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ABSTRACTS

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3-Dimensional Dosimetry For Proton Therapy.

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The dosimetry of proton therapy beams requires a detailed knowlege of patient anatomy and the properties of proton beams. With these as input data, physics models yield predictions of the absorbed dose to a patient. In characterizing proton beams at a particular therapy center, an appropriate dosimetry measurement system must be chosen that is compatible with the beam time structure, i.e., DC or pulsed, and also with the beam delivery scheme, e.g., with passive scattering, or with dynamic systems such as wobbling or voxel scanning.

Dynamic beam delivery systems promise to improve dose conformation and to make possible highly complex and nonuniform dose distributions, even to large target volumes. However, dynamic delivery comes with a price: additional care need be taken in order provide adequate patient safety. The verification of dynamic delivery systems includes 3-D dose distribution measurements, in a simple geometry (homogeneous water phantom), and for many permutations of field size, range modulation, gantry angle, and other parameters. Traditional scanning techniques, comprising a series of sequential point-measurements, are too slow for use in dynamically-delivered beams and faster dosimetry systems will have to be developed. We discuss the general requirements of the dosimetry system, the performance characteristics of some of the more promising detector technologies, and propose several systems that can meet the coming challenge of dynamic beam delivery at the Northeast Proton Therapy Center.

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3-D verification of dose delivery for proton therapy.

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Dosimetry verification in radiation therapy is that part of a quality assurance program which is intended to validate the delivery of the prescribed dose to the target volume and expected doses to normal tissues. When charged-particle beams are used to conform the dose distribution to the target volume and to provide sharp distal dose cut-off, this verification should be a 3-D study for validation of:

- the prescribed dose delivery to the reference point and to the target volume;
- the prescribed location of lateral dose fall-off;
- the prescribed distal dose fall-off .

A specific detector system, or combination of detectors is required to implement this verification procedure. The system should be tissue equivalent and should provide integrated readings with sufficient spatial resolution. The sensitivity of the detector system should be low enough to measure multiple-beam exposures and register the absolute value of the dose over the irradiated volume with appropriate accuracy and precision. The phantoms for these studies must be selected carefully , since the uncertainty in dose delivery at the distal edge is dominated by the uncertainties in interpretation of stopping powers from CT data from the phantom.

The LLUMC system of 3-D dosimetry verification employs a combination of detectors and phantom setups. Ionization chambers are used to measure prescribed dose delivery to the reference point and high-sensitivity radiochromic films and TLD's are used to validate dose distributions.

We describe two types of studies: the first is related to large field irradiation (lateral prostate beams), the second is related to proton radiosurgery with small beams.

In the first case, the accuracy of dose delivery at the distal edge is determined by combining tissue samples with plastic plates, containg detectors. Radiosurgery verification employs a water phantom containing a detector block with radiochromic films, a tissue inhomogeniety substitute, and fiducial markers, used for alignment.

Verification studies in both cases were completed within a single day following the same procedures as for a treatment patient: immobilization in a foam cradle or bite-block, thin-slice CT study, target volume delineation, design of treatment beams, fabrication of apertures and boluses, radiographic alignment using DRRs, and proton irradiation. Comparison of prescribed and measured 3-D distributions for these cases are presented and discussed .

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Large Area Detectors for Volumetric Measurements of Dose Distributions.

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Intensity modulated beams offer many new possibilities to optimize the treatment result in modern radiation therapy. Standard dosimetry systems are not very suited for such dynamic beam delivery systems, since a simultaneous measurement at many points is desired. Presently different approaches for two or three dimensional dosimetric measurements are being investigated.

For dosimetry at dynamic beam delivery systems one should take care of the following aspects, which are typical for this application: time structure of the beam, local high dose rates and dimensions of pencil beam. Also elementary decisions have strong implications for the design of the dosimetry device, for instance the purpose for on-line monitoring or for verification of treatment plan. The applicability at other modalities than protons/ions (photons, electrons, Brachy..) should also be considered, since at these modalities one faces similar dosimetry problems. Of course the desired accuracy and spatial resolution should be discussed, but also the time span between the measurement and the availability of the data. Some devices only work for special beam directions and/or need (e.g. trigger) information from the beam delivery system and others work only at high doses or at high dose rates.The current approaches can roughly be divided into three groups:

- arrays (1D/2D/3D) of ionization chambers, TLD's, diodes, etc.
- (stacks of) 2D systems: magic cube, film, scintillating screen
- 3D systems are usually based on chemical transitions in Gels (MRI, light absorption), nuclear interactions (PET) or scintillating material (light emission tomography).
- In this review three systems are described in more detail.

The Gel dosimetry [1] looks very promising. Readout of the chemical transitions (polymerization of acrylic monomers) can be done by MRI (T2 response) or by measurement of the optical density [2]. Compared to the Fricke dosimetry, the big advantage is that there is no diffusion of the polymers in the gel, which results in a very long "life time" of the dose information in the irradiated gel. Although the

results look very spectacular, the method is still very sensitive to procedure errors (gel fabrication, temperature in MRI...).

At GSI, Darmstadt, a PET scanner [3,4] is mounted around the isocenter. It has been designed for the detection of positron emitters created by the nuclear interaction of the beam particles with atomic nuclei in the tissue, but such a system also allows the detection of stopped particles from a ^{11}C beam. The device is working but the procedure to analyze and interpret the results is still in progress. Paans and Schippers found [5] that activation by proton beams would only yield a count rate in the order of 1 cps/Gy, and that the calculation of the dose is very model dependent. With heavy ions the yield is much larger: only 10^8 Carbon ions are necessary to obtain a useful signal.

At the KVI, Groningen (NL) an investigation is in progress [6] on the performance of a 2-D dosimetry system consisting of a scintillating screen (Gd_2O_2S:Tb) mounted on the beam exit side of a phantom with adjustable thickness. The light from the screen is detected by a low dark-current CCD camera with long integration time capabilities. This system allows a time-integrated measurement of the dose distribution in 2 dimensions. Experiments at different clinical beam lines have shown that the device is very useful and that important errors in the scanning pattern can be detected, even for pencil beams aimed at voxels located deeper than the screen depth.

