Latin America and the developing countries needs to be definitively incorporated in the daily practice of children cancer care. “Cure is not enough. To reduce the late effects and prepare the future of the cured patient are each time more necessary”.
This is our mission at present and to the future – hands on !!!

**BIBLIOGRAPHY**


Radiotherapy in paediatric oncology

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Radiation therapy has always been one of the most powerful tools in the fight against childhood cancer. Since the middle of the last century, we have known that most paediatric tumours are exquisitely sensitive to radiation. The early application of radiotherapy alone led to the first cures of retinoblastoma, Hodgkin lymphoma, as well as certain sarcomas and brain tumours. The generous application of radiation in conjunction with chemotherapy led to further extraordinary increases in survival rates for leukemias, Wilms tumour, sarcomas, and other paediatric malignancies. Over the past 40 years, the overall cure rate for childhood cancer has climbed from 25% to 75% in the USA. With this success, however, came the knowledge that radiation can be associated with significant late effects. We now have a much better understanding of both the benefits and risks of using radiation to treat children as we seek to optimize and refine its role in curative therapy.

Leukemias constitute approximately one third of paediatric cancer diagnoses and most of these patients are successfully treated with chemotherapy alone. Central nervous system (CNS) radiation is still recommended for patients at highest risk of CNS failure and total body radiation is useful for the small percentage of patients who require bone marrow transplant. Brain tumours also make up almost one-third of paediatric neoplasms and children with most kinds of brain tumours will require high dose radiotherapy. Many of the other types of paediatric tumours (Wilms, neuroblastoma, sarcomas, etc.) also require radiotherapy as part of curative treatment.

There have been considerable advances in radiation technology including three dimensional planning, intensity modulated radiation therapy, and protons. Individual paediatric patients may or may not benefit from advanced technologies based on numerous patient and disease related factors. Examples will be illustrated.

We must also be mindful of economic and geographic limitations. On an international level, efforts should be made to increase access to therapy for all children. We may or may not be able to help a small number of additional children with $200 million proton machines in the USA but we could certainly save thousands of children’s lives in developing countries simply by providing access to treatment with a relatively inexpensive cobalt machine or discarded linear accelerator. Member States of the IAEA are in a unique position to consider these issues and to advise on potential solutions on behalf of children around the world.
Radiotherapy related sequelae in childhood cancers: The current status

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Childhood cancers account for approximately 2% of the global cancer burden. They constitute about 5.5% of all life-years lost from cancer and, from this perspective, form a significant cause for cancer related mortality and morbidity after lung, breast, and colon cancers. The incidence of paediatric malignancies is 2–3 times lower in the low and middle income countries compared to high income countries. However, this could be a reflection of the lack of adequate and reliable data from the developing world. Owing to the large population load in the less developed countries the relative cancer burden in these countries is high compared to the developed countries, and account for approximately 85% of the global paediatric cancer burden. This figure is likely to increase in the next couple of decades owing to the increasing proportion of the younger population in the developing world.

Childhood cancers are unique in terms of their origin, histology, natural history, sites of involvement, sensitivity to therapy, treatment policies, and outcome. The management of paediatric malignancies is a good example of the importance of multimodality management of cancers comprising a delicate balance in the optimal use of a combination of chemotherapy, surgery and radiation therapy. In view of the high rates of long term cure and the innate sensitivity of the developing tissues to the adverse effects of the various cancer treatment modalities, it is of utmost importance to keep in mind issues like functional outcome, acute and late toxicities, and quality of life while defining treatment strategies for childhood cancers.

The outcome of childhood cancers has evolved and improved significantly over the last two to three decades. Currently the 10 year survival rates for childhood cancers is approximately 80% in the developed and about 40% in the developing world. This disparity in outcomes could be attributed to the differences in socio-economic factors and the scant availability of necessary infrastructure.

The improvement in outcome could be attributed to a better understanding of natural history, availability of advanced and accurate histopathogical evaluation and imaging techniques, newer chemotherapeutic agents and multiagent chemotherapy regimens, improved surgical techniques and the emergence of advanced radiotherapeutic techniques.

