EYE TUMOUR THERAPY IN BERLIN

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Abstract

The ion beam laboratory ISL at the Hahn-Meitner-Institut Berlin (HMI) supplied light and heavy ion beams for research and applications in solid state physics, industry, and medicine. Since 1998, eye tumours are treated 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.

The accelerator operation, continued with reduced manpower, required changes in the set-up of the accelerators. A new, facile injector for protons is under commissioning. Increasing the reliability will be a key issue.

The last two years of operation of ISL as a full multi-purpose accelerator will be shown and examples of the research work will be demonstrated. The conversion of a multi-ion, variable energy accelerator to a dedicated accelerator for eye tumour therapy will be discussed.

ION BEAM LABORATORY ISL

Accelerator Layout

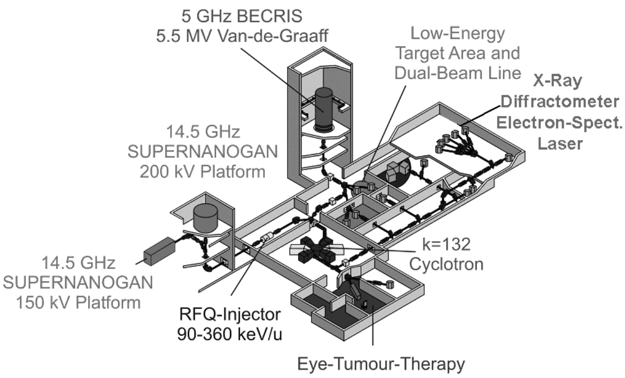

Figure 1: Layout of the ISL facility, consisting of a k=132 isochronous cyclotron served by two injectors: a Van-de-Graaff accelerator for light ions and a frequency variable RFQ with two ECR-sources for heavy ions.

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. For this purpose, ISL operated an accelerator complex serving nearly 20 target stations (see fig. 1). The properties of the ISL beams – energy range, ion species, beam emittance, pulse structure, and stability – was unique and allowed a vast variety of experiments.

Accelerator Operation

With the available manpower, about 4500 hours of beam time were scheduled each year (see fig. 2). Since 2003, always more than 3200 hours of beam on target could be achieved. The all-time high in 2006 was due to a complete stop of all R&D activities as well as the full operation of the second ECR ion source of the RFQ, leading to shorter tuning times: One source could be tuned, e.g. for a gold beam, while the other one was still delivering beam to the experiment. Gold ions were employed to about 30% of the beam time for materials modification and materials analysis, whereas for 25% of the beam time protons were used for medical purposes and materials analysis. Other ions used comprised D, rare gases, Cu, and so-called cocktail beams. The short beam times needed for solid state physics – typically a few shifts only – and the often requested changes in ion species and energy lead to the high tuning times. Beam time losses due to break-downs over the last years of ISL amounted to 5%.

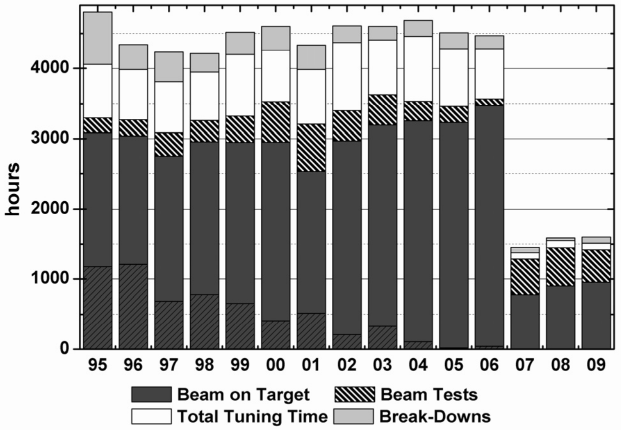

Figure 2: Operation statistics of ISL (1995-2006) and the HZB cyclotron for medical purposes only.

