PROTON THERAPY CO-OPERATIVE GROUP	Chair	Secretary
	Michael Goitein Ph. D. Department of Radiation Oncology Massachusetts General Hospital Boston MA 02114 (617) 724 - 9529 (617) 724 - 9532 Fax	Daniel Miller Ph. D. Department of Radiation Medicine Loma Linda University Medical Center Loma Linda CA 92354 (909) 824 - 4197 (909) 824 - 4083 Fax

ABSTRACTS

of the

XVIII PTCOG MEETING

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Potential efficacy of proton therapy in thoraco-abdominal tumors.

H. Tsujii, H. Tsuji, T. Okumura, A. Maruhashi, T. Inada, Y. Hayakawa, Y. Takada, J. Tada, S. Fukumoto, Proton Medical Research center, University of Tsukuba, Japan

A phase I-II clinical trial using 250 MeV proton beams has been carried out at PMRC. As of March 1993, a total of 260 patients received a partial or full treatment with proton beams with curative intent. Among them there were 95 patients with thoraco-abdominal tumors who were followed-up for 6 months or more: 22 lung ca, 25 esophageal ca, and 48 hepatocellular ca. For achievement of precision proton therapy in these tumors, we have developed a real time localize-verify system, a technique to implant metal markers for orientation of the target site, and respiration-gated irradiation system which allows irradiation synchronized with respiratory motion. While dose-fractionations employed depended upon tumor sites, a large majority of patients received substantially high doses than those traditionally used, resulting in successful local control with acceptable morbidities. This fractionation regimen has been employed because of limited availability of the accelerator, and by the expectation that the superior dose distribution possible with protons will permit administration of high radiation doses without increasing morbidities. In connection with these, the target volume was always determined by setting margins around the tumor boundary as practically small as possible. So far, our judgment is that proton therapy has proven of potential advantage in treatment of these tumors, and these accomplishment has stimulated us to design a dedicated proton therapy facility.

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An Application of Dose-Volume Histogram to the Treatment of Hepatocellular Carcinomas with Proton Therapy.

H. Tsuji, T. Okumura, A. Maruhashi, Y. Hayakawa, T Inada, H. Tsujii, Proton Medical Research center, University of Tsukuba, Japan

The survey and analysis on the influence of the proton irradiation to the liver functions was performed using Dose-Volume Histogram (DVH). 48 patients with hepatocellular carcinomas (HCC) were treated with proton therapy between 1983-1992 at our institute. All patients had concurrent chronic liver disease, of whom the majority had cirrhotic liver.

We investigated their laboratory data and estimated the influence of proton therapy on their liver functions. No patients showed clinically symptomatic radiation hepatitis, but some patients showed transient increase of transaminase (GOT, GPT) after proton irradiation. So, DVH analysis on these patients was performed, regarding to the change of GOT.

As a result, the normal tissue complication probability (NTCP) of each patient correlated with the change of GOT apparently. This result suggests the availability of NTCP for the optimization in the treatment of HCC with proton therapy.

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Should we block major arteries from radiation fields in children?

J.L. Habrand, O. Ganry, J. Lemerle, Institut Gustave Roussy, Villejuif, France

This is a review of 15 cases of chronic damages to medium and large arteries following conventional irradiation in children of 4 months to 13 years (med. 5 years) at the age of diagnosis over a 22 year period (1986-1988). All these patients had clinical symptoms revealing the complication. These symptoms were related with the location of vasculopathy : aorta in 4, infra aortic trunks in 12 and supra aortic trunks in 4. Analysis of dose effect showed that this risk exists for doses as low as 25 Gy in children < 3 years and 40 Gy above the age, given in 3 to 5 sessions per week. Although this risk is generally ignored, we recommend to carefully evaluate the dose to the major arteries when children require high dose radiation.

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Proton Therapy in 1993.

Janet Sisterson, Harvard Cyclotron Laboratory, Harvard University, 44 Oxford Street, Cambridge Massachusetts 02138 USA

The number of proton therapy facilities has been steadily increasing over the years. Long term follow-up studies for certain sites are encouraging and now world wide there are many proposals to build dedicated proton therapy facilities in hospital settings. The first such facility, at Loma Linda University Medical Center, began treating patients in 1990. There are 13 operating proton therapy facilities in 1993 and by the year 2000, there are might be 24 such facilities world wide (Figure 1). Data from the 13 operating proton therapy centers indicate that 10 of them use a cyclotron or synchrocyclotron and 5 of them have a maximum proton energy of < 100 MeV.

Figure 2 shows estimates of the cumulative totals for patients treated for both benign and malignant disease with proton and light ion beams over the past 40 years.

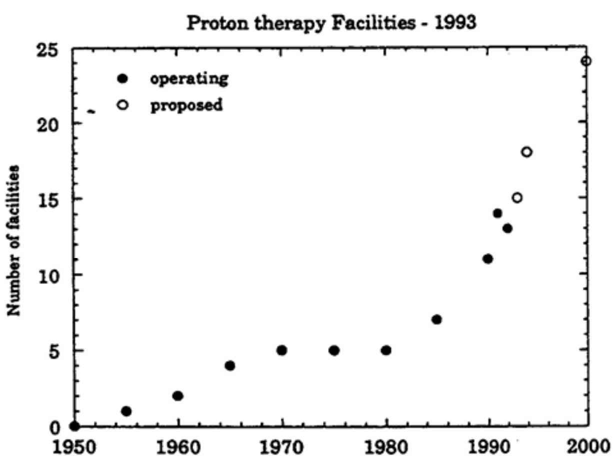

Figure 1.