Historically radiation therapy comprised the sole treatment modality for many childhood cancers like Hodgkin’s disease, Ewing’s sarcoma, and soft tissue sarcomas. With the development of newer chemotherapeutic agents/regimens and surgical techniques and the realization of the incidence of late sequelae in these probable long term survivors after high dose radiation, the use of high dose external beam radiation therapy as the sole modality of treatment has reduced. Radiation therapy now comprises an integral component in the multimodal management of paediatric malignancies. Current research in paediatric radiation oncology is focused at either reducing the volume and dose of radiation therapy amongst
children with low-risk disease or escalating treatment intensity for children with high risk disease. Examples of reduced intensity of radiation therapy are in paediatric Hodgkin’s disease, acute lymphoblastic leukemia (ALL), Wilm’s tumour, brain tumours, etc. while investigators are evaluating the need to intensify radiation therapy for malignancies like nasopharyngeal carcinoma, inoperable Ewing’s sarcoma and soft tissue sarcomas.

Modern techniques like intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT), stereotactic radiation therapy (SRT), proton beam therapy, and brachytherapy are currently being used for treatment of paediatric malignancies with the aim of improving the therapeutic ratio in terms of improving disease control and reducing both acute and late adverse effects of radiation.

With the current multi-speciality approaches and availability of high precision radiotherapy techniques, the integration of imaging and insights into tumour biology, it is expected that future studies would report improved outcomes with reduced treatment related sequelae in childhood cancers.
The view of the AFRA designated centre on how to respond to the challenges in paediatric radiation oncology in the region

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The survival of patients with paediatric tumours has improved in the last decades and the expected cure rate is to approximately 80% [1]. The multidisciplinary approach to these patients is considered the major cause of this result. The use of systemic treatment has contributed largely for these results; however the proper use of the local treatments — surgery and radiotherapy (RT) — is also crucial for the multidisciplinary management. Investigators, after reaching this high success rate, started to refine the treatment methods to minimize the side effects and improve quality of life with same or better survival rates. RT may produce late effects which are generally more severe in paediatric patients compared with adult patients.

Multiple factors may contribute to the late radiation effects of normal tissue such as treatment volume, total tumour dose, dose fractionation, volume of normal tissue included in the irradiated volume, sequence of treatment used and the age when receiving radiation.

The radiation oncologists have been changing their practice to limit the late toxicity by reducing the tumour dose, reducing the irradiated volume, excluding some normal tissues, postponing the start of RT until the patient is older and tailoring the dose according to age. The improvement of planning procedures, use of new RT techniques and combined chemo-radiotherapy regimens have been effective methods to implement these concepts [1, 2]. Different research groups have studied and proved its effectiveness. These studies have shown high survival rate with less late toxicity as in Wilm’s tumours, neuroblastoma, brain tumours and sarcomas.

Chemotherapy has been increasingly used in treatment of paediatric patients to minimize the late radiation effects. Different policies are used depending on the age of the patient, the tumour type, tumour site and stage. In view of the severe late radiation effects to children below three years; most investigators postpone RT and may use chemotherapy until the patients are older, e.g. brain tumours. Combined chemo-radiotherapy may be given instead of RT alone. The RT given according to this policy is generally lower in dose and smaller in volume which causes less morbidity, e.g. early stages of HD [3].

Different international groups have tested the tailoring of the radiation tumour dose to the age of the patient. These studies have shown high survival rate with less late toxicity as in Wilms’ tumours and neuroblastoma [4–6].

The improvement of planning procedures included better immobilization with the use of anesthesia, if needed, the use of new imaging modalities such as CT scan, MRI and PET, better delineation of target volume and organs at risk (OAR), more sophisticated treatment
planning systems, better treatment delivery methods, e.g. multi leave collimators (MLC) and accurate treatment verification methods.

Modern high precision RT techniques such as conformal RT, stereotactic radiosurgery, intense modular RT (IMRT), image guided RT (IGRT) and tomo therapy; have shown less radiation morbidity [1, 2].

Some of the local experience of the Radiation Oncology Department, National Cancer Institute, Cairo University as AFRA designated centre will be presented in the lecture.

In conclusion; the radiotherapy practice has been changing to produce consistent high survival rate and lower radiation morbidity.

REFERENCES


Session 13b:
REducing Late Radiation Toxicities
Biological approach to reduce late radiation toxicities

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Biological weighing of absorbed doses in particle-beam therapy: ICRU-IAEA recommendations on the isoeffect-dose concept


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The quantity absorbed dose D (Gy) in radiation therapy

Absorbed dose is an essential quantity in radiation therapy, and should be reported for all relevant points and/or volumes. In addition, treatment conditions should be reported as completely and accurately as possible in order to allow full understanding, interpretation and reconstruction (if necessary) of the treatment.