Experiments

Experiments were carried out at 15 high-energy target stations. The focus of the research at ISL was solid state physics: About 50% of the beam time was used for materials modifications and ion-solid interactions, e.g. the study of nanoscale self-assembly of thin oxide films under fast heavy ion irradiation [1]. The dedicated target stations for this research topic included, among others, on-line XRD spectrometer for the observation of ion induced structural changes, in-situ electron spectroscopy,

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[#] The Helmholtz-Zentrum Berlin für Materialien und Energie has been formed by the merger of the Hahn-Meitner-Institut Berlin and the Berliner Elektronenspeicherring-Gesellschaft für Synchrotronstrahlung and the spectroscopy of desorbed neutral atoms by laser ionisation. A stripper behind the cyclotron permitted the selection of the mean equilibrium charge state [2]. In cooperation with industry, polymer foils were irradiated with heavy ions for ion track filter production.

Materials analysis obtained 15% of the beam time. With Elastic Recoil Detection Analysis (ERDA), about 400 samples each year were analysed, mainly for semiconductor and photovoltaic device-developments by measuring the depth-dependent concentration from hydrogen to heavy elements up to a depth of about 3 µm [3]. The heavy ion ERDA set-up at ISL provided a flexible tool for the investigation of a broad variety of analytical questions, which was unique in Germany. High-energy Proton Induced X-ray Emission (PIXE) was applied to objects d'art and archaeological items. The advantage of high-energy PIXE is the possibility to measure heavy elements behind thick layers of material non-destructively. More than 2000 samples have been analysed for museums, mainly from Berlin/Brandenburg, but also from all over Europe, e.g. medieval silver coins from Austria [4].

High-energy protons as well as cocktail beams, e.g. 6MeV/u $^{12}C^{3+}$, $^{16}O^{4+}$, $^{36}Ar^{9+}$, $^{86}Kr^{21+}$, $^{132}Xe^{33+}$, were used for radiation hardness testing. The tested devices ranged from electronic components to solar cells for space applications [5].

Since 1998, eye tumours are treated in cooperation with the Charité, Universitätsmedizin Berlin, Campus Benjamin Franklin. In the midterm evaluation report the review committee stated: "The review committee considers the quality of research and development performed during the reporting period as excellent. In terms of the dosimetric precision achieved, the group has surpassed other groups from which they have learnt (PSI and MGH) and is currently in a leading position world-wide." However, the directors decided on the basis of the shutdown of ISL to stop the participation within the programme oriented funding topic "Health". The excellent performance both in therapy and in associated research initiated a solution to continue the eye tumour therapy as described below.

CONVERSION TO A DEDICATED MEDICAL ACCELERATOR

In order to ensure the continuation of the eye tumour therapy – Germany's first and, up to now, only therapy centre for eye tumours – a cooperation contract was signed between the Hahn-Meitner-Institut and the Charité in December 2006. The department "protons for therapy" now supplies the proton beam for the Charité. The financial circumstances lead to a reduction of the man-power for accelerator operation to a third of the original crew. Therefore, the accelerator operation was changed from a three-shift to a two-shift mode. Over night the machine idles, monitored by new control programmes.

The high-energy target stations have been disconnected from the cyclotron and the control system was reduced to the remaining components. The RFQ was removed as it cannot provide protons.

The injector for light ions, the Van-de-Graaff, provided reliably over more than 30 years a wide variety of ion species over a broad energy range. However, 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. 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 installed in the cyclotron vault, were the RFQ was originally situated. Thus, the installation of the tandetron could be executed without interruptions of the therapy schedule. In addition, this position will reduce the length of the injection line by more than 20 m. As the beam tests of the tandetron-cyclotron combination have been successful, the permit to use it for patient treatment will be applied for.

The tests performed for the dual shift operation as well as the beam tests with the tandetron account for the high number of beam tests hours as can be seen in fig. 2.

DEDICATED OPERATION FOR MEDICAL PURPOSES

In spite of the decreased manpower, operation continued smoothly. The reliability of the machine was very high: Beam time losses due to break-downs were between 2% and 5% – the latter was caused by one major failure, an internal water leak in the RF system of the cyclotron. This lead, for the first time since 1998, to an interruption of the therapy week. The small number of scheduled beam time hours results in huge effects on the beam statistics by single major breakdowns. The increase of beam time as shown in fig. 2 in the past two years is due to an increasing patient number.