In table 1 a summary is presented with some global characteristics of the three devices. The numbers presented here are meant to give an indication of ranges only. Also one should consider that all devices are still in development.

Table 1. Global indication of the parameters of three different dosimetry systems, in development for 3D (2.5D) dosimetry.

	GEL dosimetry (MRI or light absorption)	PET system	CCD + Scintillating screen
position resolution	1-2 mm	4.7 mm	0.5 mm
dose accuracy	5-8 %	?	0.5 % at 1 Gy
dose range	1-12 Gy	> 1-2 Gy	0-15 Gy (+adjustable range)
dose rate	not important	not important	not important
signal -> dose	linear; at high LET not known	complex	linear, 8% quench in Bragg peak
time span to obtain data after exposure	1 day	seconds-minute	1-3 seconds with standard software
signals from beam necessary	no	yes	no
portable	yes (phantom)	no	yes

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3D Dosimetry of scanned hadron beams using the Magic Cube.

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In a scanned hadron beam treatment the performances of the accelerator and the control system complex needs to be checked on a routine basis. Within the TERA program, it has been developed a detector (nicknamed Magic Cube) to measure the relative energy deposition in 3D. It is a sandwich of 12 parallel plate ionization chambers (25 x 25) cm^2 interleaved with tissue equivalent slabs of adjustable thickness. The anodes of the chambers are segmented into 64 strips 0.4 cm wide, which are X and Y orientated. The strips are read out by individual channels directly coupled. The chamber gap is 3 mm and filled with Nitrogen. The front end is a current to frequency converter and it implemented with the VSLI technology. A single chip contains the circuitry for one chamber and it has been placed very close to the chamber. With this solution the noise is minimized, and the sensitivity could be set as low as 0.2 pC/count. The detector has been tested on a Carbon beam at GSI, Darmstadt, Germany. Some preliminary results have been discussed and here summarized. The linearity of the detector is better than 1% for a beam intensity spanning over three orders of magnitude. The response uniformity over the chamber area, prior any corrections, is better than 3%. The beam position and width are measured with a precision of about 1 mm.

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Review of Radiobiologic and Pathologic Considerations of Subfoveal Neovascular Membranes.

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Recently, clinical trials using radiation therapy to treat subfoveal neovascular membranes have been performed with single-dose-fraction conformal proton beam and multiple-fraction x-ray dose schedules. All schedules were successful in controlling membrane progression, stabilizing vision in most patients, and increasing visual acuity in a few. The results suggest that radiation therapy could be a useful and cost-effective modality for this large patient population. However, neither the optimal time-dose schedule - either single or multiple dose fractions - nor the type of radiation - either proton conformal beam or x-ray therapy - are defined.

This presentation reviews the rationale for using radiation therapy to treat subfoveal neovascularization, and suggests parameters within which that role might be defined. To accomplish this, we examine a paradigm of interaction of radiation with tissue, review the histopathology of neovascular membranes, and document the role of growth factors in the pathophysiology of the disease. Accepting that the eye is an extracranial extension of the brain and that the microvasculature of the eye has properties similar to brain microvessels, we review the radiobiologic response of brain microvessels. Finally, we revisit the controversy between efficacy of single-dose-fraction over multi-fraction schedules and conclude that single dose fractions would be effective.

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The lateral and transversal proton RBE variation in a SOBP.

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In current clinical practice a single value of a therapeutic RBE is used. In this study we focussed on the question how the RBE varies in a SOBP in three dimensions.

Describing radiation effects one has to combine physical and biological properties. As the physical input we simulated a SOBP in water (1.5 to 2.5 cm) and the corresponding proton energy distributions at certain positions in the SOBP with the Monte Carlo code GEANT. A beam with 68 MeV (sigma=250 keV) kinetic energy and a divergency of 3 mrad has been simulated in a realistic setup including a modulator wheel and certain beam shaping devices. The biological parameters used are the radiosensitivity parameters for the CH2B2 and V79 cell lines as given in the literature. The physical and the biological parameters were used as input for the RBE calculation with the track structure model based on the Katz theory.

Due to a decreasing proton energy with penetration depth the energy transfer increases which affects the RBE. The proton dose necessary to reach the same biological effect as 60Co has been calculated. It has been shown that this dose has to decrease with depth in the SOBP. For a dose of 2 Gy we found RBE values in the SOBP up to 1.4 for CH2B2 and 1.5 for V79 at the distal end. These values decrease with increasing dose. Above 5 Gy the dose dependence is negligible. In the lateral direction we found nearly no RBE variation. In addition, surviving fractions as a function of depth have been calculated. The results obtained depend not only on the biological endpoint but on the beam parameters like initial energy, energy spread and geometrical setup.

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RBE variations with proton energy and depth: a microdosimetry and cell survival comparison.

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Cell survival data is compared with predictions from microdosimetry measurements at three diferent energies and depthd. Both the physics and biology data taken under nearly identical beam conditions at Loma Linda show that RBE variations are less than +/- 5% until the distal edge of the beam is reached. In addition, the neutron dose at 5 cm beyond the Bragg peak is measured to be about 0.2% of the peak proton dose. This indicates that the dose contribution from nuclear secondaries is quite small.

Preliminary design of a new nanometer dosimeter will also be discussed.

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Development of nanodosimetry: scientific potentials and clinical applications.

