FiR 1 reactor in service for boron neutron capture therapy (BNCT) and isotope production

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Abstract. The FiR 1 –reactor, a 250 kW Triga reactor, has been in operation since 1962. The main purpose for the existence of the reactor is now the Boron Neutron Capture Therapy (BNCT), but FiR 1 has also an important national role in providing local enterprises and research institutions in the fields of industrial measurements, pharmaceuticals, electronics etc. with isotope production and activation analysis services. In the 1990's a BNCT treatment facility was build at the FiR 1 reactor located at Technical Research Centre of Finland. A special new neutron moderator material Fluental™(Al+AlF3+Li) developed at VTT ensures the superior quality of the neutron beam. Also the treatment environment is of world top quality after a major renovation of the whole reactor building in 1997. Recently the lithiated polyethylene neutron shielding of the beam aperture was modified to ease the positioning of the patient close to the beam aperture. Increasing the reactor power to 500 kW would allow positioning of the patient further away from the beam aperture. Possibilities to accomplish a safety analysis for this is currently under considerations. Over thirty patients have been treated at FiR 1 since May 1999, when the license for patient treatment was granted to the responsible BNCT treatment organization, Boneca Corporation. Currently three clinical trial protocols for tumours in the brain as well as in the head and neck region are recruiting patients.

1. INTRODUCTION

A multidiciplinary research project to carry out clinical application of boron neutron capture therapy (BNCT) was established in Finland in the early 1990's [1,2]. It was motivated both by the need to create new applications for the Finnish research reactor FiR 1 and by the ideas to start research and production of new boron carriers for BNCT in Finland. The basic design performed by VTT showed that an epithermal neutron beam suitable for BNCT of glioma could be constructed, and even with world top performance characteristics [3] despite its low 250 kW power. The other epithermal neutron beams for BNCT had been created on rather high power research reactors: the 3 MW BMRR at BNL (USA), the 5 MW MITR-II at MIT (USA) and the 45 MW HFR at JRC Petten (NL). In Japan multimode BNCT beams, which include also epithermal modes, have been created at the KURRI (5 MW) and JRR-4 (3.5 MW) research reactors. Recently epithermal neutron beams for clinical use have been established also in Studsvik, Sweden at the 1 MW R2-0 reactor and at the 500 kW RA-6 reactor in Bariloche, Argentina.

The FiR 1 reactor is located within the about one million inhabitant Helsinki metropolitan area at Otaniemi, Espoo, about 6 kilometers from the largest hospital of Finland, the Helsinki University Central Hospital. The reactor was taken in operation in 1962. It functioned as a training and research reactor for neutron activation analysis, isotope production, and neutron physics until the mid 1990's. In 1996 an epithermal neutron beam was constructed based on a new neutron moderator material Fluental™ (Al+AlF_3+Li) developed and manufactured at VTT [1,4]. After successful demonstration of a high purity epithermal beam, the patient irradiation room was constructed by cutting partly into the original concrete shielding of the reactor (*FIG.1*). The Fluental™ moderator was shortened to create at that time the highest intensity and best purity epithermal neutron beam for BNCT. The whole reactor building was renovated creating a dedicated clinical BNCT facility at the reactor site [4]. Since May 1999 over 30 patients have been treated with BNCT at FiR 1.

The main purpose for the existence of the reactor is now BNCT. The BNCT work dominates the current utilization of the reactor: three or four days per week are reserved for BNCT purposes and the rest for other purposes such as isotope production and neutron activation analysis.

