CYCLOTRON CENTRE BRONOWICE – THE FIRST POLISH PROTON THERPAY CENTRE

The Cyclotron Centre Bronowice (*in Polish – Centrum Cyklotronowe Bronowice*, *CCB*) is a part of the Institute of Nuclear Physics of the Polish Academy of Sciences (*IFJ PAN*). The CCB is presently a major Polish accelerator facility, a modern nuclear physics research laboratory and a world-class proton radiotherapy centre. It is the first of its kind in Poland and one of only a few in Europe. The activities of the CCB are focused around two cyclotrons which now operate at IFJ PAN – the "old" in-house developed AIC-144 isochronous cyclotron (accelerating protons to the energy of 60 MeV), and the "new" Proteus C-235 cyclotron with a proton beam of variable energy (between 70 and 230 MeV), installed in 2013.

At the turn of the century, we began work to adapt the AIC-144 cyclotron to treat patients with ocular tumours using its horizontal 60 MeV proton beam, in close collaboration with the medical teams of the Department of Ophtalmology and Ophtalmic Oncology of the Jagiellonian University's Collegium Medicum and of the Centre of Oncology in Kraków. By February 2011 we were able to treat our first two ocular patients, a 38-year old male and a 42-year female patient, both suffering from eye melanoma, making proton radiotherapy clinically available to patients in Central Europe. A clinical trial engaging a total of fifteen patients preceded the present regular treatment of eye-cancer patients, under contract with the Polish National Health Fund.

The range of 60 MeV protons in water is about 29 mm which is sufficient to treat tumours in eye-ball but not tumours elsewhere in the body, where protons need to be accelerated to energies of some 250 MeV. Realising the need to develop a fully equipped modern proton radiotherapy centre, the IFJ PAN successfully applied for funds, receiving about 50 M€ (85% from EU structural funds and 15% from Polish government) to finance the installation at IFJ PAN in Krakow of a modern Proteus C-235 230 MeV proton cyclotron and two gantries, produced by the Belgian Ion Beam Application (IBA) company. We also designed a new horizontal eye treatment beam line using the C-235 cyclotron. Construction of the new cyclotron building (National Centre of Hadron Radiotherapy - Cyclotron Centre Bronowice) with patient treatment rooms and an experimental hall for nuclear physics research, began on March 17, 2011, again in close collaboration with medical experts, nuclear physicists and engineers, took five years. The fully equipped CCB was able to treat its first ocular patient in February 2016 and its first CNS (Central Nervous System) patient in November 2017.

By the end of the year 2018 a total number of 394 cancer patients were treated at CCB. Over the last year(2018) a total of 117 patients were treated, of which 34 were patients with ocular cancers, 7 were children, 25 with H&N (head and neck) cancers, 40 CNS (central nervous system) cancers, 13 with sarcomas and 5 with other cancer types. We are currently waiting for national bodies to approve proton treatment of further cancer sites.

The Henryk Niewodniczański Institute of Nuclear Physics has had quite a long tradition in hadron radiotherapy. Between the years 1976 and 1994, 550 patients with cancers located in the head-and-neck or breast had been treated with a beam of fast neutrons produced on a thick beryllium target using 12 MeV deuterons accelerated by the IFJ's U-120 cyclotron. This cyclotron was later replaced by the AIC-144 isochronous cyclotron in-house-designed at the

IFJ PAN and adapted to proton radiotherapy between 2008 and 2010. The beam delivery system and treatment room were also in-house designed and built. Our 60 MeV proton radiotherapy facility, the only one in Poland (a 40-million country) and the first to operate in Central-Eastern Europe, is not only able to treat all Polish ocular melanoma patients (some 100 cases per year) but also patients in neighbouring European countries.

Over the years 2011 - 2015 the 60 MeV proton beam of the AIC-144 cyclotron was used to irradiate patients with cancer of the eyeball. The in-house developed beam delivery system and treatment room facility were all designed and constructed by engineers, technicians and software developers at the IFJ PAN – to become the first proton radiotherapy facility to operate in Poland. In developing the clinical part of this project, the team of IFJ PAN physicists and engineers closely collaborated with radiation oncologists at the Centre of Oncology in Krakow and with ophthalmologists at the Department of Ophthalmology and Ophthalmic Oncology (Collegium Medicum of the Jagiellonian University – CMUJ). By December 2015, 128 ocular patients of the CMUJ were irradiated at the AIC-144 facility, under contract with the Polish National Health Fund.