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We propose a new method to overcome the fundamental size limitations of proportional-counter microdosimetry. The proposed method will permit, for the first time, nanodosimetric measurements of ionization statistics in small wall-less gas volumes. Preliminary studies, performed at the Weizmann Institute of Science have demonstrated that the spatial resolution can be expected to be better than 1 nm equivalent length in condensed matter. During the initial phase of the proposed project the performance of the nanodosimeter will be studied and optimized by scanning the sensitive volume with a probe beam from a low-energy ion source. A prototype single ion counting nanodosimeter will be installed on the research beam line at LLUMC. Nanodosimetric ion cluster spectra will be measured for protons of different energies. The data will be used to test a new biophysical model of cellular radiation action: the two compartment (TC) model. The model links nanodosimetric quantities, such as the relative fraction of dose deposited into large and small energy deposition events, to molecular biological endpoints, e.g., the number of reparable and irreparable double-strand breaks (DSBs) per unit dose. A crucial test of the theory will be performed by correlating the relative number of ion clusters within a small and a large cluster-size compartment with the number of fast rejoined (presumably reparable) DSBs and slowly rejoined (presumably irreparable) DSBs induced by protons of different energies. For this purpose, the linear fraction of irradiated plasmids, which corresponds to plasmids containing DSBs, will be incubated with a cell-free cellular repair extract from Xenopus eggs, and the fraction of unrejoined plasmids will be measured as a function of time. The decay of the linear fraction will be fitted to the sum of two exponential time functions, from which the relative fraction of slowly and fast rejoined DSBs can be estimated. The proposed research is important for the understanding of biological radiation effects and is anticipated to have many applications in radiation medicine and protection.

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Estimation of tissue and dose dependent RBE values for heavy charged particle tumor therapy.

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The relative biological efficiency RBE of heavy charged particles compared to photon radiation is a complex function depending on the composition of the radiation field, the dose level and the biological endpoint under consideration and thus cannot be represented by a single value. This has been demonstrated clearly by experiments using in vitro cellular systems as well as em in vivo animal systems.

Therefore, optimal application of heavy charged particles in tumor therapy requires to take into account the detailed knowledge of the RBE as a function of the tissue type and dose level.

In order to estimate RBE values, a biophysical model has been developed, which is based essentially on the radial dose profiles of particle tracks and the photon dose response curve of the biological endpoint under consideration. For a given radiation field, the RBE is expected to be determined by the width of the shoulder of the photon dose response curve, which can be expressed in terms of alpha/beta-values in the case of tissue response. Thus, RBE for radioresistant tumors with a higher repair capacity and corresponding small alpha/beta-value is expected to be significantly higher than for tumors with higher alpha/beta-value. Similarly, the RBE for late effects is expected to be higher than for early tissue response, which is in line with the clinical findings from neutron therapy.

A brief comparison of model predictions with experimental data will be presented. The main aspect of the presentation will be to discuss the expected influence of different combinations of alpha/beta-values on the RBE for the tumor and normal tissue. Results will be compared on the basis of total and biological gain factors, defined as the ratio of effective doses or RBE values in the tumor compared to the normal tissue, respectively. In addition, the significance of RBE variations within the extended peak in the tumor volume will be discussed in dependence of the alpha/beta-value of the tumor tissue.

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Dose escalation studies: sample size and tumor population heterogeneity.

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Developments have been significant and rapid and significant in the ability to plan and execute radiation treatments which irradiate progressively smaller treatment volumes while providing full coverage of the target volume. The aim of these technical advances is to increase dose to the target tumor and or decrease the volume of normal tissues or portions of a normal structure(s) in the high dose volume. The result of these advances in treatment planning is to augment tumor control probability (TCP) and/or reduce the frequency and severity of treatment related morbidity (NTCP). Assessment of the magnitude of the clinical gain is by dose escalation Phase III trials, *viz* what is the gain in TCP for a specified or lower NTCP? Here consideration is given to the design of clinical trials of radiation dose increments.

The success in demonstrating an increment in TCP is a function of several parameters in study design and characteristics of the patient population. These include: number of subject tumors at each radiation dose; number of radiation dose levels; distribution of the test doses along the true dose response curve (DRC); steepness of the (DRC); inter-tumoral heterogeneity with respect to radiation sensitivity; and the heterogeneity of the radiation dose administered among the treated tumors.

For this analysis, we employ model tumors, each comprised of 10^8 clonogens. The tumor population is uniform with respect to all parameters excepting SF_2. The median SF_2 value is 0.5; there is no intra-tumoral, only inter-tumoral, heterogeneity of SF_2. Slope of the DRC is described by the parameter γ_{50}. The γ factor is the percent point increase in TCP for a 1% increase in radiation dose. Hence, the γ_{50} is the γ factor at the mid-point of the DRC, *viz* the TCD_{50}. The steepest portion of the DRC is at the $\approx TCD_{37}$.

We demonstrate that the number of tumors required to demonstrate a gain in TCP for a 10% increment in dose is strongly dependent upon the inter-tumoral CV of the SF_2 value for any TCP for the control radiation treatment. Furthermore, the sample size is minimal at the steepest portion of the DRC or the highest γ

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The implication is clear that the most efficient study design is that with a very high level of inter-tumoral homogeneity with reference to parameters which affect TCP. The presentation will include graphic displays of the relationships between sample size and TCP for a series of CVs for the tumor population and sample size for selected TCP values.

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Preliminary Results of Carbon-Ion Therapy at NIRS.

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The clinical trial of heavy ion therapy was begun in 1994 at the National Institute of Radiological Sciences(NIRS) using carbon-ions generated by a medically dedicated accelerator (HIMAC: Heavy Ion Medical Accelerator in Chiba). Judging from the results of preparatory experiments as well as LBL experiences, we decided to use carbon ions for cancer therapy. Preclinical studies were performed on five human cell lines cultured in vitro and mouse skins to estimate RBE values of the carbon-ions which were estimated to be 3.0 for acute skin reactions at the distal part of the SOBP. Interdisciplinary working groups were organized to design protocols for phase I/II carbon ion therapy for various tumor sites including the head and neck, brain, lung, liver, uterine cervix, prostate, bone and soft tissue, and esophagus. The initial doses employed were 10-20% lower than those possibly tolerable for musculo-connective tissues. The doses were escalated by 10% increments for every 3 to 5 patients based on careful observation of the normal tissue morbidities as well as tumor responses. As of February 1997, a total of 230 patients were treated. so far, none of them experienced any type of major morbidities. As with tumor response, the preliminary results appear to demonstrate promising effects in selected tumors such as locally advanced tumors with non-squamous histology. We will continue to evaluate in what type of human cancers the differential effects could exist between the therapeutically resistant neoplasms and normal tissues that favor the latter.

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Fractionated proton radiotherapy for pituitary adenomas: five year experience.