Besides absorbed dose, the clinical outcome depends on a number of other factors such as dose per fraction, overall treatment time, dose rate, instantaneous dose rate, dose homogeneity, radiation quality (RBE) and other technical or biological conditions, e.g. degree of oxygenation. Therefore, when absorbed doses delivered under different conditions are compared or combined, weighing factors (functions) have to be applied to the quantity absorbed dose. This leads to the concept of “isoeffect absorbed dose” [1].

The isoeffect absorbed dose concept D\text{IsoE} (Gy)

The isoeffect dose D\text{IsoE} is the dose that, when delivered under reference conditions, would produce the same clinical effects as the actual treatment, all other conditions being identical. One set of conditions has to be selected as the “reference”. To facilitate exchange of information, in photons delivering 2 Gy per fraction, five daily fractions per week are recommended as the standard (“universal”) reference conditions. The isoeffect dose D\text{IsoE} is thus the product of the absorbed dose (in Gy) and a weighing factor W\text{IsoE}, which includes the effects of all parameters that could affect the clinical outcome.

\[ D_{\text{IsoE}} = D \times W_{\text{IsoE}} \]

As the isoeffect dose and absorbed dose are both expressed in Gy, it is important to clearly specify to which quantity a given numerical value corresponds [1].

Isoeffect absorbed dose (D\text{IsoE}) in fractionated external photon-beam therapy

In fractionated external photon beam therapy, the dose per fraction and overall time are the two main parameters that the radiation oncologist can adjust (they are included in W\text{IsoE}). If the dose per fraction is altered, the weighing factor for this parameter is evaluated using the
linear-quadratic ($\alpha/\beta$) model, usually assuming that $\alpha/\beta$ is 3 Gy for late effects and 10 Gy for early effects. There is little information or agreement on how to account for changes in overall treatment time. When reporting the DIsoE it is important to specify if weighing is applied for differences in doses per fraction, overall times or both.

**Isoeffect absorbed dose in proton-beam therapy**

In proton-beam therapy, in addition to the parameters involved in photon-beam therapy, the DIsoE depends on radiation quality (RBE). For protons, a generic RBE of 1.1 is assumed for the current clinical conditions and thus DIsoE = DRBE = D×1.1, all irradiation conditions (dose per fraction, overall time, etc.) being identical for protons and photons.

D and DRBE (the RBE-weighted absorbed dose) are both expressed in Gy. To avoid confusion Gy, followed by a space and the parenthetical descriptor “(RBE)” should be used when specifying DRBE. In proton-beam therapy, the term “equivalent dose” has been used in the past as the product of absorbed dose and a weighing factor accounting for differences in radiation quality (WRBE), all other conditions (including fractionation and overall time) being the same for protons and photons. The unit has been the gray equivalent, GyE [or Gy(E)], or cobalt-gray equivalent (CGE). However, the concept of “equivalent dose” as defined by the ICRP applies to radiation protection only. “Equivalent dose” may be misleading as it is only relative to photons delivered under the same conditions as the protons. Furthermore, in the International System (SI) of units, no subscript or letter/symbol can be added to a units. The symbol “GyE” is thus not permitted. The use of “equivalent dose”, “GyE” and “CGE” and similar nomenclatures is discouraged [2, 3].

**Isoeffect absorbed dose in heavier ion beam therapy**

For heavier ions as C+, the situation is more complex than with protons as the RBE varies markedly with particular type, energy, method of production, depth in the tissue, biological effect (e.g. early vs late effects), etc. However, the isoeffect dose concept can be applied as indicated above for other irradiation modalities: DIsoE = D × WIsoE [4]. The weighing factor WIsoE includes all parameters that could affect the clinical outcome. It is important to stress that the effects of some parameters — as dose per fraction — are significantly different for photons and ions. The actual and reference irradiation conditions should thus be specified completely. When photons are selected as the reference, fractionation may often be very different from the ion beam irradiation. Similar to protons, the use of “equivalent dose” and “GyE” and “CGE” is discouraged [5].

**REFERENCES**


A. Wambersie, et al.


Relating three dimensional dose/volume data to clinical outcomes: An overview of the QUANTEC effort

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Historically, RT fields/doses were selected based on clinical experience and intuition. Clinicians generally recognized the imprecision of these empiric guidelines, as they did not reflect the underlying three dimensional anatomy, physiology, and dosimetry. A great promise afforded by 3-D imaging was an improved quantitative relationship between 3-D doses/volumes and outcomes. When 3-D dosimetric information became more widely available (late 80s–90s), 3-D guidelines were needed.

