1. Introduction

The neutron therapy programme at Louvain-la-Neuve is carried out with the cyclotron "CYCLONE" of the Université Catholique de Louvain designed for physics experiments (16). The cyclotron is located in the University Campus at the Physics Institute at 25 km from the Cliniques Universitaires in Brussels.

The isochronous variable-energy cyclotron manufactured by CSF (France) accelerates different types of charged particles. Deuterons can be accelerated at energies ranging from 13 to 50 MeV and protons can be accelerated up to about 90 MeV. Beside medical applications, it is used for research in physics and chemistry as well as for isotope production.

2. Description of the facility

The treatment room and related medical facilities are located one level below the main level of the cyclotron. This permits the use of a vertical therapeutic neutron beam by bending the deuterium or the proton beam.

Up to the end of 1981, neutron beams used for therapeutic applications were produced by bombarding a 10 mm thick Beryllium target with 50 MeV deuterons (16). This Beryllium target was mounted in a 7 mm thick brass support, cooled with water. The maximum available deuteron energy at Cyclone (50 MeV) was selected.

In a second stage, from 1982 up to now, neutron beams produced by bombarding a thicker (17 mm) Beryllium target with 65 MeV protons were used (10). This change was made in order to improve the physical selectivity of the irradiation.

However to improve the p(65)+Be beam quality some modifications have been performed (9). Neutron spectra produced by protons on Beryllium differ in shape from those produced by deuterons, the former having 2 parts: a high energy extending almost to the energy of the incident protons and an intensive low energy component. A filtration with a hydrogenous material such as polythene is then necessary to attenuate this low-energy component.

The choice of the adequate filter is always a compromise between an increase in depth dose and a reduction in the dose rate: at Louvain-la-Neuve, a 2 cm thick polythene filter was selected.

Finally, in the prospect of initiating proton beam therapy (protons can be accelerated at CYCLONE up to about 90 MeV), the use of neutron beams produced by the same particles would be more practical if neutron therapy and proton therapy would be performed during the same session.

The collimation system consists of a fixed shielding and a series of interchangeable inserts (16). The shielding itself consists of a proximal part ("a precollimator") and a distal part in which the different inserts can be fitted and rotated along their vertical axis. The distal part is conical and consists of a steel mould filled with a mixture (50%) of epoxy and borax.

The precollimator, 50 cm steel, which determines the largest available field (25 cm x 25 cm) contains two independent transmission ionization chambers used as monitors and located about 25 cm below the target.

The interchangeable inserts are cylindrical in shape; their height is 80 cm and their external diameter 40 cm. The proximal part (50 cm) is a mixture of iron and epoxy and the distal part (30 cm) is a mixture (50%) of borax and epoxy, which ensures an efficient definition of the beam. A set of 12 inserts is available with field sizes ranging from 6 cm x 8 cm to 16 cm x 20 cm (at a TSD of 157 cm). The field sizes can be modified -6% to +13% by varying the TSD from 147 cm to 177 cm. Due to their weight, positioning of the inserts requires an electro-hydraulic device.

3. Characteristics of the beams

The physical selectivity which can be reached with 50 MeV neutron beams is slightly better than that obtained, in usual conditions, with 60 Co (10). For example, for a 10 cm x 10 cm field at a TSD of 157 cm, the 50% absorbed dose, on the axis, is obtained at 13.6 cm in depth.

Irregular shaped fields are frequently used by inserting iron or better tungsten shielding blocks (12 cm thick) (3) (4). These blocks are used to protect critical normal tissues. They are positioned on a perspex table just above the patient. The interposition of this perspex table (of 5 mm thick required to support the heavy shielding blocks) destroys nearly completely the skin sparing.

This fact could be clearly noticed clinically (more heavy skin reactions), and was confirmed by measurements performed with a parallel plate ionization chamber.
For 50 MeV neutron beams skin sparing can be recovered completely (or even improved) by inserting 2mm lead beneath the perspex of the table; the surface dose than decreases down to 43%.

Improvement of skin sparing (surface dose: 41%) is observed by closing the collimator aperture with a 2 mm lead shield, which absorbs the charged particles produced inside the collimator.

4. Activation problems:

Production of neutron beams from protons on Beryllium raises some activation problems (9). It has been observed that after several treatments with p(65)+Be neutrons, activation in the treatment room raised by a factor 2 if compared with activation levels after d(50)+Be treatments. In the beam axis, a significantly increase of activation irradiation was observed. Measurements indicated that this was mainly due to activation of the brass support of the Be target. A mechanical system, supporting two targets was then constructed in such a way that after each treatment, the irradiated target is automatically removed out of the beam line. A new target configuration was used since 1982.

