QUALITY ASSURANCE AND RADIATION SAFETY IN POSITRON EMISSION TOMOGRAPHY

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Scientific studies, clinical experience and economic analysis have shown that the positron emission tomography (PET) is clinically and cost effective cancer diagnostics method. Combined PET and computed tomography (PET/CT) has proven clinical utility, particularly in the diagnosis, staging or restaging malignant disease and metastases, surgical planning, radiation therapy planning and evaluation of treatment response. The use of PET/CT has grown substantially in the past few years, with an increasing number of hospitals and installations of PET/CT imaging centers each year. In the same time combination of 2 procedures, each of which impart a radiation dose and, as a result, increases the deleterious influence for health, creates additional radiation safety issues. In these conditions the role of quality assurance (QA) and quality control (QC) programs is getting more and more important. We considered main QA and radiation safety requirements for whole PET technology chain from radio-pharmacy facilities to PET/CT scanning and patient release criteria. All these issues were considered and assessed having the example of PET facilities and technology chain of All-Ukrainian Center for Radiosurgery of the Clinical Hospital "Feofania".

1. Introduction

Positron emission tomography has become one of the most important diagnostic tools in the cancer detection and treatment in last ten-fifteen years. Main advantage and uniqueness of this method is possibility to find and identify any malignant neoplasms of small sizes (for new metastatic formations less than one centimeter), which are in the stage of active growth phase, studying a tumor`s activity, clear identification of the stage of specific disease, prognostication of the effectiveness of treatment targeted to finally define the quality of medical process in a post-therapeutic period. In the recent years the active progress and development of new PET-procedures take place and the characteristics of equipment and analyzing software are being improved with increasing rate. The combination of positron emission tomograph with computerized X-ray tomographic system into one tandem has provided essential advantages and improvement of scanner `characteristics for positron emission tomography. At the present stage of progress practically all such systems are produced with X-ray computer tomograph (CT) with modified name PET/CT scanner (or PET/CT tomograph). For the past few years with appearance of effective semiconductor electronic photomultipliers (SiPM), which have a small sensitivity to magnetic field, the tendency of integration PET scanner and magnetic resonance tomograph appears, new time-of-flight methods allow to improve background conditions for obtaining high quality diagnostic scans.

2. Basic physical and biological principles of PET tomography

In the early thirties of the last century it was noticed that the significant part of malignant neoplasms is characterized with higher level of glucose uptake. It is due to quick growth and reproduction of cancer cells, and such a rapid metabolism requires large quantity of biological construction and energy resources, among which glucose occupies the most important place. In the seventies years it was suggested to use labeled glucose analogues for the metabolism study in a human organism. Initially radioactive carbon was used as an irradiation source, but application of radioactive isotope ^{18}F in the fluorodeoxyglucose (FDG) has become especially widespread. FDG is a glucose analogue at several stages of its metabolism, but unlike glucose FDG metabolism is broke off too soon and its product with the radioactive marker of fluorine being accumulated in live tissues. If one defines the concentration of fluorine-18 in tissue then ^{18}F accumulation in the tumor can be localized with quite good accuracy and high value of probability (corresponding to high metabolism level). Some important organs of human body (like brain, heart) also have high metabolism level. That complicates partly the determination of malignant tumors in such areas, but it allows studying cerebral and cardiac activity directly in a dynamics which is very important for corresponding fields of medicine. A nucleus of fluorine-18 emits positrons of sufficiently low energy while decaying. This process makes it possible to identify the point where a nucleus disintegrated with quite good accuracy and low background. Let's consider the physics of this process. As a result of β^+-decay a positron is emitted with energy not higher than 0.63 MeV. It is captured in a human body and annihilates with one of environment electrons after achievement of kinetic energy close to zero. As a result of annihilation two photons with the same energy equal 511keV escape in opposite directions (angle 180^0). Matrix of scintillation detectors forms a circle around patient, in these detectors the energy of photons and time of their appearance are detected. According to a signal coincidence from two matrix detectors the straight line is defined (at two "points"-detectors). There is a radiation source on that line, and place of the cross points of such lines is to be used to determine the point of positron emission.