In 1991, multiple investigators pooled the available, albeit sometimes limited, information regarding the often-quoted “Emami paper” (IJROBP 1991).

During the last 17 years, additional 3-D dose/volume/outcome data has become available. In order to summarize the available information, ASTRO and the AAPM sponsored the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) effort. A central goal of QUANTEC is to summarize this information in a clinically useful manner. For each organ, the literature providing meaningful dose/volume/outcome data is reviewed. Clinical/treatment variables that may impact the application of the data are discussed. Where available, NTCP-model parameters are provided. We hope this information will improve patient care by providing clinicians and treatment planners with the tools necessary to determine the “optimal” 3-D dose distribution for each individual case.

Further, opportunities for research and suggestions on how to score toxicities were afforded.

Nevertheless, the information provided by QUANTEC is not ideal, and care must be taken to apply it correctly. Unfortunately, the data are incomplete for essentially almost every organ.
The user must recognize the limitations inherent in extracting/pooling literature data. For some complications, some studies summarize their findings in terms of models that can be used to estimate risk. Extreme care should be taken when such models are applied clinically, especially when clinical dose/volume parameters are beyond the range used to generate the model. Models that rely on DVH data discard all spatial information (and hence inherently assume that all regions of an organ are functionally equally important), and often do not consider variations in fraction size (a particular concern with the increasing use of hypofractionated schedules).

Similarly, the increasing use of RT combined with concurrent chemotherapy, with rapidly evolving drugs/doses, questions the validity of historical data to modern times.

For essentially all patients with curative cancers, a marginal miss is a more serious complication than is a normal tissue injury. Care must be taken to reasonably balance the need for target coverage with the normal tissue risks. Furthermore, palliation in patients with recurrent/metastatic/incurable disease, with limited expected survival often requires one to exceed “tolerances”, as concern for late effects may not be applicable (e.g. RT fields for locally advanced lung cancer may include large volumes of lung and heart and withholding RT due to the risk of pericarditis, or pneumonitis, may not be “therapeutically rational”). These concerns are most applicable to our youngest generation of recently trained radiation oncologists. Such individuals have become accustomed to having 3-D dosimetric information available for every case, and rely on such data for many of their clinical decisions.

These physicians may be uncomfortable in clinical settings wherein large radiation fields need to be applied in a relatively rapid fashion (i.e. without 3-D dosimetry) in order to provide effective palliation.

An overview of the QUANTEC effort, and a summary of some organ-specific findings, will be presented.

Supported in part by grants from ASTRO, AAPM, and NIH (CA 69579).

QUANTEC Steering Committee Members:

Lawrence B. Marks, Joseph O. Deasy, Soren M. Bentzen, Ellen D. Yorke, Andrew Jackson, Randall K. Ten Haken, Louis S. Constine, Avraham Eisbruch.
Acute and late toxicity after fractionated total body irradiation as conditioning for bone marrow transplantation

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Objective: Total body irradiation (TBI) followed by bone marrow transplantation (BMT) is well established as part of the conditioning regimen in high dose therapy. The objective is to report the acute and late toxicity investigated prospectively in patients who had conditioning regimes including fractionated TBI (FTBI) and chemotherapy.

Materials and methods: From October 2002 to December 2007, 18 patients received FTBI in our institution. There were 11 males and 7 females with median age of 20 years (range: 8-50). The present study includes 11 patients with initial diagnoses acute lymphoid leukemia (ALL), 4 – acute myeloid leukemia (AML) and 3 – chronic myeloid leukemia (CML). At the time of BMT 11 patients were in complete response (CR), 4 in progression and 3 in chronic phase.

The conditioning regimens applied by us for allogeneic BMT include cyclophosphamide, vepesid and TBI (10 patients), cyclophosphamide and TBI (3 patients), melphalan, fludarabine, ATG and TBI (2 patients) and fludarabine and “mini” TBI (3 patients).

TBI was performed on a $^{60}$Co unit in alternate prone and supine position. Three patients received non-myeloablative regimen including “min” TBI of 2 Gy as a minimal intensive conditioning regimen followed by allogeneic blood stem cell transplantation (BSCT), and 15 received myeloablative regimen of 10–12 Gy FTBI. Five patients received a total of 10 Gy (six fractions of 1.67 Gy twice daily for three consecutive days), eight patients received a total of 12 Gy (six fractions of 2 Gy twice daily for three consecutive days) and two patients received a total of 10 Gy (five fractions of 2 Gy in five consecutive days). The dose rate requirement was met for TBI 5–10 cGy/min.

