# STATUS OF THE HZB# CYCLOTRON: EYE TUMOUR THERAPY IN BERLIN

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*Abstract*

The mission of the ion beam laboratory (Ionenstrahllabor) ISL was the provision of fast ions for solid state physics, materials analysis and medical applications in basic as well as applied research. Eye tumours are treated since 1998 with 68 MeV protons in collaboration with the University Hospital Benjamin Franklin, now Charité - Campus Benjamin Franklin. In autumn 2004 the board of directors of the HMI decided to close down ISL at the end of 2006. In December 2006, a cooperation contract between the Charité and the HMI was signed to assure the continuity of the eye tumour therapy, at this moment being the only facility in Germany.

We have now experienced the first three years under the new boundary conditions; treating more than 600 patients in that time. The main challenge is to supply protons for the therapy with less man-power but keeping the same high reliability as before. The conversion process is not yet finished. The installation and commissioning of a new, facile injector for protons will be discussed. In addition to the routine treatment, proton therapy of ocular tumours for very young children under general anaesthesia was performed.

## ACCELERATOR OPERATION

Since 2007, the cyclotron was operated for the most part for medical purpose. Hence, the scheduled beam time hours decreased tremendously (fig. 1). The new financial boundary conditions lead to a reduction of the man-power for accelerator operation to a third of the original crew. Hence, the accelerator operation was changed from a three-shift to a two-shift mode. Over night the machine idles, monitored by new control programmes.

Nevertheless, operation continued smoothly. The reliability of the machine was kept at a high level: Beam time losses due to break-downs were between 2% and 5%. Due to the small number of scheduled beam time hours, single major breakdowns have huge impacts on the beam statistics. An example is an internal water leak in the RF system of the cyclotron, leading, for the first time since 1998, to an interruption of the therapy week. In 2008, one fifth of the unscheduled down time was caused by failures in the electric power supply of the laboratory. Some of these failures lasted for almost 1 sec. Beam tests were performed for the change from the three-shift to two-shift mode in order to test the monitoring control programs. Further tests were made for the commissioning of the tandetron (see below).

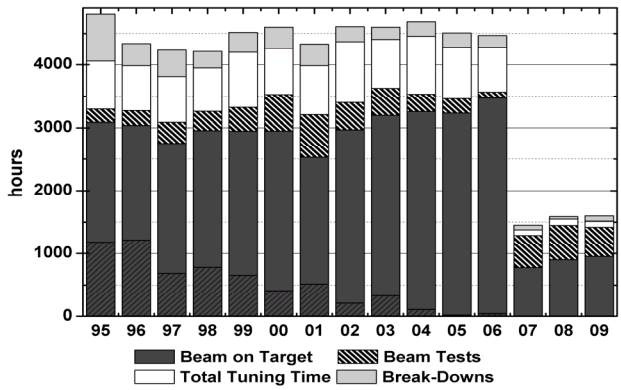


Figure 1: Operation statistics of ISL (1995-2006) and the HZB cyclotron (since 2007)

## EXPERIMENTS

The increase of beam time as shown in fig. 1 in the past two years is due to an increasing patient number. In addition, a small number of experiments were carried out. These experiments comprised radiation hardness tests for the Deutsches Zentrum für Luft- und Raumfahrt as well as detector tests and dosimetry.

In addition, a new way to correlate the axis of the proton beam to the x-ray positioning system was developed: The patient positioning is performed with the aid of tantalum tumour position markers observed by two, orthogonal X-ray systems. Usually one X-ray system is mounted in the axial direction, anti parallel to the proton beam, creating an inverse beams eye view. For patient positioning it is important that the axes of the proton beam as well as the axial X-ray system are identical. With a CCD system [1] consisting of a scintillating foil, a mirror, and a CCD camera, the two dimensional dose distributions can be measured and analysed with high precision in a very fast way. The CCD system is mounted on the patient chair thus allowing the checking of position and direction of the proton beam. A 0.2 mm tantalum cross-hair is mounted in front of the CCD camera. By moving the patient chair both cross-hair and CCD camera are moved. The chair is brought into a position where the centre of the mounted cross-hair superimposes the centre of the beam-line's cross-hair, as observed by the axial X-ray system. Thus the centre of the mounted cross-hair lies on the central axis of the axial X-ray system. In this position the dose distribution is measured by the CCD camera. The tantalum cross-hair in front of the CCD can be seen clearly in the resulting CCD image.

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Its centre can be evaluated, thus transferring the centre of the X-ray system to the CCD. The cross-hair is removed and the dose distribution is measured anew, enabling the determination of the centre of the proton beam. From the two CCD images differences between the two centres can be calculated.

With this method it is possible to ascertain the differences between the X-ray axis and the proton axis with an accuracy of up to 0.1 mm. The whole procedure takes less than 10 minutes. The former method – looking for the field centre with two one-dimensional high resolution diode scans, positioning the diode in the field centre and checking the centre with the axial X-ray system – required nearly one hour.