For the synthesis of FDG which is to be injected into a patient, it is necessary to produce radioactive fluorine-18 every day with activity about of 1 - 4 Ci, because the half-life of ^{18}F is 110 min, i.e. this isotope decays fast enough.

Quite short half life on the one hand leads to the relative isotope safety (within few days nuclei of fluorine-18 will mostly decay), on the other hand it limits the distances to use fluorine-18 produced in one PET center and implies the requirement to produce FDG close to clinics equipped with PET scanners (within one-two hours of a transport movement). Therefore different medical cyclotrons and automated FDG synthesis systems are dedicated for the production of fluorine-18 in one large clinical institution. One of the most justified methods of ^{18}F production is 15 MeV protons irradiation of nuclei ^{18}O (as a rule in water, containing stable isotope ^{18}O with enrichment exceeding 90 %). In nuclear reaction $p+^{18}O \rightarrow n+^{18}F$ the needed fluorine isotope is produced but meanwhile a considerable neutron flux is generated as a side harmful process. Once irradiated, the water (containing ^{18}O converted into ^{18}F) needs to be squeezed out into automated FDG synthesis system where all the processes of material cleaning and pharmaceutical synthesis take place without human help in the automatic mode. Then prepared pharmaceuticals do pass the quality control to be lately packed for utilizing in the same medical institute where FDG was produced or for transportation to other medical institute which has PET scanners. FDG is injected into a patient by using a syringe for effective extension in blood-vascular system and after 20-40 minutes (for the achievement of the corresponding metabolism stages) diagnostic scanning is ready to be carried out at PET (PET/CT) tomograph. All technological chain to get diagnostic PET images of high quality is difficult enough and has substantial differences from the processes of X-ray imaging not only in basic physical principles but also in the area of radiation safety and development of quality assurance management systems.

3. Radiation safety in PET application

Numerous features of PET technology chain do require special rigorous measures to provide high level of radiation safety for patients, personnel and other people in the hospital and nearby. This includes very thorough consideration of corresponding building design, system for radiation monitoring, internal and external audits, prevention of accidental radioactive releases into atmosphere, etc. One can note first of all the following issues:

1. Annihilation gamma-quanta (with energy 511 keV) are major contributors to radioactive irradiation from positron emitting isotopes. This energy is high enough relative to x-ray generated by roentgen diagnostic equipment and even gamma ray energy of the most widespread isotopes in nuclear medicine (such as ^{99m}Tc). For 511 keV gamma ray energy attenuation a contribution of photoabsorption does not prevail and a part of Compton scattering is quite significant. Therefore strong dependence (ordinary for radiation safety specialists in the field of nuclear medicine and x-ray diagnostics) of quanta absorption from atomic number of material is absent practically. From this conclusion such result arises – low effectiveness of lead and barite plaster (standard materials for X-ray diagnostics field). For example the tenth value layer (TVL) for radiation of ^{99m}Tc is nearly 0.9 mm of lead, for X-ray tube with anode voltage 100 kV TVL in lead less than 0.25 mm (with 2mm aluminium filtration), but for annihilation gamma-quanta of ^{18}F this value is nearly 1.6 cm. One can derive the following conclusions from this:

a. the most effective shielding against annihilation gamma-quanta is concrete walls and main optimal effective method is to increase a distance between radiation source and point of dose applying, taking into account the ratio shield/shield cost;

b. radiation safety system for personnel is complicated, first of all for nurses who applies syringe injection of FDG to patient blood. Thus, lead or tungsten syringe covers make it possible to solve this problem partially only (herewith the injection procedure is essentially complicated due to large mass of cover), minimization of injection time is main approach in these conditions to minimize radiation dose on nurse fingers and hands;

c. radiation doses for patients in PET are not very high – the dose rate from ^{18}F is about one order of magnitude higher than for ^{99m}Tc, but due to short half-life the total cumulative patient dose nearly equals to value of Technetium.

One can find more detail information about radiation safety and shielding of PET diagnostics in ref. [1, 2].