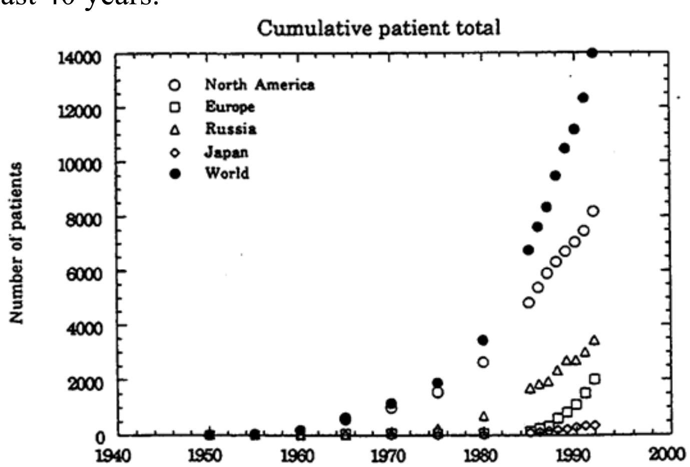

Figure 2.

The data presented here indicate that there continues to be much interest in the world for using proton beams to treat both benign and malignant disease. Many new hospital-based dedicated proton therapy facilities are being planned world-wide so that it would seem that this interest should continue or expand.

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Status Report of the Proton and Neutron Therapy Project on the AIC 144 Krakow Cyclotron.

J. Huczkowski, Centre of Oncology, Maria Sklodowska-Curie Memorial Institute,
Garncarska 11, 31-115 Krakow, Poland

Joint Radiation Oncology Group in the Centre of Oncology and in the Institute of Nuclear Physics, where the U-120 classic cyclotron was used for neutron cancer therapy for 15-years. In 1992 the new isochronic machine was built. We are now preparing the machine for neutron and proton therapy (60 MeV proton beam for eye melanoma treatment).

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The Light-Ion Therapy Project at GSI.

D. Schardt, GSI Darmstadt, Planckstrasse 1, 6100 Darmstadt, Germany

During the last years we have performed both physical-technical studies (raster scan, range verification with PET, fragmentation, etc.) and biological studies for the preparation of a light-ion therapy, using high-energy ion beams delivered by the synchrotron SIS. It is now planned to build up a dedicated treatment cave in the SIS target hall and use one horizontal beamline for an “experimental” therapy. This facility will be operational in 2-3 years from now, making use of the new techniques for a tumor-conform exposure.

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Radiation medicine projects at PSI. Status report.

H. Blattmann, G. Munkel, E. Pedroni, T. Böhringer, A. Coray, E. Egger, S. Lin,
A. Lomax, S. Scheib, U. Schneider, U. Ulmer, Paul Sherrer Institute, 5232 Villigen PSI, Switzerland

Charged particle radiotherapy at PSI now enters - for the treatment of deep seated tumors - a transition period going from pions to 200 MeV protons. The techniques used for pion treatment are critically analyzed in view of the future proton treatments in terms of precision requirements and practicability. The experience gained in the treatment of the nearly 500 patients with conformation therapy with pions is evaluated.

The proton treatment of uveal melanoma is continuing at a constant referral rate, and the OPTIS beam is increasingly used also for detector testing for the 200 MeV proton beam and for radiobiology.

While the gantry is being installed on the treatment area, electronics, dosimetry and calibration equipment is prepared.

The development of patient handling is underway, i.e. patient positioning, fixation and position verification. Treatment planning for voxel scanning but also - in collaboration with Heidelberg - a platform for treatment planning intercomparison with other irradiation modalities is set up.

Support in clinically related areas and in radiobiological questions is coming from members of our Proton Therapy Users Group and from various university institutes.

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Comparison of proton beam data for supp. 17 B.J.R.

A. Kacperek, J. Shaw, Douglas Cyclotron Unit, Clatterbridge Centre for Oncology, Clatterbridge Road, Bebington, Wirral L63 4JY, UK

Preliminary work is presented following an examination of proton Bragg peak from twelve therapy centres. The problems of how to present this data to a wider radiotherapy audience is discussed, as well as characteristic differences between various centres and how these may affect proton therapy.

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The RBE of Protons - Directions for Future Clinical Trials.

R.W.M. Schulte, Loma Linda University Medical Center, Loma Linda, CA 92354

With increasing interest in the use of protons and other heavy charged particles for the treatment of cancer patients, the relative biological effectiveness (RBE) of protons becomes an important factor of clinical protocols. In general, heavy particles like protons differ in their biological efficiency compared to sparsely ionizing radiation like X or gamma rays and electrons. During the late 70s and early 80s the Harvard group performed a series of radiobiological measurements of the proton RBE in cultured mammalian cells and murine tissues using the 160 MeV spread out proton Bragg peak, indicating that the RBE of the proton beam relative to Co-60 was between 1.0 and 1.2. No dependence of RBE on dose or endpoint was found. Since then, a RBE value of 1.1 has been used in most clinical proton protocols. On the other hand, because of the nonlinear relationship between dose and log cell survival, one can expect that the RBE of protons should depend on dose and on the cell survival parameters alpha and beta. Using recent relevant radiobiological measurements, a model of radiation damage and -repair was designed. The model predicts that for acute-responding tissues and tumors the RBE is, in fact, almost independent of dose and cell survival parameters. However, for late-responding tissue a higher RBE value and an increase of RBE with decreasing dose is predicted. The implications of these findings for future clinical protocols will be discussed.

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Quality Control, Chambers, Calorimeters, Micro-Dosimetry & Radiobiology

A. Mazal, J.L. Habrand, S. Delacroix for the CPO, and partner's teams, Centre de Protonthérapie d'Orsay, Centre Universitaire, Bât. 101, 91400 Orsay, France

From September 1991 to April 1993, 218 patients have been treated with the ophthalmological line at CPO. At present, 2 series of 8 patients each are treated per month (see statistics and methods in Dr. Desjardins's and Dr. Delacroix's abstracts).