## INSTALLATION OF A TANDETRON

The injector for light ions, the Van-de-Graaff, provided steadily over more than 30 years a wide variety of ion species over a broad energy range. Although the 5 Ghz ECR-source itself runs very reliable, the position of the source on the high-voltage terminal including a RF bunching system, the moving belt, and the elaborated fast high-voltage regulation system require careful maintenance. In order to reduce the required manpower, a 2 MV tandetron accelerator was bought from the Bundesanstalt für Materialforschung und -prüfung (Federal Institute for Materials Research and Testing). It was dismantled and transported to the cyclotron vault. The installation took place on the position of the former heavy ion injector, the RFQ. Thus, the installation of the tandetron could be executed without interruptions of the therapy schedule. This position will reduce the length of the injection line by more than 20 m. The beam emittance of the RFQ and the tandetron are different, the latter having larger beam spot and emittance [2,3]. Furthermore, the size of the tandetron made it impossible to maintain the focus on the same position in the beam line, requiring a different focusing into the beam line to the cyclotron.

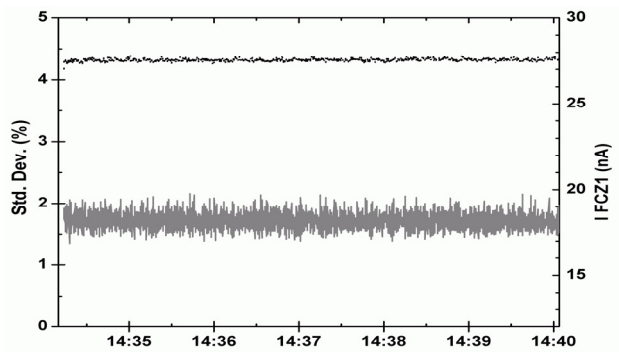


Figure 2: Short term beam stability (grey line) and beam intensity (black line) of the proton beam from the tandetron-cyclotron combination

Fig. 2 shows the extracted beam of the cyclotron using the tandetron as injector with the typical intensity used for therapy. The beam was scanned with 10 kHz and the update rate was about 10 Hz. The short-term stability is excellent; the beam changes only for 2 %. Slow variations over longer times, e.g. several hours, are in the order of 5 %.

When comparing the proton beam delivered either by the Van-de-Graaff-cyclotron or the tandetron-cyclotron combination, they are similar: Differences in the dose distribution are negligible (fig. 3).

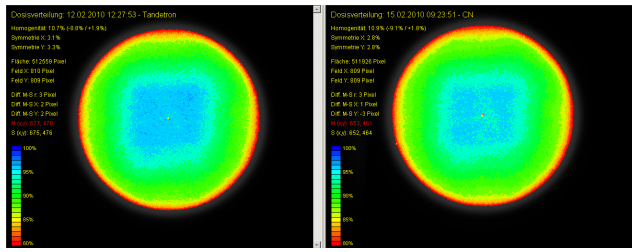

Figure 3: Dose distribution at the therapy station measured for both injectors: Van-de-Graaff (right) and tandetron (left)

The single Bragg peak of the 68 MeV proton beam was determined for both injectors, and they are identical. Due to the acceptance of the cyclotron, small changes on the tandetron voltage will not affect the energy, i.e. the range, of the extracted beam. The distal fall off from 90 % of the dose to 10 % of the dose is in both cases 0.95 mm. This sharp distal fall off provides best possibilities to spare healthy tissue.

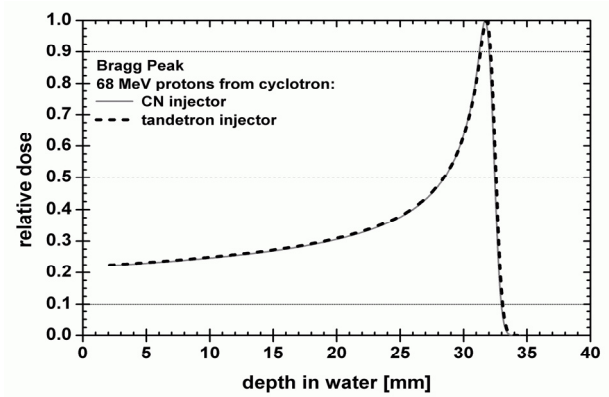


Figure 4: Bragg peak at the therapy station determined for both injectors: Van-de-Graaff (solid grey) and tandetron (dashed black)

## INDICATIONS, DEVELOPMENT OF PATIENT NUMBERS AND SPECIAL CASES

In 2007, eleven therapy weeks were scheduled: Quality assurance is performed on Monday, whereas the patients receive their irradiation in four fractions of about 40 s from Tuesday to Friday. The number of patients rose to more than 210 per year (fig. 5). Hence, the number of therapy weeks was increased to twelve. More than 90% of the indications are choroidal melanomas. The case-subgroup of large uveal melanomas increased, mostly followed by surgical removal (endoresection or

transscleral resection) of the inactivated tumour mass to prevent toxic reactions.