2. If one use reaction $p+^{18}O \rightarrow n+^{18}F$ to obtain ^{18}F, intensive neutron flux is generated as side harmful product. For example for production of ^{18}F few Ci, a neutron fluence may reach about 10^{15} neutrons in 4π solid angle. Intensive flux of thermal and resonance neutrons may be formed due to slow down at the cyclotron construction elements and shielding vault. Neutron capture reactions lead to formation of several radioactive isotopes. All such interactions (neutron capture and reactions with primary neutrons) cause essential radioactive background of induced radiation in the cyclotron vault. To lowering this background the vendors prefer to manufacture the target unit materials with low neutron cross section values or with short living radioactive isotopes in output channel of neutron induced reactions. One must avoid using in the vault (especially around target unit) the elements with high values of cross sections for cyclotrons without built-in shielding. Besides constructive materials of accelerator and vault itself, the activation of air causes accumulation of radioactive isotope ^{41}Ar with half-life nearly two hours [3] in the cyclotron vault. To minimize the influence of such radioactive sources a using of built-in complex neutron cyclotron shielding is considered as the most effective approach. For this case only small air inner volume in shield is irradiated in area around target (dozens liters). Then the air with induced activity has to be diluted in a large volume of clean air to obtain the permitted concentrations of ^{41}Ar and further release into the atmosphere. Another approach is used for cyclotrons without built-in shielding. In this case volume of air in cyclotron vault can exceed dozens of cubic meters and its dilution to get permitted concentrations of radiation in air can be problematic or even impossible. The alternative solution of such problem could be the ventilation of cyclotron systems without releasing the air into the atmosphere. Then upon completion of ^{18}F production the air with induced activity is to be pumped into large balloons and after cooling time (as

a rule – one day and night for argone-41 decay) the air may be released into the atmosphere with continuous radiation monitoring.

3. During technology chain of positron emitting isotopes, especially in the processes with gases or volatile components (frequently in ^{11}C production chain) the risk of leakage of highly radioactive discharges to ventilation system might be essential. The consequences of accident like this can lead to radioactive pollution of PET chain rooms and even outer atmosphere [4]. Therefore continuous radiation monitoring in ventilation system is mandatory. It is not simple task because direct measurements by detector systems without concentration of radioactive isotopes is very problematic for pollution concentrations nearly permitted values [5].

4. Quality assurance procedures in the PET technology chain

Taking into account a very complex PET technology chain one have to build Quality Assurance (QA) system in the all segments of chain in their interconnections. This QA system should cover all the activities from the development of PET diagnostics departments and further to operate routine procedures with equipment and software. Some leading organizations of national and international level developed sets of documents, which are devoted to these problems. Among them: the IAEA documents [6, 7], accreditation procedures of American College of Radiology (ACR accreditation, [8]), standards of 2001 and 2007 years of the Association of Electrical Equipment and Medical Imaging Manufacturers (NEMA standards for positron emission tomography, [9]).

5. PET diagnostics in All-Ukrainian Center for Radiosurgery of the Clinical Hospital "Feofania"

More than one year department of PET/CT diagnostics is in operation at All-Ukrainian Center for Radiosurgery of the Clinical Hospital "Feofania" in Kyiv. Complete technological chain (from a fluorine-18 production with medical cyclotron and FDG synthesis to the scanning procedures on the PET/CT tomograph) is developed, recognized and fully certified. . The cyclotron has its own built-in protection that substantially improves and simplifies the conditions to provide high level of radiation safety. Ukrainian normative documents and best international practices [5 - 8] were taken into account for the development of QA procedures. Biograph 64 TruePoint PET/CT by Siemens is used for a tomographic scanning. Within the framework of quality control system the NEMA IEC Body phantom according to the standard of NEMA NU2-2007, ACR phantom «Flangeless Deluxe ECT Phantom» according to the ACR accreditation program of nuclear medicine, dose calibrator Atomlab™ 500 Calibrator (Biodex) and other modern equipment are in full scope operation for patients treatment and experience gaining.

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