Patients were grafted from HLA matched related (13) and mismatched related (5) donors. A standardized supportive therapy was administered.

Results: Premedication was carried out in all patients including antiemetics (mainly serotonin receptor antagonists – ondansetron, granisetron, tropisetron) and corticosteroids (8 to 20 mg). The most frequent reactions determining acute toxicity due to the conditioning regimens and the induced bone-marrow aplasia, which are observed in the patients, are presented in Table 1.

During the transplantation period on day 0 and +1 of the clinical protocol the realized transplantation of the donor cells pool passed without complications in 16 of the patients and was accompanied by allergic reactions in 2 patients. Induced bone marrow aplasia was observed in all patients during the post-transplantation period. On day +14 to +24...
“entgraftment” was established in 16 patients. In 2 patients until the 35th day after the transplantation, no symptoms of the grafting were observed, which imposed reinfusion of donor cells pool.

TABLE 1. CLINICAL TOLERANCE IN TOTAL BODY IRRADIATION PRIOR TO ALLOGENEIC BMT

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Indisposition</td>
<td>93%</td>
</tr>
<tr>
<td>Fatigue syndrome</td>
<td>68%</td>
</tr>
<tr>
<td>Headache</td>
<td>16%</td>
</tr>
<tr>
<td>Loss of appetite</td>
<td>58%</td>
</tr>
<tr>
<td>Nausea</td>
<td>75%</td>
</tr>
<tr>
<td>Emesis</td>
<td>58%</td>
</tr>
<tr>
<td>Mucositis</td>
<td>50%</td>
</tr>
<tr>
<td>Oesophagitis</td>
<td>8%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>50%</td>
</tr>
<tr>
<td>Parotidis</td>
<td>8%</td>
</tr>
<tr>
<td>Pruritus</td>
<td>33%</td>
</tr>
</tbody>
</table>

Seven (7) patients developed acute GvHD, 2 developed idiopathic pneumonia syndrome and 1 developed acute liver toxicity and another, neurological toxicity. No development of cardiovascular, renal or other type of toxicity was established. The development of fatal organ toxicity (FOT) was found in five patients.

From the 18 patients subjected to TBI and allogeneic BMT, development of late morbidity was recorded in 8 patients during the six year period of clinical observation. Six (6) patients (35%) developed chronic GvHD. In all the six patients it was successfully controlled and it was not the reason for the fatal outcome in any of these patients. We observed the development of cataract in one patient and late liver toxicity in the form of hepatitis C reactivation in one other patient.

Conclusion: FTBI is a well tolerated therapeutic regimen in high dose therapy. The observed acute and late toxicity in the 18 patients is similar to that cited in reference literature.

REFERENCES


Lunch Forum II:
ALTERED FRACTIONATION IN CURE
AND PALLIATION
The rationale and radiobiology of altered fractionation in cure and palliation

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Major developments in radiotherapy fractionation have taken place during the past three decades. A milestone was the survey of isoeffect relationships for various normal tissues [3]. This covered experimental studies in which the overall time was kept short, therefore highlighting the influence of dose per fraction on response and mostly excluding the influence of overall treatment time. In each study, and for each chosen dose per fraction, the total radiation dose that produced a defined level of normal-tissue damage was determined. The results of this survey showed that the isoeffective total dose increases more rapidly with decreasing dose per fraction for late normal-tissue effects than for early effects. If this isoeffective total dose is regarded as a tissue tolerance dose, then using lower doses per fraction (hyperfractionation) should tend to spare late reactions if the total dose is adjusted to keep the early reactions constant. The linear-quadratic (LQ) model forms a quantitative environment for considering the balance between late and early reactions (and tumour effect) as dose per fraction and total dose are changed. In the LQ model, the $\alpha/\beta$ ratio quantifies the magnitude of the fractionation effect: late-reacting tissues have $\alpha/\beta$ ratios averaging about 3 Gy, whereas early reacting tissues have $\alpha/\beta$ ratios averaging about 10 Gy. The fractionation response of carcinomas of head & neck, and lung, are thought to be similar to that of early responding normal tissues, sometimes with an even higher $\alpha/\beta$ ratio.