Some works done or under evaluation include:

a) C.Q. of patient positioning (clips positions before each treatment & chair coordinates).

b) Monitor Units calculations for each day/each patient from the measurement of a reference condition and the values of absorber and modulation.

c) Dosimetric intercomparisons (between chambers: better than ±1%; calorimeter-chamber: the differences changes from -5% to -1% depending on the protocol, w/e and the s/ρ values adopted).

d) Microdosimetric intercomparison Orsay-Clatterbridge showing an excellent coincidence of spectra (y_D = 13,75 and 13,62 kev/µm respectively).
e) Microdosimetric values inside the SOBF (from 3 to 6,6 kev/µm) and after the pic (e.g.: 17,6 kev/µm).
f) Obtention of biological weighting functions from microdosimetric and radiobiological correlations (photon + neutron + proton beams).
g)In vivo radiobiological measurements (early intestinal tolerance by crypt regeneration in mice, SOBP protons vs. Cobalt, RBE=1,15).
h) Modification of the present ophthalmological line for the treatment of intracranial and base of the skull tumors (E=180 MeV, field sizes ≤10 cm, passive scattering).
i) Treatment planning software under development, based on existing photon & electron treatment planning systems in use at the hospitals partners of the project.

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Treatment Planning for spot scanning: Present and future developments at PSI.

E. Pedroni, H. Blattmann, T. Böhringer, A. Coray, S. Lin, A. Lomax, G. Munkel, S. Scheib, U. Schneider, Paul Scherrer Institute, CH-5232 Villigen-PSI, Switzerland

The dose application technique (Spot Scanning method) developed at PSI is based on the superposition of elementary pencil beams. The beam is focused on the patient and is scanned in three dimensions by the use of a sweeper magnet, a range shifter device and by moving the patient couch. The position and the dosage of each Bragg peak spot can be chosen freely in the treatment planning system. The dose distribution of each spot is calculated in all 3 dimensions. The pencil beam dose calculation (integral dose and beam width as a function of the depth in the patient) is performed using a physics formalism (with a few slightly tuned parameters). The model agrees experimentally very well with measurements done at PSI and at other institutions. Body inhomogeneities are taken into account in the dose model using the CT density distribution along the axis of a single pencil beam. A recursive dose optimization algorithm χ^2 minimization) is included in the treatment planning system, with the dosage of each spot being chosen automatically by the computer. In this way a better shaping of the dose to the assigned target volume can be achieved. The optimization procedure is expected also to improve the dose fall-off at the edge of the field and eventually to compensate automatically part of the dose distribution effects due to body inhomogeneities. The file formats used in the treatment planning system are designed to permit easy exchange between different software-hardware platforms (in our case VMS and UNIX systems). Commercially available software packages, PVWAVE and AVS, known in physics laboratories for their flexibility, have been chosen for the implementation of the three-dimensional graphics and widgets used in the treatment planning system. Future planned developments concern the implementation of collimators and compensators in the treatment planning system (an option for the spot scanning system), and the calculation of dose errors (organ movements simulation, Monte Carlo based dose calculation for complex geometries, etc.) A major effort will be devoted to the problem of patient positioning (calculation of simulated radiographies with photons and protons) with the aim to correct patient positioning errors with the steering system of the pencil beam. Simultaneous optimization of multiple dose fields and dose optimization based on biological criteria are ideally suited for the spot scanning technique but quite labour intensive. They will be investigated with lower priority over a longer time scale.

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Status report on proton therapy at NAC.

C. Stannard, National Accelerator Centre, Faure, South Africa

Situated between the 2 teaching hospitals in the Cape
Physics research up to 200 MeV. Radioisotope production 66 MeV: 22 hospitals.
Medical neutrons : 66 MeV
protons : 200 MeV.
Beam available 24 hours/day, 7 days/week except scheduled breaks for services :
Monday evening to Thursday afternoon : 66 MeV
Thursday night to Monday morning : 200 MeV or less.
1986 : beam available
1988 : first patient treated with neutrons
1989 : regular neutron therapy

PROTONS: 2 treatment rooms :1 horizontal - fixed, 1 vertical/gantry ? Start in 2 months
Initially :
1) Once a week on Friday
2) Shoot through
3) Boost to intracranial metastasis
Small AVM'S

Stereotactic treatment with computerized controlled chair, cast with markers for planning CT and treatment.

FUTURE:
1) SOBP : end of 1993 or early 1994
2) Beam : 3 x per week
3) Single fraction : small AVM'S

Fractionated : large AVM'S, recurrent pituitary tumors , skull base tumors, head and neck, deep seated tumors. No plan for choroidal malignant melanomas (10-12/yr.), use I-125 plaques.

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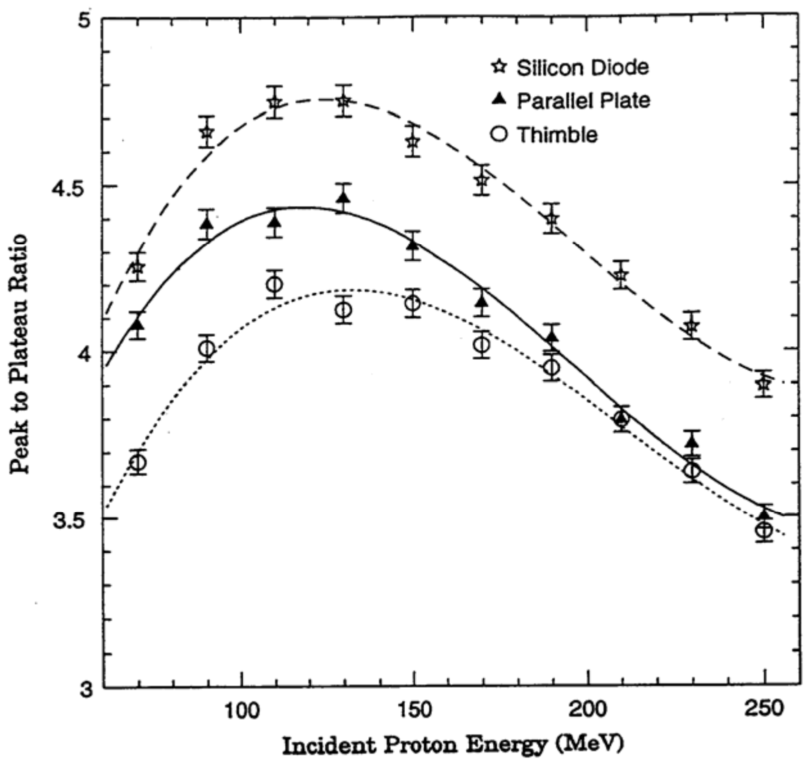
Effects of Detector Geometry and Ionization Potential on Bragg Curve Measurements.