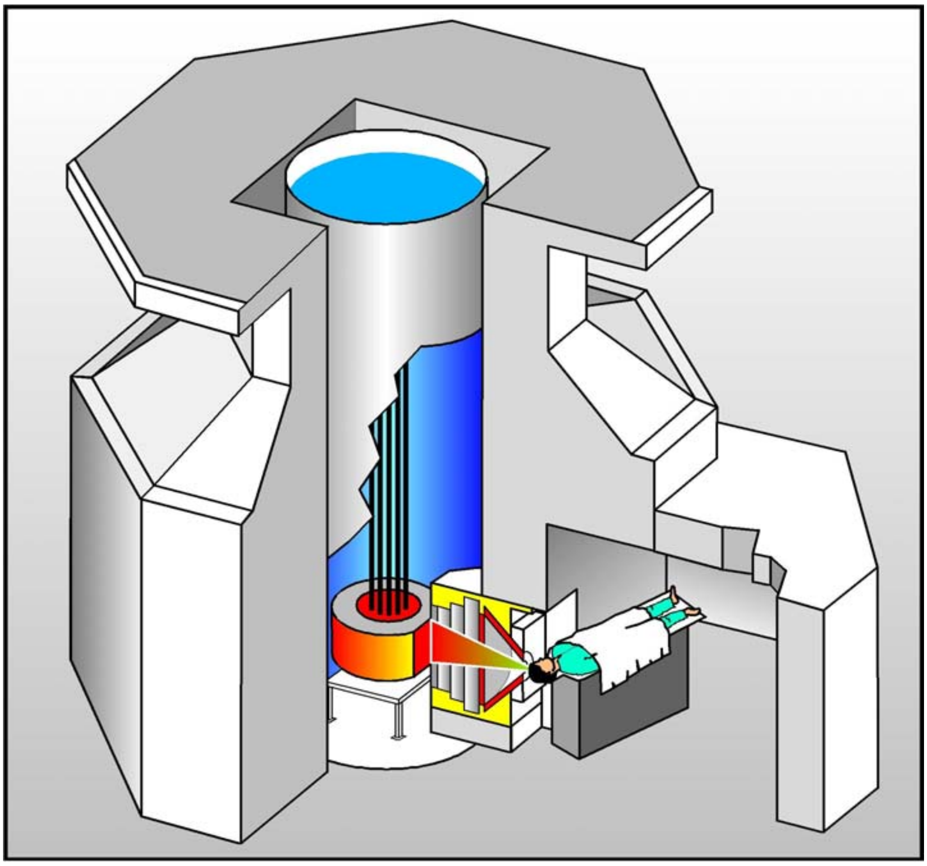

FIG. 1. BNCT Facility at the FiR 1 –reactor.

2. FiR 1 RESEARH REACTOR

The Finnish Research Reactor 1 (FiR 1) operated by the Technical Research Centre of Finland (VTT) is a 250 kW TRIGA II open pool reactor with a graphite reflector and a core loading of 15 kg U containing 3 kg ^{235}U (20% enrichment) in the special TRIGA uranium-zirconium hydride fuel (8-12 w% U, 91% Zr, 1% H). The advantages of the TRIGA design for BNCT include large flux-per-Watt feature and inherent safety of the TRIGA fuel. Due to the strong and fast negative temperature coefficient of the reactivity of the TRIGA fuel and easy operation of this type of a relatively low power reactor FiR 1 is a safe neutron source for a clinical BNCT facility. The reactor has a good safety and availability record from 42 years.

3. THE BNCT FACILITY

The old training and research reactor facility has undergone major changes in becoming a BNCT clinic. The clinical facilities for BNCT are located on the ground floor of the reactor building with easy access from the driveway through the new BNCT facility entrance. There are the patient preparation and treatment simulation room, the irradiation room, the BNCT monitoring room, the boron analysis laboratory and room for physical dosimetry equipment and laboratory work.

Patient positioning on the treatment coach relative to the neutron beam aperture is performed in the treatment simulation room using a beam aperture simulator. Then the coach with the patient is rolled into the irradiation room into the same position relative to the beam aperture. A crosshair laser system provides an identical coordinate system for patient positioning both in the simulation room and in the irradiation room.

3.1. The epithermal neutron beam

The epithermal neutron field is produced by replacing the original thermal column graphite in the thermal column cavity starting from the very bottom with the patented Fluental™ neutron moderator (*FIG. 2*) [9-11]. The thermal neutron load from the graphite reflector of the reactor core is removed with a boral plate. By placing the wide moderator closer to the reactor core more neutrons are caught into it. These neutrons have a wide energy spectrum that is then compacted to the epithermal range due to collisions and capture reactions in the moderator. The bismuth shield passes through neutrons but attenuates efficiently the gammas originating from the reactor core and neutron activated structures. A conical beam collimator enables to use the epithermal field for human irradiations. The diameter of the beam exit aperture can be selected from 20 cm down to 8 cm in steps of 3 cm by the number of aperture collars in place. The FiR 1 neutron beam is well characterised and particularly well suited for BNCT because of its low hydrogen-recoil and incident gamma doses, and its high intensity and penetrating neutron spectrum characteristics [5-8]. The measured thermal (< 0.5 eV), epithermal (0.5 eV-10 keV), and fast neutron (>10 keV) fluxes at the exit plane of the 140 mm diameter collimator at 250 kW power, are 8.1×10^7 n/cm^{2}s, 1.1×10^9 n/cm^{2}s, and 3.4×10^7 n/cm^{2}s, respectively.. The undesired fast neutron dose is 2×10^{-13} Gy/epithermal n/cm^2 and the gamma contamination 0.5×10^{-13} Gy/epithermal n/cm^2.