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Between 1990 and 1995 40 patients with pituitary tumors were treated with fractionated proton beam therapy at the Loma Linda University Medical Center. Thirty-five patients with incompletely removed or regrowing tumor were treated after surgery, whereas five patients received proton therapy as their primary treatment. Twenty-nine of the 35 tumors that were histologically confirmed at the time of surgery were pituitary adenomas, one tumor was classified as pituitary carcinoma, and 5 tumors were diagnosed as craniopharyngiomas. Seventeen patients presented with signs and symptoms of hormonal hyperfunction, including 8 patients with acromegaly, 6 patients with hyperprolactinemia, and 2 patients with Cushing's disease, and one patient with Nelson's syndrome. Thirty-eight patients were treated to a nominal dose of 50-54 CGE (RBE = 1.1) in 25-30 fractions, and two patients, both with craniopharyngioma, received a

dose of 59.4 CGE in 33 fractions. The median follow-up time in 39 patients was 34 months (range: 8-66 months). One patient was lost to follow-up. Two patients, one with craniopharyngioma and one with pituitary carcinoma, died with clinical signs of local tumor progression at 13 and 23 months after treatment, respectively. In 37 patients tumor response could be evaluated with regular MRI or CT studies. At a median follow-up time of 25 months (range: 6-57 months), none of these patients showed signs of tumor progression or recurrence; 23 tumors showed no or minimal size reduction, 5 tumors responded partially (> 50% reduction of tumor volume), and 9 tumors were no longer visible at the time of the latest MRI. Ten out of 17 patients with hormonally active tumors could be evaluated endocrinologically at a median follow-up time of 32.5 months (range: 7-56 months): six patients had a complete remission, three patients improved, and one patient showed no change of hormonal hyperfunction. Visual outcome could be assessed in 34 patients. Vision remained unchanged in 27 patients, and improved in 3 patients with initially compromised vision. Vision deteriorated in four patients: possibly treatment related in three patients, and due to tumor progression in one patient. All three patients with deteriorated vision and absence of tumor progression received doses less than 50 CGE to the optic chiasm but had complicating factors, such as supra-sellar tumor extension, long-standing Cushing's disease, and Nelson's syndrome. Pituitary function could be assessed in 33 patients: out of 14 patients with normal function at the time of treatment, 13 patients retained normal function and one patient developed new signs of hypopituitarism; out of 19 patients with subnormal function at the time of treatment, 16 patients remained unchanged, one patient improved, and two patients developed additional signs of hypopituitarism. Long-term follow-up is in progress.

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Management of Atypical and Malignant Meningioma: Potential Role of High-Dose, 3D Conformal Radiation Therapy.

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Purpose / Objective: Atypical and malignant meningiomas are at high risk of local failure. Due to its relative rarity, role and dose levels of radiation therapy to improve disease control are poorly defined. This study reviews the experience of radiation therapy in the management of these tumors. Material and Methods: Between 1974 and 1995, 31 patients underwent fractionated radiation therapy (RT) for atypical (AM, 15 pts.) and malignant meningioma (MM, 16 pts.) of the cranium at Massachusetts General Hospital. All pathologic specimen were reviewed. Age at diagnosis ranged from 6 to 79 years (mean: 49 yrs.). Sixteen patients presented with primary and 15 with recurrent disease. Eight patients received RT following total and 21 patients after subtotal resection; 2 patients were treated following biopsy only. RT was given using megavoltage photons in 15 patients and combined photons and 160 MeV protons in 16 patients. Total target doses ranged from 50 to 68 (AM, mean: 62) and from 40 to 72 (MM, mean: 58) Gy or CGE (= Cobalt Gray Equivalent), excluding one patient who died during RT at 25 Gy. Results: With mean observation time of 59 months (range: 7-155 months) actuarial local control rates at 5- and 8- years were similar for both histologies with 38% and 19% for atypical and 52 and 17% for malignant meningioma. However, significant improved local control rates were observed for use of proton versus

photon RT (80% versus 17% at 5 years, P = 0.003) and target doses > 60 Gy for both, atypical (P = 0.025) and malignant meningioma (P = 0.0006).

At time of analysis, 14/15 patients (93%) with AM and 6/16 (38%) with MM were alive. Three patients (19%) with MM developed distant metastasis. Four patients with AM were alive with disease, but all patients with MM and local failure succumbed to disease. Actuarial 5- and 8- year survival rates for MM were significantly improved by use of proton over photon RT and radiation doses > 60 CGE. Three patients developed symptomatic radiation damage after 59.3, 68.4 and 72 Gy/CGE. Conclusion: Conformal, high dose radiation therapy, delivered by combined, fractionated proton and photon radiation therapy resulted in significant improvement of local control for both, atypical and malignant meningiomas. Increased local control resulted also in improved rates of survival for patients with malignant meningioma.

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Long term results of proton radiosurgery and fractionated proton irradiation for vestibular schwannomas.

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Between 1976 and 1990 26 vestibular schwannomas were treated in 25 patients were treated with single fraction160 MeV proton irradiation at the Harvard Cyclotron. Of these 9 patients had neurofibromatosis II. An additional 7 lesions in 6 patients (3 with NF II) received fractionated stereotactic radiotherapy with 160 Mev protons and 3D-planned megavoltage photons. The mean dose of stereotactic radiosurgery was 31.4 CGE to the 90% isodose line. In the fractionated group the doses varied from 57.1 - 72.0 CGE delivered at 1.7 - 1.9 CGE/day.

With a median follow-up of 10.6 years the 1, 5, 10 and 18 year overall actuarial survivals of the group with NF II were 91, 82, 63 and 42%, respectively. For the non-NF II group the same interval actuarial figures were 100, 100, 94 and 63%, respectively. Actuarial event-free survival for the patients with NF II was 54% at 1 year and remained at 46% from 5 - 18 years. For the other group the 1, 5, and 10 year event free survivals were 73%, 67% and 58%, respectively. These differences are not statistically significant.

Hearing was maintained in 22% of the NF II group and in 1 out of 4 patients who had hearing before treatment in the non-NF II group. Permanent facial nerve deficits occurred in 16% of the NF II goup. Permanent and temporary CN VII palsies occurred in 32% and 50%, respectively, of the non-NF II group. Trigeminal nerve occurred in 3% of the whole group transiently and 6% of the patients permanently. Ataxia worsened in 22% of the patients with time.