The fixed horizontal beam line and the limited range in tissue of the 60 MeV protons from the AIC-144 cyclotron precluded any applications of this beam in cancer radiotherapy apart from ocular treatments. In 2010 the IFJ PAN successfully applied and received a grant of about 30 M€ to purchase and install a modern IBA (Ion Beam Applications, Belgium) Proteus C-235 cyclotron to supply proton beams to an experimental hall and to a new eye treatment facility. Following the ground-breaking ceremony on March 18, 2011, the C-235 cyclotron was delivered from Belgium, installed on May 11, 2012 and began operation in December 2012. The C-235 cyclotron is able to accelerate protons to the energy of 230 MeV and is equipped with a degrader and energy selector which allows the energy of the proton beam to be varied continuously over the range 70 – 230 MeV. Basing on our earlier experience gained from the AIC-144 ocular radiotherapy project, a new eye treatment room was designed, fully equipped and commissioned by the physicists, engineers and technicians of our Institute. Finally, working together with IBA, the new eye treatment unit was commissioned and approved, in conformity with CE Medical standards. The first ocular patient was irradiated at the new facility on February 14, 2016.

While the application of cyclotron-produced proton beams for ocular radiotherapy was our immediate goal, the choice of the modern IBA C-235 cyclotron was dictated by the possibility of applying its variable-energy proton beams for proton radiotherapy at all sites using a rotating gantry and Pencil Beam Scanning (PBS) technology, as well as for basic and applied research in nuclear physics, radiobiology, medical physics and radiation detectors. The success of the C-235 cyclotron project enabled the management of the Institute to apply for financing of a much broader project involving the construction of a building for medical applications of the C-235 beams, together with housing and installation of two rotating gantries with PBS therapy units able to treat tumours at all treatment sites, as well as building a modern, well equipped experimental hall for basic and applied research in nuclear physics. Commencing in 2013, two state-of-art rotating gantries were also purchased from IBA. They successively underwent installation, approval, and final commissioning in September 2015. This medical centre was officially opened on October 15, 2015. However, it took one year (until July 1, 2016) for the Polish Ministry of Health to publish an ordinance which formally enabled Polish medical centres to perform a limited number of proton radiotherapy procedures under public funding.

The proton radiotherapy contract between IFJ PAN and the Centre of Oncology, Krakow Division (COOK) was signed on September 30, 2016. The first patient with a base of scull tumour was irradiated at the CCB on November 4, 2016.

The Cyclotron Centre Bronowice now consists of two Departments: of the AIC-144 Cyclotron and of the Proteus C-235 Cyclotron, and of four Sections: of Dosimetry, of Treatment Planning, of Quality Assurance, and of Administration. Currently, within about 60 members of the CCB staff at the IFJ PAN are medical physicists, medical doctors, engineers, technicians, and Ph.D. students. We believe that the CCB – a unique in Poland, state-of-art proton radiotherapy installation located within the IFJ PAN – a leading nuclear physics research institute, together offer the unique possibility of combining cutting-edge proton radiotherapy with expertise in accelerator physics and with extensive basic and applied research capability in hadron radiotherapy, nuclear physics, radiation physics, clinical dosimetry, medical physics, radiobiology, microdosimetry, and materials engineering.

The AIC-144 cyclotron is an isochronous cyclotron designed and constructed at IFJ in the early 90's to accelerate light ions (protons, deuterons and alpha particles) for research in nuclear physics. Its design, with a single dee, is unconventional. This cyclotron was used until 2010 mainly for the production of rare radioactive isotopes for scientific purposes. Later, its construction was modified and optimised to produce a 60 MeV proton beam at a current of 80 nA, stable to within 5%, for purposes of proton radiotherapy. The AIC-144 cyclotron is currently operated as a user facility for research and development in radiation physics, dosimetry, medical physics and radiobiology. Two beam lines are currently available: at the AIC-144 ocular proton therapy room and at the AIC-144 experimental room. In their vicinity, several rooms are available for preparing experiments in physics and biology. The cyclotron is operated by the AIC-144 Department engineering team of 11 accelerator engineers, technicians and support personnel, closely collaborating with engineers of the Proteus C-235 facility.