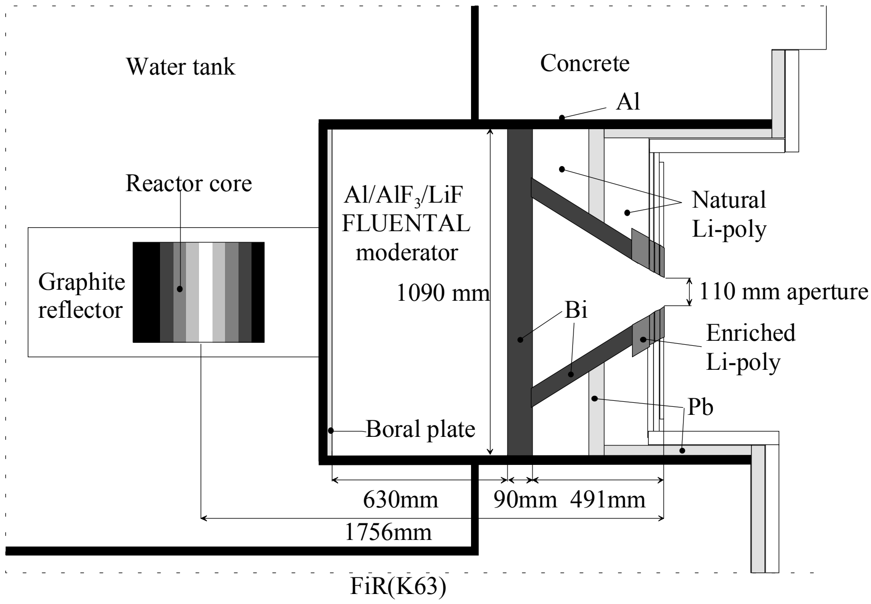

FIG. 2. The epithermal neutron irradiation facility in its current configuration with a 63 cm thick FLUENTAL™ moderator. In patient treatments normally 14 and 11 cm diameter beams are used.

3.2. The irradiation room

Several cubic meters of the concrete biological shield had to be cut away in order to allow positioning of the patient at the beam aperture in proper bodily orientation. Limiting factor in the removal was the stability of the original biological shield. Structural strength analysis performed by Olli Majamäki (IVO Power Engineering Ltd) showed that the thermal column could be widened only so far that a suspending arch is still formed over the irradiation position. Therefore the cutting was limited to halfway of the side faces.

A heavy concrete shielded therapy room was built around the irradiation position (*FIG. 1*) [13]. By casting heavy concrete into steel tubes good structural strength was combined with high density (4.35 g/cm^3). No load was allowed to put on the biological shield of the reactor so large beam lengths were used. The achieved high density ensured that with the 80 cm wall and roof thickness the dose rate levels outside are actually lower than outside the original biological shield. The neutron field in the irradiation room is depressed by a factor of 200 by lining the inner walls and the ceiling with in house made 30 mm thick lithium plastic elements. The floor is made of steel plate box elements filled with the same lithium plastic mixture. Lithium was selected as the neutron absorbing isotope throughout the beam collimator and irradiation room to enable background free boron prompt gamma monitoring in the future. The complications created by the tritium production from the lithium have been manageable and no tritium contamination of the personnel has been detected.

3.3. Improving patient positioning with recesses for shoulders

To reach more efficient patient positioning, shoulder recesses were constructed in year 2003 around the beam aperture so that the patient's shoulders are fitted to recesses when positioning is performed to a lateral field and the patient is in supine position [14]. The lithiated plastic parts where the shoulder recesses were constructed were contaminated by tritium induced by the ^{6}Li(n,α)^{3}H reaction. Therefore the beam aperture collar supports which could be easily detached were remade of virgin material. The basic shielding layers behind the collar supports (see *FIG 2.*) had to be machined *in situ*. At the surface of these parts up to 8 Bq/cm^2 of tritium was measured. An underpressurized glove box was constructed and machine tools with local exhaust were used to confine the sawdust. The tritium contamination of the irradiation room and the personnel was controlled with measurements and no contamination was observed.

3.4. Easy operation for patient irradiations

During the irradiation the reactor is operated at full 250 kW thermal power. The reactor power is maintained at the specified level by the reactor automation, but the initial starting procedure has to be done manually by the reactor operator. The length of the irradiation is controlled based on the beam monitor units given by the beam monitor system [15,16]. When the specified amount of beam monitor units is reached a manual reactor scram is initiated by the BNCT operator. A rather rapid operation is achieved without beam shutter. Start-up after closing the irradiation room door takes 3 minutes. The patient can be removed latest 5 minutes after reactor scram without uncomfortable doses to personnel.