In summary the long term follow-up of this group of patients suggests similar survival and complication rates to other surgical and irradiation techniques. Surprisingly, the relatively high doses used in this early single fraction effort did not realize either improved control or worse complication rates compared to more contemporary series.

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Results of 90 Gy proton/photon radiation therapy for glioblastoma multiforme.

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Purpose/Objective: To determine if irradiation to 90 Cobalt Gray Equivalent (CGE) will improve local control and survival in selected patients with Grade 4 astrocytoma.

Materials and Methods: 23 patients with Grade 4 Astrocytoma on the Daumas-Duport scale were treated postoperatively on an institutional protocol to 90 CGE to residual tumor volume with a combined proton/photon therapy approach. Median preoperative T1-gadolinium tumor volume was 33 cc. Eligibility criteria included: 1) surgical resection, resulting in post-operative tumor diameter < 5 cm 2) age 18-70 3) post-operative Karnofsky > 70 4) unilateral, unicentric tumor not involving the corpus callosum and without subependymal spread. Irradiation was 1.8 CGE perfection bid with 7 hours interfraction interval. 3-D, CT-based treatment planning was completed incorporating standard MRI, echoplanar MRI, and F18-PET data. The area of first radiographic failure was correlated to the planning scan to determine the corresponding isodose.

Results: Median survival time from first surgery was 19 months with actuarial survival at 1, 2, 3 years of 78%, 33%, and 14%, respectively. Median follow-up for patients alive (N=6) is 22 months. Of patients alive, one leads a normal life 52 months after treatment, with the other 5 remaining steroid dependent. All of the 23 patients demonstrated expanding, enlarging masses by conventional MR imaging at a mean of 7 months after starting radiation. 12 of these patients then had second-surgeries (biopsies or resections) - 2 had autopsies. Of these 14 specimen for review, 10 revealed only necrotic material, 4 indicated both tumor and necrosis. Necrosis persisted, either alone (4), or with tumor (3) in 7 of these 12 patients operated upon for a third time. One had fourth-surgery showing necrosis only. In summary, 7 of 14 patients with pathological material following radiation never had demonstrable tumor in their specimens. 3 of these patients died. There was a trend towards prolonged survival in patients without demonstrated tumor compared to the whole group. Patterns of radiographic failure of the entire group suggest a continued prevalence of locoregional failure with 9 patients failing in the 90 CGE bid volume and only 2 patients first recurring in an isodose below 50 CGE.

Conclusion: The survival data for this group of patients is comparable to the survival data of the best brachytherapy series, with a trend towards larger and less accessible tumors in our patient population. Patterns of failure continue to support locoregional recurrence. The toxicity of this regimen dictates modification in dose per fraction and further restriction of the treatment volumes.

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Brainstem Tolerance to conformal Proton Therapy.

J. Debus[2], E.B. Hug, N.J. Liebsch, D. O'Farrel, D. Finkelstein, J. Efird, J.E. Munzenrider, Massachusetts General Hospital, Boston, MA; Harvard Cyclotron Labratory, Cambridge, MA, USA and [2]University of Heidelberg, Germany

Purpose / Objective: The tolerance of the brainstem to inhomogenous radiation doses applied by modern conformal radiotherapy has not yet been examined prospectively. The aim of this study was to analyse the incidence of brainstem toxicity in patients treated for skull base tumors with high dose conformal radiotherapy .

Materials & Methods: Between 1974 and 1995, 367 patients with chordomas (n=195) and chondrosarcomas (n=172) of the base of skull have been treated with combined megavoltage photon and 160 MeV proton radiotherapy. All patients had previously undergone biopsy or subtotal or total tumor removal. 104 patients had two ore more surgical procedures before radiotherapy. Following 3d treatment planning with delineation of target volumes and critical non-target structures dose distributions and dose volume histograms were prospectively calculated. Radiotherapy was given once a day, 1.8 Gy or CGE (=Cobalt Gray Equivalent) per fraction, 5 fractions per week, with prescribed target doses ranging from 63 CGE to 79.2 CGE (mean = 67.8 CGE). A relative biological effectiveness (RBE) of photon vs. proton Gray of 1.1 was assumed. Doses to the brainstem surface were limited to ≤64 CGE and to the brainstem center to ≤ 53 CGE. Brainstem toxicity was scored according to the RTOG grading system.

Results: Follow-up ranges from 6 months to 21.4 years (mean = 42.5 months). Brainstem symptoms developed in 16 of 282 patients with local tumor control (5.7%) attributable to the treatment, resulting in death of three patients. The mean time to onset of symptoms was 17 months (range: 4.5 to 177 months). These symptoms appeared in 89.5 % within 3 years. Grading of the brainstem toxicity is listed in table 1. Actuarial rates of 5 and 10 year survival were 87% and 82 % respectively. Increased risk of brainstem toxicity was significantly associated with maximum dose, volume of the brainstem receiving ≥50 CGE, ≥55 CGE and ≥60 CGE, number of surgical procedures and prevalence of diabetes or high blood pressure. Multivariate analysis identified three factors as possibly important prognosticators (table 2). The relative risk was 13.1 at a p=0.0009 if more than 1 cc of brainstem was irradiated to doses higher than 60 CGE. No toxity was observed in 32 patients with doses less than 60 CGE.

Table 1: Grading and incidence of brainstem toxicity

RTOG grade	I	II	III	IV	V
Patients (No.)	1	4	6	3	3

Table 2: Multivariate analysis: risk factors for brainstem toxicity

Variable	risk ratio	p-value
number of surgical procedures	2.6	0.001
volume above 60 CGE	1.7	0.001
diabetes	5.7	0.02

Conclusion: Tolerance of the brainstem to fractionated radiotherapy appears to depend not only on maximum doses but is also a function of tissue volume included in high dose regions. In addition presence of predisposing factors as as extend of surgical manipulation can significantly lower brainstem

tolerance in the individual patient. These factors should be considered in the design of future clinical trial with conformal radiotherapy.