James Case, Friedel von Goeler, Monroe S. Z. Rabin, Department of Physics and Astronomy, University of Massachusetts, Amherst MA 01002.

When measuring the shape of the Bragg curve it is important to take into account the effects on the results of both the geometry and the ionization potential of the detector. Measurements at both the Harvard Cyclotron Laboratory and the Loma Linda University Medical Center have yielded different Bragg curve shapes depending on the type of detector used (thimble ionization chambers, silicon photodiodes, and a parallel-plate ionization chamber). By using our Monte Carlo simulation program to describe the energy deposition of a beam of protons in both water and the various detectors, we understand the origins of the different shapes seen.

Compared to the shape of the Bragg curve measured with a parallel-plate air ionization chamber (ionization potential $\geq$ 100 eV), the thimble ionization chamber's non-planar geometry distorts the Bragg curve at low incident proton energies, and the silicon photodiode's low effective "ionization potential" (it is the effective band-gap potential, 3.67 eV, rather than the 175 eV ionization potential of silicon that is important) distorts the shape at high incident proton energies.



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Kidney Mobility during Respiration.

L.H. Schwartz [1,3], J. Richaud[1,2], L. Buffat[1], E. Touboul[1], (1) département de radiothérapie, (2) département de radiobiologie - Hôpital Tenon, 4 rue de la Chine 75020 Paris, France, (3) Centre de Protonthérapie d'Orsay, Centre Universitaire-Bât 101, 91400 Orsay, France

The motion of kidney during respiration has not been well quantified. Fourteen patients volunteered for the study. Nine MRI imaging of the kidney were done: three in the axial plan (all in deep inspiration), six in the coronal plan (three in deep inspiration, three in deep expiration). The maximal vertical motion of the superior pole is 39 mm (i.d. superior to a vertebral body). In deep inspiration, the positioning of the right and left kidneys appear reproducible. The standard deviation in every single direction is less than 3 mm.

Table I : Range of vertical motion of the kidney between deep expiration and inspiration

		Standard deviation	*Maximal*
Right kidney :			
	superior pole	*16 mm*	*39 mm*
	inferior pole	*17 mm*	*43 mm*
Left kidney :			
	superior pole	*14 mm*	*39 mm*
	inferior pole	*17 mm*	*42 mm*

Table II : Mobility of the kidney in deep inspiration

		Standard deviation	*Range*
Right kidney			
	internal border	*1,84 mm*	*0-2,9 mm*
	external border	*2,93 mm*	*0-2,7 mm*
	anterior border	*2,86 mm*	*0-5,7 mm*
	posterior border	*2,22 mm*	*0-4,6 mm*
	superior border	*2,87 mm*	*0-4,6 mm*
	inferior border	*3,00 mm*	*0-6,9 mm*
Left kidney			
	internal border	*1,94 mm*	*0-2,8 mm*
	external border	*1,86 mm*	*0-2,9 mm*
	anterior border	*2,40 mm*	*0-5,6 mm*
	posterior border	*2,12 mm*	*0-3,8 mm*
	superior border	*2,75 mm*	*0-4,6 mm*
	inferior border	*2,97 mm*	*0-6,9 mm*

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Abdominal Fixation - a Way to Reduce Organ Motions and to Minimize Mismatching between Target and High Dose Volume.

G. Munkel, H. Blattmann, S. Scheib, A. Lomax, E. Pedroni, U. Ulmer, Paul Scherrer Institute, Division of Radiation Medicine, CH-5232 Villigen PSI, Switzerland

In first investigations about the physiological organ motions and the influence on precision radiotherapy, we defined needs for patient positioning and fixation such as moulage and a tolerable compression of the abdominal area. The effect of abdominal fixation on respiration movement, target displacement, and matching with the target dose are shown. The isodose distributions for the corresponding respiration situation and the non corresponding one are compared. The latter is, according to the progress of the PSI planning program, corrected for the different anatomical situations. The same target contoure and the same spot positions are bases for a true dose calculation for the non corresponding respiration situation. Dose volume histograms will show the effect of abdominal compression more quantitatively.

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A New Technique for Localization and Orientation of the Target in Thoraco-Abdominal Organs.

T. Okumura, H. Tsuji, Y. Hayakawa, A. Maruhashi, T Inada, H. Tsujii, Proton Medical Research Center, University of Tsukuba, Japan

For precise proton irradiation, the important characteristics of the thoraco-abdominal organs are their physiological movement (such as respiratory motion and peristalsis of gut), and their alternation in shape according to their contents or surrounding structures.
We present our techniques how to minimize the treatment volume of mobile target, and how to identify the target on verification images.

To make treatment volume minimal, control of respiratory motion is essential especially for tumor around diaphragm. We developed the respiration-gated irradiation system (ReGIS) for proton therapy. This system consists of monitoring system of the patient's respiratory motion and triggering system of proton Synchrotron. We evaluate the efficacy of this system using DVH analysis and follow-up CAT scans.

Techniques available to identify the target volume on fluoroscopic imaging system mounted in the treatment room are as follows : (1) transarterial infusion or direct injection of oily contrast material for liver and adrenal tumors,(2) insertion of small radio-opaque seeds in or around the liver, esophagus, stomach, uterus and bladder tumors.

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Installation of the PSI Compact Gantry for Spot Scanning.