The medical team together with the reactor personnel has been trained for incidences and emergency situations with the reactor. Emphasis has been on the communication between the reactor staff and the BNCT-facility personnel. If the situation allows the shift supervisor of the reactor will consult the persons responsible for the patient irradiation, the radiation oncologist and the medical physicist, before he makes decisions about shutting down the reactor or evacuation of the reactor building in case of emergency.

3.5. Possibilities to increase the reactor power

To improve the capabilities of the facility, the option to increase the penetration of the epithermal neutron field using a spectrum hardening filter has been studied. Calculations using a 5 mm thick ^{6}Li-filter at the beam exit show that the power of the reactor should be increased by a factor of two, at least, to maintain the current irradiation times [17]. Also irradiations, where the patient has to be positioned at a distance, like 5 to 10 cm, from the beam aperture, would benefit from a higher reactor power.

When FiR 1 started operation in 1962 its licensed power was 100 kW. In 1967 the power was increased to 250 kW but already then part of the required modifications were designed for 1000 kW. In the 1996-97 renovation the cooling system was rated for 400 kW with most of the parts capable for even higher power. The large heat capacity of the reactor tank allows for limited periods, like duration of a patient irradiation, operation at a higher power than is the capacity of the cooling system.

The feasibility of a power increase has been studied considering both reactor technical (like fuel safety and economy, core reactivity and control, cooling system) and radiation safety issues (both during normal operation and in exceptional cases) together with the requirements of the licensing authorities. An essential economic factor is the capability to still use the old aluminium clad fuel elements left in the current loading (48 of the total 79 fuel elements). The key issue in licensing is the safety of the aluminium clad fuel. Using steel clad elements in the regions with highest power, like already in the current core configuration, the safety margin for the use of the aluminium clad elements can be increased. General Atomics (USA), the manufacturer of the reactor, has experiences in using the aluminium clad fuel at power levels of 500 kW to 1000 kW [18]. From the licensing point of view it is clear that a thorough safety analysis for the aluminium clad fuel elements is required. Current control rods will be sufficient for safe and reliable power control of the reactor also at elevated power levels.

Especially the temperature of the fuel meat is of concern due to the lower phase transition temperature (537-550 ºC) of the uranium-zirconium hydride used in the aluminium clad elements. A MCNP[1]-model has been developed at VTT to calculate the power of individual fuel elements. According to this model at 500 kW reactor power by replacing four of the aluminium clad elements with steel clad elements the power of the remaining individual aluminium clad elements will stay lower than the maximum power in a standard 250 kW core configuration (5.6 kW). Further thermal hydraulic and fuel rod thermal analysis is required. A model to predict the fuel temperature is required and it should be verified in a power increasing experiment.

4. LICENSING

The Radiation and Nuclear Safety Authority (STUK) gave in May 1999 to the BNCT facility at FiR 1 the licence to perform BNCT radiotherapy complying with experimental protocols accepted by the ethical committees. The licence required also an inspection and approval by the municipal health care authorities as well as an approval by the regional governmental medical authority.

The operating license of the reactor was renewed beginning of 2000. The reactor is now explicitly licensed also to be used also as part of a BNCT treatment facility. The reactor personnel has now the right to judge the benefits of a completed patient irradiation by for example continuing the running of the reactor even in a emergency situation like fuel element leakage against risks in radiation and reactor safety. The operating license is by the Technical Research Centre of Finland (VTT), an independent government research organisation under the ministry for trade and industry. The management organisation of the reactor can be seen in *FIG. 3*. A special management position, the BNCT Manager, was set up for managing the BNCT facility.

[1] MCNP—A General Monte Carlo N-Particle Transport Code, Los Alamos National Laboratory, USA.

The radio therapy license is hold by Boneca Corporation. Boneca Corporation is a firm owned by the Clinical Research Institute at Helsinki University Central Hospital, VTT and Sitra, the Finnish National Fund for Research and Development. The management organisation for the radiotherapy license is shown also in *FIG. 3*.