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The idea of proton-knife radiotherapy.

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The main advantage of proton irradiation is the special dose distribution of Bragg peak. There is still a relative high dose in front of the Bragg peak, so the normal tissue especially in front of the tumor could be irradiated in relatively high dose. The radiation oncologist are concerning the radiation damage especially for some tumors located in the brain and eye.

The principles of this system we are designing is named "proton-knife" system or stereotactic focused proton system, The main parts of this system for clinical application are the following: (1) 360o rotated gantry; (2) 360o rotated couch; (3) body frame for patient localization; (4) air bag for patient fixation; (5) 3D-TPS for field arrangement and dose calculation.

The fractionations for proton treatment we are considering in this system are the following: (1) 3 -6 fractions; (2) 1000 - 1500 cGE per fraction; (3) total treatment time is 1-2 weeks.

This system had the following main clinical advantages: (1) reliable and reproducible fixation; (2) precise localization; (3) perfect dose distribution; (4) shorter treatment time.

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Modelling cell survival with mixed LET radiation.

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For more accurate treatment planning with high-LET radiations it is desirable to take into account the relative biological effect of all dose fractions of varying quality at each point in the dose distribution. For range modulated proton beams this has not been done so far. A single RBE value of 1.1 is currently used in clinical practice. Looking at the steepness of the dose-response curves for tumours and organs at risk, the clinical relevancy of the varying proton LET over the SOBP cannot be excluded. Therefore we aim to investigate the consequences of using biologically effective dose in the treatment planning for protons. To do so a model is needed on how to predict survival in the case of a mixture of different LET radiations. In this study we irradiated V79 cells with a mixture of ^{60}Co and nitrogen ions with a LET of either 78 keV/□m or 165 keV/□m. The measured survival curves were compared to the predicted survival curves from the Katz track structure theory, the Kellerer and Rossi dual radiation action based formalism and the lesion additivity model by Lam. The results showed that the lesion additivity model and the dual radiation action based model yield survival curves that are close to each other and to the measured survival curves for the different mixtures of low and high LET beams. Survival curves calculated from the track structure model have less curvature than the others, and in one case, with a mix of ^{60}Co and nitrogen ions with a LET of 165 keV/□m, the predicted curve falls partly outside the error bars of the measured curve.

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Risks and Benefits of a Lowered Dose Regimen in Irradiation Therapy of Choroidal Melanomas: A Controlled Clinical Trial.

E. S. Gragoudas[1], K. M. Egan[1], J. M. Seddon[1], J. Munzenrider[2], [2]Massachusetts Eye and Ear Infirmary, [2]Massachusetts General Hospital, Boston.

Purpose: Proton irradiation for choroidal melanoma achieves excellent local tumor control (97%) with preservation of useful vision in many treated eyes. However, radiation complications and visual loss may be inevitable in eyes with tumors close to the macula and optic nerve. We undertook a randomized clinical trial to determine whether lowering the total dose in patients with these tumors improves visual outcome without jeopardizing local control and systemic metastasis.

Methods: Patient with tumors under 15 mm in diameter and 5 mm in height, in proximity to the optic disc or macula (within 6 mm of either) were recruited for the study. Statistical considerations dictated a trial of 188 patients (1:1 ratio) for power to detect significant reductions in visual loss and worsening of local control. Those enrolled were randomized to receive either the conventional dose (70 CGE) or a reduced dose (50 CGE) regimen. Patient and physician were masked to the dose assignment. After completing treatment, patients were examined according to a standard protocol at six-month intervals, with the first interim analysis planned for the end of year 6 (median follow up: 3 years).

Results: Dose groups (94 per arm) were well balanced on age and other factors associated with visual outcome. By two years, patients in the reduced dose group has lost significantly fewer letters of vision from baseline (P=0.008), and had significantly improved visual field performance (P=0.21). No differences were observed in the number of local recurrences (4 total) or systemic (8 total) metastases.

Conclusion: A dose of 50 CGE improves visual outcome in patients with posterior choroidal melanoma. More extended follow up will determine whether the benefits of dose reduction must be weighed against any excess risk of tumor recurrence.

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Patient positioning system at CPO : tests and commissioning.

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A new patient positioning system for the second treatment room in development at the CPO is based upon a standard six axis industrial robot (Fanuc Robotics, Japan).

Based upon the following technical characteristics :

- maximal load 300 kg
- -six axis articulated robot driven by AC servo motors - movements : +/- 1m for x,y (horizontal), +/- 0.5 m in z (vertical) due to the position of the robot in the treatment room (1,3 m under the ground)
- -360 degrees for rotation around the vertical axis, tilt and roll limited to +/- 20 degrees (intrinsically 360) several specifics features have been developed : 4 accessories (carbon fiber table, chair, dosimetry phantom, setup box) linked to the robot by a pneumatic coupler. man

machine interface via PC (specific software) with 1 local (teach pendant) and two remote controllers.

- ethernet link to get the corrections for another computer.

The CPO is now undergoing the first commissioning : the preliminary results showed a bending of the table of 5 mm (at the end of the table) without correction and for a distributed load of 150 kg. We obtained also a repeatability better than 0.05 mm for the full procedure (including move movements such as coupling and decoupling). Concerning the positioning procedure and the working envelope, the robot seems to follow well the initial specs.

Efforts have been devoted to the safety system in order to fit the requirements of a medical application :

- concerning the procedure, the patient positioning system is going to have a classification as a "class I" product in the CE marking. This marking includes domains such as mechanical tests, electrical tests (shutdowns, cables,...), conception and procedures, "crash tests", electromagnetic compatibility,... and is done in cooperation between the CPO, the company and the GMED. Furthermore, an independent risk analysis committee (physicists, physicians, robotics experts, experts in medical equipment safety systems) has been set up. Technical and procedural recommendations for safety systems such as patient immobilization, covering of the device,... have been expressed.

- concerning the technique, some safety systems are "intrinsic" : hard and soft limitations of the speed, interlocks, default detection, automatic brakes if a default occurs,... Additional safety systems have been included : acceleration sensors, inclinometers and speedometers, collision sensors on the accessories and the robot, limitation of the working envelope, patient immobilization with belts, emergency manual procedure setup in case of an electrical shutdown,...