A 17mm thick Beryllium target was used to raise the dose rate. Carbon was chosen as backing material to lower the gamma component and to reduce the low-energy component in the neutron spectra. The neutron beam was filtered with a hydrogenous material to further eliminate this low-energy component. The 17mm Beryllium target together with the 10mm Be target are inserted in a movable brass support which allows the production of neutrons either by 65 MeV protons or by 50 MeV deuterons. The design of the new target assembly offers the possibility of transmitting the accelerated protons directly.

5. Radiobiology:

Determine types of RBE determinations were performed: they were a part of the pretherapeutic radiobiological program carried out at Louvain-La-Neuve.

The RBE varies, within large limits, as a function of the dose per fraction and the biological effect. For example, the RBE for the late tolerance of the central nervous system is particularly high. Relations between RBE and dose per fraction for early intestinal tolerance in mice were measured. Early intestinal tolerance was assessed from LD50 after selective abdominal irradiation. RBE increases with increasing dose per fraction but reaches a plateau value of 2.6 when the gamma dose per fraction becomes smaller than about 3 Gy.

Different RBE values were observed depending on biological system. For all the systems, RBE increases when decreasing dose.

The variation of neutron RBE as a function of energy was determined for different neutron beams. An increasing RBE with decreasing neutron energy of the beam was observed.

6. Clinical results

From the radiobiological data available, one could expect that hypoxic, slowly growing and well differentiated tumours would be a good indication for fast neutrotherapy.

It is now well recognized that the main indications for neutron therapy are:

1. Salivary gland tumours
2. Some head and neck tumours
3. Malignant melanomas
4. Soft tissue sarcomas
5. Prostatic adenocarcinomas

From March 1978 to December 1989, a total number of 1125 patients were treated at Louvain-La-Neuve (Table I).

A. Prostatic adenocarcinomas

From October 1979 to December 1988, 159 patients were treated for prostatic adenocarcinomas: 33 stage A, 12 stage B, 62 stage C and 32 stage D (8).

The present analysis, performed in March 1989, includes 62 patients with stage C, having a minimum follow-up of one year.

In 14 patients, the tumour was present at the moment of neutron therapy and in 28 patients, the treatment was started after TURP. The local control rate reaches 98% at one year, 95% at two years, 82% at three years and 85% at 4 years.

The survival rate reaches 93% at one year, 82% at two years and 66.5% at three years and 57% at 4 years.

B. Soft tissue sarcomas

Hundred evaluable patients with locally advanced soft tissue sarcomas were treated from March 1978 to March 1987 (6). They were analyzed in September 1987. The minimum follow-up was 6 months.

Excluding 22 intra-abdominal and 3 intrathoracic localizations, 259 patients are analyzed.

In a first group of 47 patients treated after radical surgery, a persistent local control was achieved in 91.5%.

In a second group of 28 patients with "gross" tumour present at the time of neutron therapy, the local control was observed in only 10%.

Survival rate is nearly independent on the presence or not of "gross" tumour at the time of neutron therapy (70% and 65% in the first and second group respectively).

Severe complications were observed in 12 cases (16%).

A correlation between complication rate and field size was observed. The large field sizes reflect generally the large initial tumour extent.
The multileaf variable collimator designed by Dr. RRAHME is now under construction in our workshop in Louvain-La-Neuve. Of course, the horizontal beam is available. The Bragg Peak appears to be suitable to treat choroidal melanomas, some cerebral tumors have been measured at 6 cm in depth in phantom. This proton beam will be used with a set of interchangeable inserts.

Combination of a fixed vertical beam and of a fixed horizontal beam was preferred to an isocentric mounting. The vertical beam will be adjacent to the first one. This room will be equipped with a horizontal beam and will be operational for 65 MeV neutrons in 1989.

Two 430 bending magnets bring the proton beam the main Cyclotron level down to the level of the treatment room. The multileaf variable collimator designed by Dr. BRAHME is now under construction in our workshop in Louvain-La-Neuve. Of course, the length of the leaves had to be increased and adapted to 65 MeV neutron beams.

Proton beam therapy is foreseen in the second irradiation room with horizontal beam. 90 MeV protons are available. The Bragg Peak was measured at 6 cm in depth in phantom. This proton beam appears to be suitable to treat choroidal melanomas, some cerebral lesions in children as well as some superficial tumours of the head and neck area.

References