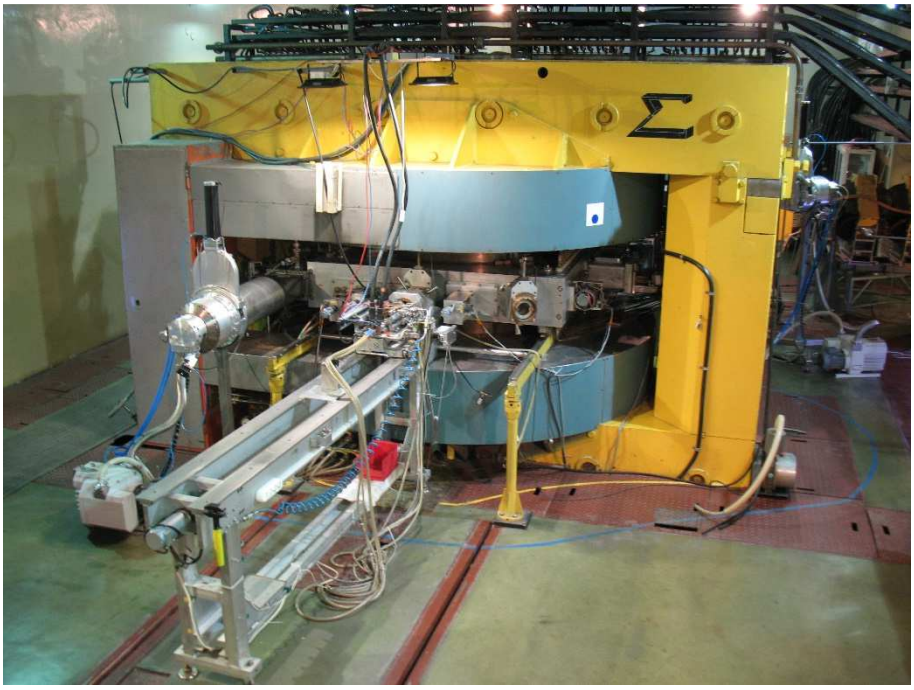

Fig.1. The AIC-144 isochronous cyclotron. Shown are the main magnet, magnet coils, the vacuum vessel and the ion source – at the centre. (*copyright: J. Sulikowski*)

The **new building of the Cyclotron Centre Bronowice** houses the technical part and the medical area. The technical part contains the cyclotron vault and an experimental hall, together with preparation laboratories for experiments in physics and biology. The medical area provides the space necessary for the radiation therapy facility, including two scanning gantry therapy units, and for the required diagnostics and preparation of radiotherapy patients.

Fig.2 A view of the CCB building, December 2016 (*copyright: M. Ptaszkiewicz*)

The Proteus C-235 cyclotron was designed and produced by IBA (Ion Beam Applications S.A., Belgium) specifically for medical applications. It is an isochronous cyclotron with a compact conventional magnet, able to accelerate protons to an energy of 230 MeV. Protons of this energy have a range of some 32 cm in water, which enables their radiotherapy applications at all sites in the patient. An energy degrader and selector, allowing the beam energy to be downgraded continuously to 70 MeV, is an integral part of this installation. The basic parameters of the Proteus C-235 cyclotron are: weight – 220 tons, outer magnet yoke diameter – 4.34 m, magnetic field – up to 3.1 T, maximum current in the main coil magnet – 800 A, operating frequency – 106 MHz, radially-dependent dee voltage amplitude 50-100 kV, PIG-type internal source, extraction efficiency – 70%, external beam current at 230 MeV –500 nA, total operating power consumption – 1.3 MW.

The Proteus C-325 Cyclotron Department which maintains and operates this cyclotron employs ten engineers. The variable energy beams of the Proteus C-235 cyclotron are directed to the physics experimental hall, to the C-235 eye treatment room and to two gantries.

The Experimental Hall, of floor area 100 m^2 and a height of 5 meters, uses a single horizontal proton beam line of variable energy, mainly for basic research in nuclear physics. Two preparatory rooms for physical experiments and two rooms for biological experiments are available in close vicinity to this experimental hall.