Radiation induced normal-tissue regeneration (“repopulation”) may modulate radiation tolerance. This is seen in early responding tissues but not in late responding tissues within the usual duration of seven weeks of conventional radiotherapy. In tumours, the existence of a time factor in clinical radiotherapy was also deduced for squamous cell carcinomas of the head and neck [5]. As overall time increased, a greater total radiation dose had been required to control these tumours. For treatment times longer than four weeks, the effect of proliferation was equivalent to a loss of radiation dose of about 0.6 Gy per day. Therefore accelerating radiotherapy to less than seven weeks may improve tumour response. For treatment times shorter than 3–4 weeks, tumour proliferation had less effect and, as shown for experimental tumours, it may take time for repopulation to accelerate in human tumours.

To test these ideas, many clinical trials of altered fractionation have been set up. In a meta-analysis of 15 randomized trials [1], there was a significant benefit for loco-regional control in favour of altered fractionation. The survival advantage was more pronounced with hyperfractionation (8% at five years) than with accelerated fractionation (2% for regimens without dose reduction and 1.7% for regimens with dose reduction). However, many clinical studies with accelerated radiotherapy protocols, i.e. with a shortened overall treatment time, have resulted in increased early radiation side effects as expected.

Some human tumour types like melanoma and sarcomas exhibit low $\alpha/\beta$ ratios, and this is also suggested for early-stage prostate [4] and breast cancer [2], maybe with $\alpha/\beta$ even lower than for late normal tissue reactions. Therefore hypofractionation, using doses per fraction
>2 Gy, may be as good or even better than conventional fractionation in curative radiotherapy of these early-stage cancers, and this hypothesis is currently being tested in randomized trials. Hypofractionated schedules have the additional advantage of being more convenient for the patient and they help to spare resources.

Single-dose irradiation or hypofractionation with only few large fractions is also widely applied in palliative radiotherapy. These schedules use lower total doses than those applied in curative radiotherapy. For this reason, and because the patients have a limited life expectancy, late normal-tissue damage is of less concern. Randomized trials have shown that symptom control after palliative hypofractionated schedules is comparable to that achieved with more highly fractionated schedules.

For stereotactic radiotherapy of small tumours, e.g. in lung, where very steep dose gradients can be achieved and hence smaller volumes of surrounding normal tissue are at risk of damage, single doses or hypofractionation with few large fractions are becoming more used. There is also growing interest in using moderate hypofractionation to escalate total doses in conformal radiation therapy. For example, utilizing a field-in-field technique or intensity modulated radiotherapy (IMRT), a higher dose per fraction can be applied for boosting the macroscopic tumour while potential microscopic tumour extensions are treated at conventional doses per fraction. Such hypofractionated approaches for dose escalation avoid prolonging the overall treatment time and conserve treatment resources. However, these advantages must be carefully weighed against the increased risk of late normal-tissue injury, and further clinical trials are required to fully evaluate the therapeutic gain compared with standard approaches.

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Altered fractionated RT: What is the magnitude of the benefit in head and neck carcinoma?

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Applications of hypofractionation in the curative treatment of cancer

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For decades the standard fraction size has been 2 Gy per fraction. Many studies have demonstrated efficacy when delivered five days per week for 5–8 weeks to the total dose based on estimation of tumour volume. When accessibility is a problem, whether from lack of radiation therapy resources or from the ability of the patient to access treatment for socioeconomic or physical reasons, alternative fraction schemes reducing number of radiation therapy fractions appear attractive.

Recent presentations and publications of accelerated treatment for breast cancer have challenged the conventional delivery of five weeks of daily radiation therapy. Not only did the Canadian and British trials show comparable control in the breast, there was no increased toxicity in these very well analysed studies. Whelan, et al. showed that 42.5 Gy in three weeks was equivalent to 50 Gy in five weeks. The START trials showed that 40 Gy in three weeks, or 39 and 42 Gy in five weeks delivered on alternative days, was equivalent to 50 Gy in five weeks. Follow-up was 5–12 years in these studies with modern dosimetry. A French trial of once weekly radiation therapy in elderly patients showed good local control, again challenging the older standards.

Single large fractions to a limited volume are becoming increasingly easy to deliver due to image guidance and respiratory gating during radiation therapy. Many preliminary reports of “radiosurgery” for lung cancer are appearing and the RTOG is currently studying hypofractionation for limited size lung cancers. Many mature studies for “radiosurgery” for brain malignancies have been reported and dose recommendations have been made.

As successes are increasingly reported for hypofractionation schedules to small fields for lung, liver, and brain cancers, the application of these schedules in other tumours will likely increase and be reported. Improvements in technology have allowed exploration of new schedules without increased risk to normal tissue.