E. Pedroni, H. Blattmann, T. Böhringer, A. Coray, S. Lin, A. Lomax, G. Munkel, S. Scheib, U. Schneider, Paul Scherrer Institute, CH-5232 Villigen-PSI, Switzerland

The rotating support of the PSI compact gantry was installed last month in the new area dedicated to proton therapy. The gantry body consists of a compact all-welded frame connected to two discs rotating on separate supports. The counterweight for the magnets of the beam line is part of the supporting structure itself. These elements were aligned exactly on the geometrical axis of the gantry and screwed together. Since only one beam port will be available at PSI no compromises were entered in the design of the rotating body, which is manufactured very precisely and is extremely rigid. This will hopefully permit very precise treatments not yet specified to be performed on the gantry in the future. The next step of the installation program is now being performed with the installation of cables and power supplies. The magnets are being assembled in Germany and Denmark and should arrive at PSI in May. The patient table system is also being manufactured and should be installed at PSI next fall. With 5 degrees of freedom (2 rotations and 3 translations) the full capability of horizontal beam line and isocentric treatments will be combined in the same single beam port. We have recently decided to separate the vacuum of the gantry from the vacuum of the beam line feeding the gantry. We will use the space in air at the coupling point to the gantry for the installation of a second beam shutter (slower than the fast kicker used for dynamic treatment) and for the installation of retractable devices used to measure and/or to collimate the beam at this point. The construction of the moving supports (mounted on the gantry) for X-ray tube, image amplifier (at the beginning film holder) and for the devices for proton radiography is underway. These elements will be used for controlling the positioning of the patient directly on the gantry. The parallel program for controlling the patient positioning outside of the treatment room has been started by purchasing our own CT. A separate VME processor will be used for the steering of the (11) motors of the gantry. This system will receive commands from the general steering system for the dynamic scanning (remote control) or will be driven directly by the operator using a wireless hand station (local control).

Everything is on schedule, in accordance with our plans which aim at the complete installation of the gantry by the end of the year and first patient treatments at mid 1994.

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Performance Specifications for Proton Medical Facility.

B. Ludewigt, Lawrence Berkeley Lab, MS 64-121, Berkeley, California 94720, USA

Performance specifications of technical components of a modern proton radiotherapy facility will be presented. The technical items specified include: the accelerator, the beam transport system with a rotating gantry, and the treatment nozzle systems with beam scattering, beam scanning, and dosimetric instrumentation. The justifications for the more important specifications and their relationships to the published clinical specifications ("New proton medical facilities for the Massachusetts General Hospital and the University of California Davis Medical Center", NIM, in press) will be explained.

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Control System Specifications for a Medical Accelerator.

T. Renner, B. Chu, B. Ludewigt, M. Nyman, R.P. Singh, Lawrence Berkeley Lab, MS 64-121, Berkeley, California 94720, USA

The accuracy and safety of a patient treatment is determined in part by the system controlling the irradiation. This system is many things to many people. From the accelerator physicists viewpoint, it is a number (the dose) to be entered and a start and stop button. For the technical staff, it is lots of software and hardware with a human interface (a patient) and a doctor hovering nearby. For the radiation therapist, it is a clinical physicist's toy to play with and their nightmare to operate. Given all these diverse views a system for doing all things for all people is clearly required. Based on our experience at the Lawrence Berkeley Laboratory Bevalac, we have set forth the functional requirements necessary for a heavy-charged particle radiotherapy facility control system. How these requirements are actually implemented and prioritized we leave to the bill payer.

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Magnetic Scanning System for Heavy lon Therapy at GSI.

Th. Haberer, W. Becher, D. Schardt and G. Kraft, GSI Darmstadt, Germany

The advantages of heavy ion therapy are most pronounced if the beam is delivered in a tumor-conform way by active beam scanning At GSI an active beam delivery system is installed using a fast magnetic scanning system to spread the beam laterally. The beam is guided over the irradiation field in a preselected pattern which is subdivided in up to 16k beam positions. For each position control values representing the x-, y-position and the required number of ions is precalculated. The beam is moved without interruption from position to position when the appropriate number of particles is reached. With this hybrid technique of raster and pixel scan mode it is possible to produce scan patterns having irregularly shaped boundaries and well defined homogeneous or inhomogenous particle coverings. The range of the particles in tissue is changed by an active variation of the beam energy in the synchrotron from pulse to pulse. First results using the lateral beam scanning method as well as the combination of the active energy variation with the magnetic beam scanning will be presented.

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A 200 MeV Proton Therapy Facility at the AGOR Cyclotron in the Nederlands.

J.M. Schippers[1], B.G. Szabó[2], (1) KVI, 9747 Groningen, (2) Radiotherapy Department, University Hospital, 9700 RB Groningen, the Netherlands

In 1994, proton beams with Emax=200 MeV will become available from the superconducting AGOR cyclotron at the Kernfysisch Versneller Instituut (KVI) in Groningen, the Nederlands. Their coming availability offers a unique possibility to perform radiotherapeutic treatments with protons in this part of Europe. A collaboration between KVI, the Radiotherapy Departments of the University Hospitals of Groningen (AZG) and Utrecht and the Daniel den Hoed Kliniek in Rotterdam, has initiated plans to establish a radiotherapy facility with 200 MeV proton beams at the KVI.

A proposal for a dual-beam facility, using the proton beams from AGOR, is in progress. Presently, we are aiming at an annex to the KVI with two treatment rooms: one with a gantry and one with a fixed beam line. As a first step towards the facility, some subprojects have already been started: instrumentation development for beam diagnostics and dosimetry for a spot-scanning system and a study of PET measurements of radioactivity induced by protons in tissue.

An outline of the project and the present status of the plans will be presented.

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Quality Control of the Proton Beam and Daily Dose Calculation.

N. Brassart, J. Herault, JM Gabillat, P. Chauvel. Centre Antoine-Lacassagne - Cyclotron Biomedical, 227 av. de la Lanterne, 06200 NICE-F.

The characteristics of the proton beamline in Nice have previously been described (Particles n°9). The beam is under vacuum until the range shifter/modulator combination (RS/MC). The position of this unit in the optical bench is a compromise between profiles quality and energy loss: the compromise adopted was to install the RS/MC at 190 cm of the last collimator. The range in eye tissue is then 30.8 mm, sufficient to treat all the ocular tumors, even when using bolus. The penumbra is 1.6 mm for a non modulated beam and 2.3 mm for a full range modulation. The beam falls off from the 90% to the 10% isodose in 0.8 mm which is a critical parameter when using reduced safety margins for tumors located close to the optic nerve.