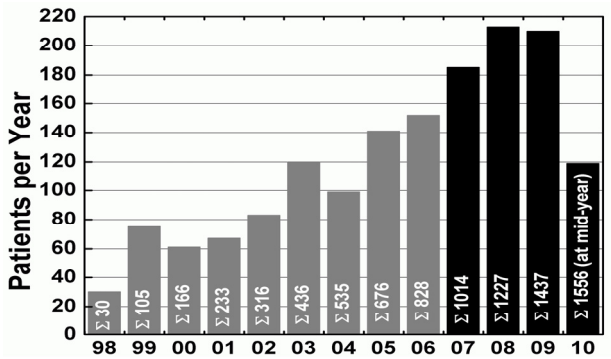


Figure 5: Patient figures treated per years (bars) and in total (white numbers).

In the treatment of ocular melanomas, the cooperation of the patient is absolutely necessary. As small children are unable to cooperate in the appropriate way; they must be treated under general anaesthesia. The treatment room was equipped with a mobile anaesthesia workstation. Car seats, for different body sizes, were modified to fit to the treatment chair.

The anaesthesia procedure has to take place in the treatment room on a separate couch for anaesthesia. The anaesthetised child is transferred into one of the modified car seats. Within the seat the child is still in a lying position, fixed by seat belts. A thermoplastic mask attached to the car seat immobilizes the head. The car seat with the child is then mounted at the treatment chair and moved into a nearly sitting position. In treatment position the eyelids are kept out of the irradiation field by lid retractors. A suction cup is attached to the cornea to adjust the gazing angle of the eye for treatment (see fig. 6). After verification of the localization the irradiation takes place. The position of the eye and the vital signs are continuously monitored in the treatment and in the control room. Following irradiation the child is transferred to the couch for recovery from anaesthesia. As soon as the child can breathe by itself and has protective reflexes, it is transported to a recovery room for observation until an ambulance carries the patient back to the eye hospital.

Prior to the treatment course a simulation session with the child under general anaesthesia is necessary to fit the immobilization mask and test the feasibility of the treatment plan. The treatment procedure itself takes about two hours: one hour for anaesthesia and positioning, one minute irradiation, few minutes dismounting and roughly 45 minutes for recovery from anaesthesia. Simulating an emergency situation showed that the child can be dismounted in less than a minute, giving full access of the anaesthesiologist to the child for emergency procedures.

With this set-up we treated three children (10 months, 5 years, and 7 months). Treatment was tolerated well. With the frontal irradiation approach we can use the benefits of a dedicated eye beam line: sharp lateral penumbra and sharp distal fall-off, enabling us to spare the bones of the skull completely.

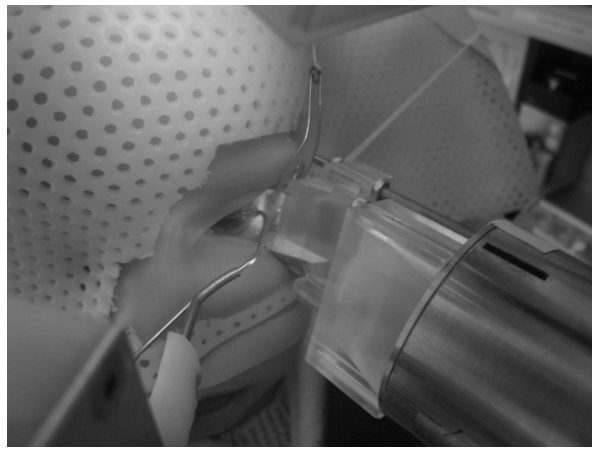

Figure 6: One of the children in treatment position. The proton beam arrives from the lower right. A suction cup fixes the eye in the desired position.

## SUMMARY

This activity is based upon more than 10 years of accelerator development and common R&D of the accelerator scientists and the Eye Clinic of the Benjamin Franklin University Hospital within the Charité. The joined effort created Germany's only facility for this kind of therapy. In spite of major structural changes we could keep a high quality standard and even increased the number of treated patients. Proton therapy of ocular tumours for complicated cases like very young children under general anaesthesia is feasible on a horizontal eye beam line.

We have now experienced the first three years under the new boundary conditions; treating more than 600 patients in that time. The conversion process from a multi-purpose, multi-ion machine to a single ion, single energy accelerator is not yet terminated. Nevertheless, the accelerator operation went quite smoothly. A tandetron was installed as new injector and the beam tests were successful. As the beam tests of the tandetron-cyclotron combination have been successful, we now apply for the permit to use it for patient treatment.

We will continue to provide unique therapeutic possibilities for the patients in Germany.

## ACLNOWLEDGEMENTS

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