The commissioning is going on now (tests of the whole software, measurements of the absolute accuracy, bending with different loads,..). We are still in the schedule (call for bids in January 96, choice of the company in April 96, robot delivery in November 96, first commissioning in April 97). We plan to be "ready to treat" in this second room in September 97 and to treat by the end of this year.

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Nuclear Data For Radiotherapy: ICRU and IAEA Initiatives.

D. T. L. Jones[1] and M. B. Chadwick[2] for the ICRU and IAEA Committees [1]National Accelerator Centre, Faure, South Africa [2]Los Alamos National Laboratory, NM, USA

Nuclear data for neutron and proton reactions are needed for a number of applications including radiation therapy. Early in 1996 the ICRU formed a Report Committee on "Nuclear Data for Fast Neutron and Proton Radiotherapy".

The current chairman of this committee is M B Chadwick who has taken over from H H Barschall (deceased). This report, which is nearing completion, reviews the current status of these nuclear data and recommends cross sections and kerma coefficients for neutrons up to 100 MeV, and cross sections for protons up to 250 MeV,on tissue elements and elements used in collimators, shields and beam modifiers. Some important data on tissue elements are provided up to proton energies of 300 MeV, to meet the requirements of proton tomography. The nuclear data evaluations are based on experimental measurements and nuclear model calculations, and facilitate calculation of absorbed dose and the transport of radiation through matter. Recent experimental results, along with new advances in the modelling of nuclear reactions, are also described.

More recently the IAEA formed a Consultants' Panel to assess the "Status of Nuclear Data need for Radiation Therapy and Existing Data Development Activities in Member States". D T L Jones is chairman of the panel which has held one meeting at which it was resolved to concentrate on reviewing nuclear data for radiotherapy applications not currently being considered by other ICRU and IAEA groups. These applications include neutron capture therapy, heavy-ion therapy and radionuclide therapy.

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Fast 2D Dosimetry for Dynamic Beam Delivery Systems.

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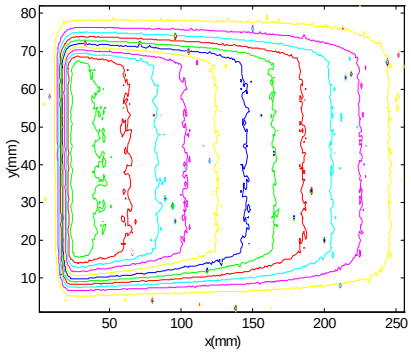
The introduction of dynamic treatment techniques in protontherapy requires improvements of the conventional water phantom dosimetry for quality control. We have developed a system which consists of a scintillating screen (Gd_2O_2S:Tb) mounted on the beam exit side of a phantom and observed by a low noise CCD camera with long integration time (1). This system allows a measurement of the dose distribution in 2 dimensions simultaneously, which is very advantageous for dynamic systems.



'Wedge' field produced by the spot scanning method and measured with the CCD-scintillator dosimetry system.

We have tested this system at the first clinical system using dynamic beam delivery: the 200 MeV proton gantry at the Paul Scherrer Institute in Switzerland. It uses the 'spot-scanning' method, in which the proton pencil beam is moved by a scanning magnet and table motion to cover the target volume. We have compared the CCD yield for a calibrated dose with earlier tests at the The Svedberg Laboratory in Uppsala, Sweden. The results obtained with the scanned pencil beam turned out to be consistent with those of the passive scattered proton beam within 1%. We have also measured homogeneous fields to look at the detection limits of beam positioning and preset errors. They are determined by the signal-to-noise ratio and well below the clinical maximum.

The greatest advantage of this system, however, is the capability of measuring more complex dose distributions. An example of such a distribution can be seen here. It is a dose distribution, in which the dose preset value varies linearly with the distance in the x-direction, comparable to a X-ray field with a wedge. With the PSI spot scanning system this sequence takes about 1.5 minute. This integration time can easily be reached by our system. It can be seen that the linearity of the system is very good. The sensitivity to small dose variations is clear from the detailed scanning structure, which becomes visible at high dose values.

The system demonstrates to be a useful tool for developing complicated dose distributions thanks to the fast availability of the results. We plan to enhance the system further in order to allow simultaneous 3D measurements.

Reference:
(1) S.N. Boon et al, submitted to Medical Physics.

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Continuous or stepped range modulator?

D. Prieels, IBA, Louvain-la-Neuve, Belgium

In proton therapy, the depth dose distribution is achieved by spreading out Bragg peaks. The number of Bragg peaks that are used and the specific weight attributed to each of them influence the dose uniformity. A natural question to ask is therefore if a continuous modulator, that is using an infinite number of Bragg peaks, gives a better result than the classical stepped modulator.

Simulations were performed using conventional optimization techniques. they show that both modulator designs give comparable results with a slight advantage for the stepped configuration.

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Radiation Effects from Secondary Nuclear Fragments in Proton-Induced Reactions.

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We review the status of nucleon-induced reactions from MeVs up to 300 MeV. Cross sections from these reactions provide crucial inputs to several important technological applications: 1) microdosimetry studies and particle-beam radiology, and 2) studies of single event upsets in microelectronic systems. We give a status report on our experimental and theoretical programs. Using reverse kinematics techniques, recoil spectra from 80 MeV protons on Si are measured at the National Superconducting Cyclotron Laboratory of Michigan State University. The data compare well with the predictions of a nuclear spallation reaction model NUSPA. Based on the NUSPA model, we have done new simulations of thick water targets irradiated by high-energy protons (50 - 250 MeV). The results show significant radiation energies due to the secondary nuclear fragments (heavy recoil nuclei and light ions such as alphas), a fundamental problem which needs to be addressed systematically. We discuss the significance of the recoil spectra and the implications of the simulation results.

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The use of GEANT for proton dosimetry.