Each day before treatments are measured the Bragg peak (particularly range and thickness of the 50% isodose), the half-modulated peak and the profiles of the beam. Two independent parallel plate transmission ionization chambers monitor the beam continuously: the beam monitoring system is daily checked by measuring the dose per monitor unit in standard conditions on the middle of the plateau of a half modulated beam. Two tissue equivalent ionization chambers (FWT IC 18 and X.Radin T2) are used. This daily measurement called the “top” takes into account variations for temperature, pressure and beam characteristics; it allows us to daily correct the dose per monitor unit measured on the first treatment day for each patient and so to simplify the procedure of the daily measurement of the dose. A study on 115 patients shows, for the majority of the patients, a variation between +/- 1% of the ratio of each day measured dose to each day calculated dose using the daily value of the “top” and the first day measured dose.

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Summary of the Questionnaire on Practical Aspects of Ophthalmologic Treatment Planning with Protons.

S. Delacroix, Centre de Protonthérapie d'Orsay, Centre Universitaire-Bât 101, 91400 Orsay, France

A questionnaire, concerning the very practical aspects of the ophthalmologic treatments was sent to the different centres performing eye treatments.

The different topics included: personalized beam modifiers, use of eye retractors, collimators safety margins, control quality beam and patient set up.

Among the 8 participating groups, one can observe a quite good uniformity in the answers.

- 50% of the centres used wedges
- The number of patients with a portion of eyelid irradiated is still high, even if this can be reduced by using rotation of the mask and/or the chair but it seems that retractors specially designed will be able to improve this problem.

- The average standard value for collimator safety margin is around 2.5 mm and every body agrees to be extremely vigilant when reducing this margin.
- A complete quality control is performing every day, every where, even if a previous calculation has been done.
- And at least, the accuracy in the daily positioning of the patient varies from 0.5 to 2 mm, although the set up time is around 15 to 20 min.

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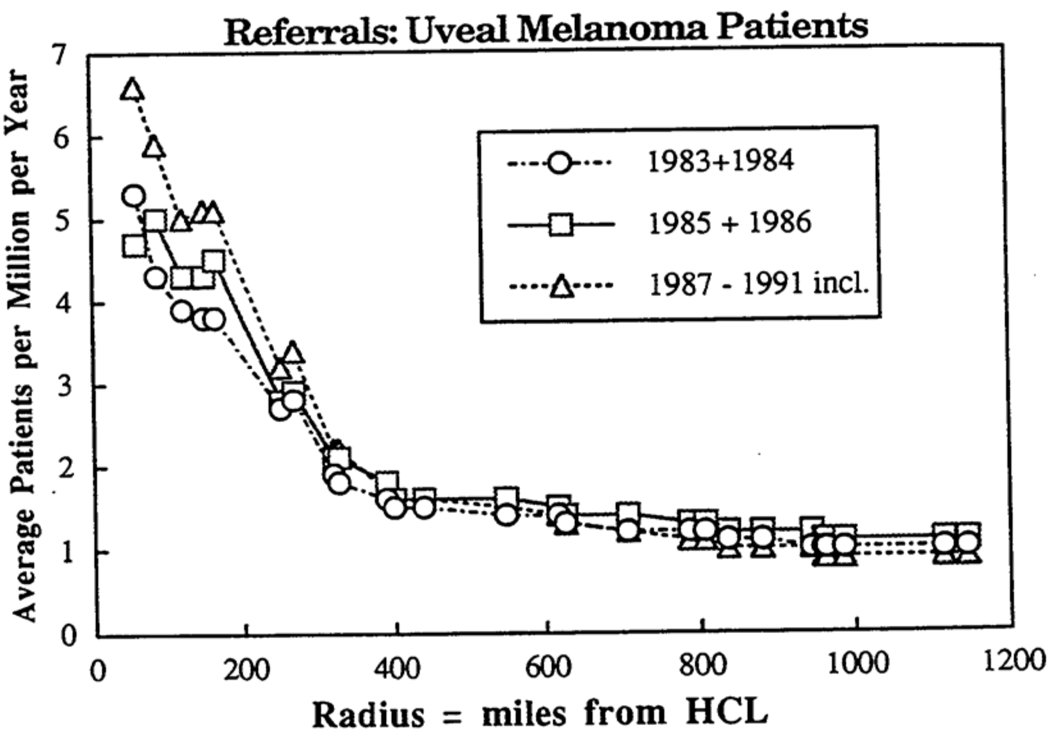
Uveal Melanomas: Trends in Patient referral for Proton Beam Therapy at HCL.

J. M. Sisterson, K. N. Johnson, A. M. Koehler, Harvard Cyclotron Laboratory, Cambridge MA 02138.

From 1975 through December 1992, a total of 5742 patients have been treated with proton beams by the MGH/HCL/MEEI group in four clinical programs, 1870 of these patients have been treated for uveal melanomas. Over the past 10 years, an average of ~150 uveal melanomas have been treated at HCL each year.



The patient data has been analyzed to study the geographical trends in patient referral over this 17 year time period. As might be expected, few patients are referred to HCL from the Western States, but a significant number of patients are referred from other countries. The data for Massachusetts show that most new cases of uveal melanoma are treated at HCL or that the incidence in Massachusetts is higher than that currently estimated of ~6 patients/million population/year. An attempt has been made to compare the referral of patients over different distances to HCL in a manner to include the population densities of each state. Figure 1 shows that there has been little significant change in referral pattern over this 17 year period and indicates that within a 300 mile radius of Boston have a good chance of being referred to HCL for treatment.

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Why small uveal melanomas are best indicated for proton beam irradiation. Discussion of functional results.

E. Egger, OPTIS, Department of Radiation Medicine, PSI, CH-5232 Villigen - PSI

In Western Europe proton beam irradiation is mainly used to treat conservatively large melanomas or tumors near the optic disc and/or macula. Despite the fact that the mean volume of the tumors treated with protons is about three times larger than the volume of tumors treated with radioactive plaques, survival of the proton patients is comparable to the survival of the other patients. Using Cox proportional hazard model we can show that a recurrence has a negative influence on patient survival, we suppose that the high rate of local tumor control (~98% for proton beam irradiation versus ~90% for plaque therapy) is responsible for the good survival of the proton patients.