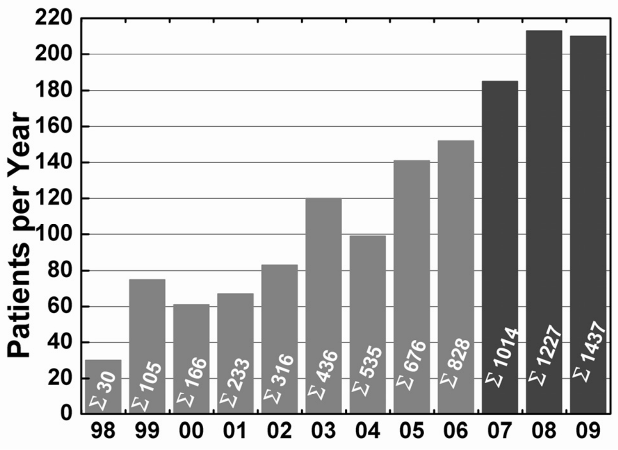

Figure 3: Patient figures treated per years (bars) and in total (white numbers).

In 2007, eleven therapy weeks were scheduled: Monday is reserved for quality assurance; patients receive their irradiation in four fractions from Tuesday to Friday. As can be seen in fig. 3, the number of patients rose to more than 210 per year. Hence, the number of therapy weeks was increased to twelve. Nearly 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.

Special Patients: Children - 7 months to 5 years

With its high local control rates of about 95% and high dose conformation proton therapy is a very powerful tool in the treatment of ocular tumours. Generally, to achieve these results the cooperation of the patient is absolutely necessary. Small children are unable to cooperate in the appropriate way; therefore, they must be treated under general anaesthesia. To prepare the treatment room for the therapy of anaesthetized children a mobile anaesthesia workstation was installed. Car seats, for different body sizes, were modified to fit to the treatment chair.

The anaesthesia procedure takes place on a separate couch for anaesthesia in the treatment room. Under general anaesthesia the child is transferred into one of the modified car seats. Within the seat the child is still in a lying position, the body is fixed by seat belts. A thermoplastic mask fixed at 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 moved 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. 4). 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.

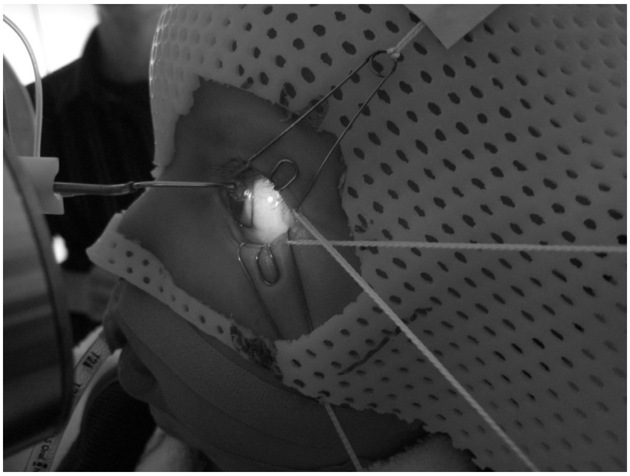

Figure 4: One of the children in treatment position.

Following treatment 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 transferred to a recovery room for observation until an ambulance transports 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 mmobilization 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.

SUMMARY

ISL fulfilled its duty to the users till the very end. All planned research activities have been finished. A very fruitful phase of research using fast ions was terminated. We thank our users for fascinating experiments and the ISL accelerator crew for their efforts. By the end of 2006 the ISL as a multi-purpose accelerator facility was closed. Therefore, with the beginning of 2007, the proton therapy was reorganised: the Charité is in charge for the therapy, the Helmholtz-Zentrum Berlin is in charge for delivering the beam.

We have now experienced the first three years under the new boundary conditions; treating more than 600 patients in that time. The conversion process is not yet finished. The accelerator operation went quite smoothly. We will continue to provide unique therapeutic possibilities for the patients in Germany.

This activity is based upon 10 years of accelerator development and common R&D of the ISL 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 very young children under general anaesthesia on a horizontal eye beam line is feasible. The neighbouring bones of orbit and skull are kept free of irradiation.

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