Fig. 3. The Proteus C-235 isochronous cyclotron at the Cyclotron Centre Bronowice, IFJ PAN. (*copyright: K. Guguła*)

At the western, medical part of the new CCB building, the **proton treatment units** and auxiliary medical rooms are located. The medical part consists of three treatment rooms, one with a horizontal 70 MeV proton beam line for eye treatment, and two rooms equipped with rotating gantries, which allow the patient to be irradiated from any direction (0^0- 360^0). Both gantries are equipped with dedicated IBA nozzles which are able to apply fields of up to 30 cm x 40 cm using proton Pencil Scanning Beams. The patient is positioned with the aid of a robotic positioner, orthogonal X-ray imaging sets and a Vision-RT optical verification system. For treatment of paediatric patients, anaesthetic columns and units are installed with access to anaesthetising gases. Imaging for treatment planning is conducted using a Siemens Somatom AS Open wide-bore computer tomography (CT) scanner which enables fast scanning using a dual-energy protocol. The CT room also contains lasers for virtual simulation and an optical patient positioning verification system for alignment and gating purposes. In the CT room there is also full access to anaesthesiology procedures. A dedicated room has been prepared for

paediatric patients, with a mobile anaesthesiology unit, allowing out-of-the-room patient preparation. After treatment the paediatric patients are transferred to a wake-up room equipped with monitored intensive-care beds. Patient-specific immobilization devices, such as thermoplastic masks, cushions or vacuum bags, are prepared in a dedicated modelling room equipped with a movable patient couch, alignment lasers, a water bath, vacuum pumps and other accessories. The patient treatment facility has been fully operational since October 2015. Up to 500-700 patients a year can be treated here, depending on their site of treatment and treatment schemes.

Fig. 4 Positioning of a head phantom at the gantry room at the Cyclotron Centre Bronowice. (*copyright: T. Kajdrowicz*)

Fig.5. Preparation of a Computed Tomography scan of a head phantom at the Cyclotron Centre Bronowice. (*copyright: T. Kajdrowicz*)

Development of the Proteus C-235 cyclotron-based proton ocular radiotherapy facility

The basic advantage of proton ocular radiotherapy is in its exceptional sub-millimetre accuracy, unattainable by conventional radiotherapy using external photon beams. The C-235 ocular proton radiotherapy facility has been in-house developed at IFJ PAN and incorporated within the IBA Proteus C-235 therapy system.

The 230 MeV proton beam from the C-235 cyclotron installed at CCB in 2012 is degraded to an energy of 70 MeV and delivered to a specially designed eye therapy room where it is suitably formed and monitored. The eye therapy facility is equipped with several in-house – developed beam forming elements. After its preparation, the beam line allows a small tumour volume in the patient's eyeball to be irradiated at dose rates ranging between 6 – 32 Gy/min. The proton beam range in water (90% at the distal edge) is 31.5 mm, the distal fall-off (90%–10%) is less than 1.8 mm and lateral penumbrae measured in air (90%–10%) do not exceed 2 mm. These parameters are in line with other ocular radiotherapy centres worldwide.

The input beam energy is individually selected for the patient by a range shifter. Passive spreading of the Bragg peak is achieved by rotating wedge modulators also individually designed and machined for each patient. The beam dose is continuously monitored by PTW beam monitors and a four-segment ionization chamber. The patient is immobilized and positioned to a precision of 0.1 mm using a Patient Positioning System equipped with a BFI robotic eye therapy chair with a fixed isocentre position. Precise positioning of the patient's eyeball, which relies on X-ray images of fiducial markers attached earlier to the treated eyeball and on patient's active cooperation, is achieved by a Varian RAD-14 Diamond X-ray system using silicon flat panel detectors. The beam control system and the autonomous safety system are based on National Instruments hardware and on in-house developed dedicated software, using the LabView platform. The Varian Medical Systems Eclipse Ocular Proton Planning system has been configured to plan ocular radiotherapy at the CCB.

The C-235 proton eye therapy facility has been certified as a part of the Proteus C-235 therapy system of established CE medical certificate conformity, as a class IIb device, complying with the requirements of the European Council Directive 93/42 (approval number LRQ0960676).

Figure 6 The C-235 eye-treatment room at the CCB facility (*copyright: J. Swakoń*)