The functional results however are disappointing. Even with protons it is not possible to keep a good visual acuity if the optic disc, the macula or a large part of the globe volume have to be irradiated.

We will present some selected cases of patients who could have been treated with other means than with proton beam irradiation and we will show how good the functional results are. The patients were selected as follows: larger tumor diameter less than 16 mm, tumor height less than 7 mm, distance to the macula greater than 4 mm, distance to optic disc greater than 4 mm, visual acuity before treatment better or equal to 0.80, the applied dose is 60 Gy in 4 fractions, no recurrence after treatment. 53 of the 1263 patients treated at PSI between March 1984 and December 1992 satisfied these selection criteria. 13 of them had a loss of visual acuity to less than 0.80 in the years following proton beam irradiation, 8 because of a cataract, 1 because of an inflammation of the anterior chamber (the visual acuity improved again to 0.80 after healing), 1 because of a mechanical detachment of the macula, 1 because of a total retinal detachment, 1 because of a partial detachment of the retina (the visual acuity improved again to 1.00 after reapplication of the retina) and 1 because of an hemorrhage on the tumor.

As now several centers offer proton beam therapy in Western Europe, these results indicate that time has come to perform a randomized study comparing proton beam irradiation to radioactive plaque therapy not only to show that survival is the same but especially to find out which treatment modality leads to the better functional results in order to offer optimal treatment to the patients.

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Improvement of Treatment Planning by Tomographic Measurements Using B-scan Ultrasonography.

W. Friedrichs(1), W. Sauerwein(2), N. Bornfeld(3), P. Chauvel(4) (1) Dept. of Ophthalmology, University of Essen, Germany. (2) Dept. of Radiotherapy, University of Essen, Germany. (3) Dept. of Ophthalmology, Universitatsklinikum Steglitz, Berlin, Germany. (4) Centre Antoine-Lacassagne-Biomedical Cyclotron, Nice, France

Choroidal or retinal lesions adjacent to the optic disc or to the macula are common indications for proton therapy. In the case of small posterior lesions the clips defining the tumor base have to be placed quite posteriorly. The intraoperative measurement of the resulting large distances of the clips to the limbus may be difficult and necessitates to roll the eye by strongly pulling on one or two muscles. This maneuver will increase the radius of the turned eye which can result in falsely high distance values.

B-scan ultrasonography permits to visualize posteriorly located clips and to measure the distances between the clips and the center of the optic disc without influence on the shape of the globe thus providing a better idea of the topography of the posterior pole. In our experience these additional informations may increase the accuracy of treatment planning and the safety of irradiation in terms of protection of the optic disc and the macula.

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The Treatment of Choroidal Melanoma by Proton Beam at Orsay - Preliminary Results.

L. Desjardins, C. Levy, F. D'Hermies, B. Asselain, A. Mazal, P. Schlienger, L. Schwartz, J.L. Habrand, S. Delacroix, C. Cohen-Solal, Centre de Protonthérapie d'Orsay, Centre Universitaire-Bât 101, 91400 Orsay, France

Since September 1991, we have started to treat choroidal melanoma by proton beam in the proton beam therapy center at Orsay.

More than 200 patients have been treated up to now. We report our experience and we give the preliminary results on tumor local control and on the visual results in 38 patients followed for one year or more.

The results at one year appears good on tumor local control. More follow up will be necessary to evaluate functional results and metastatic rate.

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Status Report of the Proton therapy Facility in Nice: Clinical and Technical Considerations on the first 216 patients treated.

P. Chauvel[1,2], N. Brassart[1,2], J. Hérault[1,2], A. Courdi[1,2], J. D. Grange[1], J. P. Caujolle[1], L. Diallo-Rosier[1], F. Porta[1], N. Bornfeld[1], J. Sahel[1], F. Bacin[1], J. P. Gerard[1], W. Sauerwein[1], W. Friedrichs[1], V. Vitale[1], C. Carrie[1], G. Kantor[1], R. Rozan[1], J. L. Lagrange[1,2], R. J. Bensadoun[1,2], E. Teissier[1,2], F. Demard[1,2].
SERAG[(1)] and Centre Antoine-Lacassagne - Cyclotron Biomedical (CAL)[(2)], 227 av. de la Lanterne, 06200 NICE-F.

Proton therapy of ocular melanomas started for France, by June 17th 1991, in Nice, using the 65 MeV H^- cyclotron built and installed in CAL for biomedical purposes. Simulation and treatment planning are performed 10 to 15 days after tantalum rings have been inserted by the surgeons participating in the Cooperative Group (SERAG - South Europe Radiotherapy Group), now including the Cancer Comprehensive Centres and University Hospitals in South of France and adjacent regions in Germany, Italy and Spain. The treatments are delivered on the basis of 60 Cobalt Gray Equivalent given in four consecutive fractions of around 20 sec. Parallel-plate chambers, brass collimators, X-ray film holder, light systems and the final brass pipe bearing patient collimator are placed in a 60 cm box ending at 7 cm of the isocentre while the range shifter and the modulator are installed 190 cm before the isocentre to optimize the quality of the beam. Depth dose curves and profiles are measured using small silicon photo-diode and minibeam explorers.