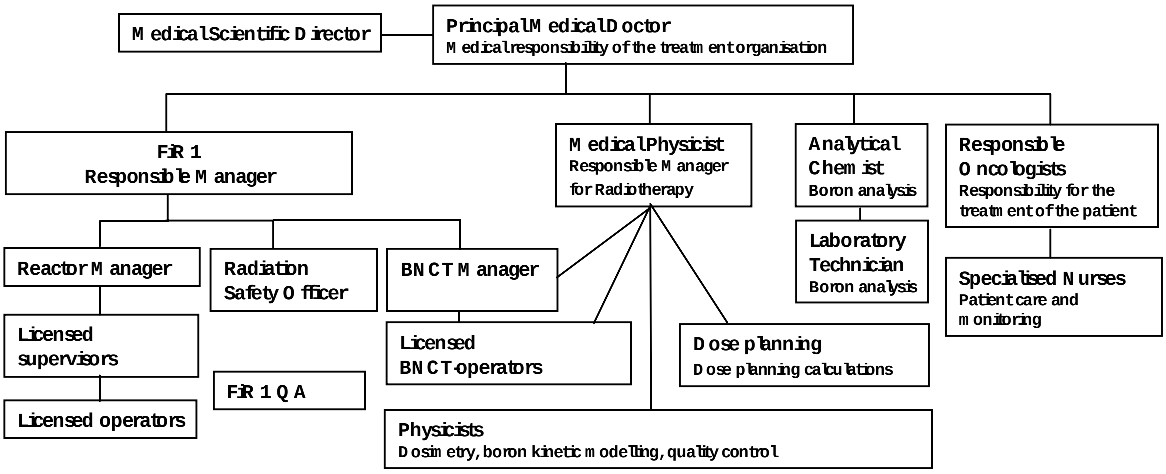

FIG. 3. The management organisation for the radiotherapy license.

As can be seen the two organisations overlap and are partly included in each others licensing documents. VTT is responsible for the maintenance, operation and safety of the reactor and for the radiation safety of the BNCT irradiation facility. Boneca Corporation is responsible for the patient irradiations, especially for the dose the patients are receiving, e.g. dosimetry, treatment planning, boron determination and patient positioning into the neutron field.

5. CLINICAL TRIALS

Three clinical trials are currently underway at the FiR 1 BNCT-facility [19,20]. Since May 1999 over 20 patients with glioblastoma, an until now uncurable brain tumour, have been treated with BNCT using boronophenylalanine (BPA) as the boron carrier compound within a context of a prospective clinical trial (protocol P-01). BPA-fructose is given at the BNCT-facility as 2-hour infusion prior to neutron beam irradiation. Blood samples are analyzed for blood boron concentration using inductively coupled plasma-atomic emission spectrometry (ICP-AES) in a dedicated analytical laboratory at the reactor. The irradiation is given in one or two fractions from two fields. The irradiation procedure typically lasts for about one hour. In another trial (protocol P-03) already some patients with recurring or progressing glioblastoma following surgery and conventional cranial radiotherapy have been treated with BPA-based BNCT. Recently also a trial for adult patients with histologically confirmed recurrent inoperable head and neck carcinoma after standard external beam radiotherapy has been started (HN-BPA-01-2003 trial).

The conclusion has been that BPA-based BNCT has been relatively well tolerated both in previously irradiated and unirradiated patients. Efficacy comparisons with conventional photon radiation are difficult to perform due to patient selection and confounding factors such as other treatments given, but the general results support continuation of clinical research on BPA-based BNCT [19]. With the head and neck carcinomas very promising results have been obtained [21].

6. PRODUCTION OF ISOTOPES AND OTHER IRRADIATION SERVICES

Although BNCT dominates the current utilization of the reactor, one or two days per week are used for other purposes such as isotope production and neutron activation analysis. The main routinely produced isotope is Br-82, either in the form of KBr or ethylene bromide. They are used by customers for flow measurements in industry. Typical produced activity per irradiation capsule is around 40 GBq. Also other isotopes used in measurements in industry are produced. The volume of neutron activation analysis is dramatically smaller than in the 70's and 80's when the reactor was operated close to daily only for activation analysis [22]. Occasionally special isotopes or other irradiation services are produced for customers' R&D projects.

7. CONCLUSIONS

Over thirty patients have been treated at FiR 1 since May 1999, when the license for patient treatment was granted to the Boneca Corporation. VTT as the reactor operator has a long term contract with the Boneca Corp. to provide the facility and irradiation services for the patient treatments. The BNCT facility has been licensed for clinical use and is being surveyed by several national public health authorities including the Radiation and Nuclear Safety Authority. The treatments are given in collaboration with the Helsinki University Central Hospital, located only about 6 kilometers from the reactor.

FiR 1 has also an important national role in providing local enterprises and research institutions in the fields of industrial measurements, pharmaceuticals, electronics etc. with isotope production and activation analysis services. The reactor is considered at VTT as a self supportive service unit without basic funding from VTT or other government sources. The funding is based on the sales and contracts with the customers.

ACKNOWLEDGEMENTS

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