By April 15, 1993, a total number of 216 patients (209 uveal melanomas) have completed their treatments; 130/209 presented a posterior pole tumor and 141 a T3. 2 patients were treated for multi-relapsing conjunctival melanomas, 1 for a relapsing retinoblastoma and 4 for a von Hippel-Lindau syndrome. The mean age for uveal melanomas is 57.5 years, the sex ratio being 1.0. 77 patients had their clips inserted in Lyon, 66 in Nice, 19 in Essen, 16 in Berlin, 13 in Bordeaux, 12 in Genova, 6 in Strasbourg, 6 in Clermont-Ferrand, 1 in Paris. The maximum range needed was 30.7 mm of eye tissue, the modulation varying from 25% to 100% of the range. Some technical particularities have been set-up in Nice: - from the opening of the facility, a second simulation has been introduced, using a shadow collimator in order to check the eyelid position in the beam and the feasibility of the plan before the final simulation; - the use of bolus, either in wax or ultrasonographic gel or both, has been developed since 1991, in order to transform the entrance of the beam in a plane, whatever could the eyelid position and contour be; - a new design of plexiglas wedge filters mounted on two 4 mm diameter iron rods transfixing the personal collimator, avoiding any movement of the filter and allowing to position it as close as possible to the eye to decrease the scattering induced by the plexiglas; - the design of concave or convex spherical plexiglas compensators calculated either to shape the posterior pole of the eye or to irradiate only the thickness of the coats. For respectively 1991, 92 and 93, the use of bolus was 6%, 66% and 98%, the use of filters being 0%, 48% and 68%, while a classical safety margin of 2.5 mm on the range was used in 68%, 30% and 28% of the patients. All these efforts were made on the request of the ophthalmologists of the group, in order to try to better protect the post-therapeutic function of the eye, particularly for posterior pole tumors, and seemed to be technically acceptable, due to the sharpness of the beam.

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Conventional Radiotherapy of Primary Intraocular Tumors.

W. Sauerwein[1], H. Sack[1], U. Quast[1], D. Fluhs[1], C. Wieczorek[1], H. Henrich[1],
W. Friedrichs[2], A. Wessing[2], N. Bornfeld[2], Strahlenlclinik[1] und Zentrum fur Augenheilkunde[2],
Universitätsklinikum Essen, Germany

As a result of the pioneering work of MEYER-SCHWICKERATH, treatment of intraocular tumors become high importance at the University of Essen in the last 3 decades. More than 800 retinoblastoma and 1500 uveal melanoma have been treated using different treatments. Aside from surgical approaches, i.e. coagulation techniques, the most important modality always has been radiotherapy. The techniques which are used actually will be presented, the pros and cons will be discussed in view to look if there is any need of proton irradiation for our patients.

In most cases of bilateral hereditary retinoblastoma, the target volume is the whole retina. Here a highly accurate beam alignment technique developed from the proposals of SCHIPPER seems to be appropriated to minimize the irradiated volume and to spare lens and lachrymal gland. This technique allows a homogeneous dose distribution at the whole retina and the macroscopic tumors and an optimal dose fractionation schedule (5 x 2 Gy/week up to 50 Gy) even in very young children. In few cases and in cases of unilateral unifocal non hereditary retinoblastoma, a reduced target volume can be defined and further reduction of the irradiation volume is mandatory. This goal may be reached using brachytherapy. A very specific problem are recurrent tumors after primary external beam irradiation. Here a need for proton irradiation may be given.

A different approach is needed in uveal melanoma. The target volume is only the tumor while all other structures should be kept out of the irradiated volume. To destroy the tumor a very high dose is needed, which cannot be applied by external photon beam without seriously damaging other anatomical structures. As a very efficient technique brachytherapy using high energy, β-rays (^{106}Ru-plaques) or low energy γ-rays (^{125}I plaques) is in routine use. Established indications for brachytherapy are equatorial tumors of less then 6 mm thickness. Juxtapapillary tumors can be treated effectively in terms of salvaging the eye but visual prognosis is limited. In these cases proton irradiation may lead to a function salvaging radiotherapy.

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Considerations on the Treatment Policy for Posterior Pole Tumors.

P. Chauvel[1,2], N. Brassart[1,2], J. Hérault[1,2], A. Courdi[1,2], J. D. Grange[1], J. P. Caujolle[1], L. Diallo-Rosier[1], F. Porta[1], N. Bornfeld[1], J. Sahel[1], F. Bacin[1], J. P. Gerard[1], W. Sauerwein[1], W. Friedrichs[1], V. Vitale[1], C. Carrie[1], G. Kantor[1], R. Rozan[1], J. L. Lagrange[1,2], R. J. Bensadoun[1,2], E. Teissier[1,2], F. Demard[1,2].
SERAG[(l)] and Centre Antoine-Lacassagne - Cyclotron Biomedical (CAL)[(2)], 227 av. de la Lanterne, 06200 NICE-F.

Two thirds of the ocular diseases referred to Nice for a proton therapy are located on the posterior pole of the eye and the visual outcome could be severely affected by the treatment. The classical therapeutic attitude had been developed in order to obtain an as good as possible cure rate of the tumor; as a result the standard safety margin proposed on range calculation is 2.5 mm. If the tumor reaches or involves partly the macula or the disc, the use of such a margin means that there is almost no chance to retain a vision in the near future, these structures and the optic nerve being irradiated at a toxic level. The accuracy of the proton beam set-up in Nice indicated that it was perhaps possible to try to decrease these safety margins and to refine the use of the wedge filters combined to the use of bolus to protect the critical structures of vision. In parallel have been developed some verification procedures or instruments (use of ultrasonographic measurements of the distance between the posterior clips and the disc, superimposition of the reconstructions of tumor and clips position on fundus photographs, measurements on the polaroid films of the distance between the clips and the plane tangent to the anterior part of the eye using a special mechanical device) allowing to verify the accuracy of the reconstruction of the eye. Another point has to be underlined: the reconstruction of the tumor assumes that the whole thickness of the sclera is involved, which is most often an overestimate; the sclera constitutes in facts quite a 1 mm safety margin, essentially at the periphery of the tumor. In the future it could be relevant to take in account the real thickness of the sclera and to represent it on the 3-D drawings of the EYEPLAN program. The positioning of the clip system from day-to-day is also very cautious and often needs a lot of fine adjustments of the fixation diode and of the chair in order to obtain an almost perfect repositioning able to guarantee the reproducibility and accuracy of the planned dose delivery. All these precautions and a very cautious follow-up during which the ophthalmologist is ready to realize a laser surgery on a limited marginal failure are the means of this effort towards a better visual outcome after proton therapy.

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