S.N. Boon, J.M. Schippers, Kernfysisch Versneller Instituut, Groningen

We have investigated the use of the GEANT Monte Carlo code system as a tool in proton dosimetry. The GEANT (1) code has the possibility of incorporating other codes for the treatment of nuclear

interactions. We have chosen the GCALOR (2) code which is valid in the proton therapy energy region of interest. The transport of electromagnetic interacting particles is performed by GEANT itself.

The threshold energy for separate scoring of the delta electrons was set to 10 keV. We have examined the relative contribution of primary protons and secondary particles to the total dose for 78 MeV and 175 MeV proton beams in a simple 1D geometry. With respect to the nuclear interactions the calculations show that only the secondary protons have a significant contribution to the dose. In contrast to PTRAN (3) calculations, GEANT shows that their contribution varies with depth. At small depth a "build-up" effect is observed and for 175 MeV protons at 10 cm depth 10% of the total dose is due to secondary protons. At the end of the range this contribution decreases again. The second conclusion is that delta electrons with an energy larger than 10 keV do play an important role in the dose distribution, but since their range is not more than 1.5 mm, it remains a local effect. Work is in progress of comparing the GEANT results with depth dose curves measured with an NACP-02 ionization chamber. With respect to this we need to know the initial beam energy spread to obtain the right peak-plateau ratio. We hope to learn more on the influence of the secondary protons and electrons to model the different responses of ionization chambers and diodes.

(1) GEANT Version 3.2150, CERN, Geneva (1995)
(2) GEANT - CALOR Interface Version 1.04/08 by C. Zeitnitz, T.A.Gabriel (1995)
(3) PTRAN by M.J. Berger - NISTIR 5113 (1993)

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35 Years of Patient Treatments at the Harvard Cyclotron Laboratory: A geographical perspective.

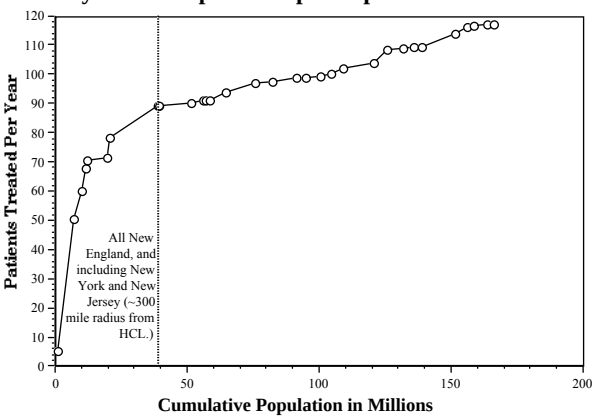
K. N. Johnson, Harvard Cyclotron Laboratory, Cambridge, MA 02138.

The Harvard Cyclotron Laboratory has treated 6972 patients since 1961:

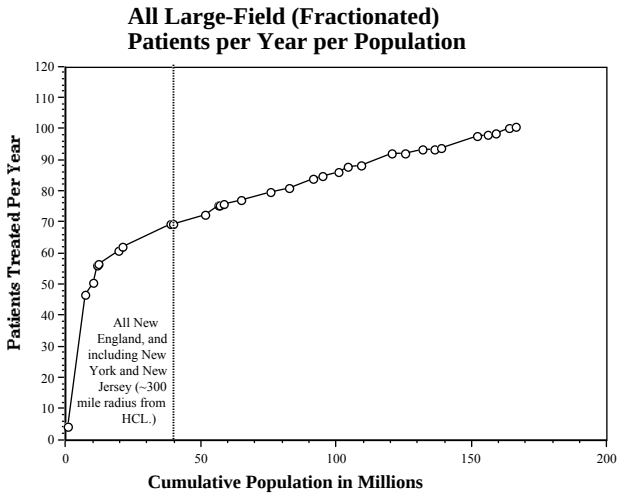
Uveal Melanoma:	2360	At the present time, we average a total of 310
Neurosurgical:	3124	patients per year encompassing all 3 programs,
Miscellaneous:	1488	where approximately 10% are neurosurgical,
(large field)		40% are uveal melanomas and 50% are
TOTAL	**6972**	miscellaneous.

Uveal Melanoma: of the 2360 patients, 93% have come from the United States with 32 foreign countries represented. On average, the HCL has saturated the 6 state New England area (total population, 13.2 million), in regards to uveal melanoma patient referral. (The currently accepted occurrence rate is 6 cases per million population per year.)

Miscellaneous: of the 1488 patients, 85% have come from the United States with 33 foreign countries represented.



Uveal Melanoma:
Patients treated during the last 5 years (604) were used to compute the average number of patients per year on the the Y axis. Home locations for these patients were plotted on the X axis, in cumulative state populations. From the graph one can see that we treated about 90 patients per year from within a population of some 39 million which includes all 6 states of New England, as well as New York and New Jersey. This encompasses a distance of about 300 miles from the HCL.



Large Field (Radiation Oncology):
Patients treated during the last 5 years (543) were used to compute the average number of patients per year. Home locations for these patients were plotted on the X axis, in cumulative state populations. We averaged about 70 patients per year for the last 5 years from within a population of some 39 million.

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Status report of NAC particle therapy programme.

D. T. L. Jones, A. N. Schreuder, J. E. Symons, E. A. de Kock, F. J. A. Vernimmen[1], C. Stannard[2], J. Wilson[2] and G. Schmitt, National Accelerator Centre, Faure, South Africa [1]Tygerberg Hospital, [2]Groote Schuur Hospital

The 200 MeV cyclotron facility at the National Accelerator Centre has been operational since 1987. Between September 1988 and March 1997 a total of 851 patients (24599 fields) had been treated on the p(66)/Be isocentric neutron therapy system. The physical beam characteristics are very similar to those of 8 MV x-rays. The facility has operated very reliably with more than 96% of the scheduled treatments having been successfully completed. Several randomised clinical trials are currently being undertaken, including head and neck, salivary gland, breast, soft tissue sarcomas, uterine sarcomas and paranasal sinuses. A new protocol for prostate treatment will soon be implemented. A multiblade post-collimator trimmer is under construction and will be installed this year. This will provide improved beam shaping capability. At present neutron therapy is conducted 3 times per week (1 day, 2 nights).

Between September 1993 and March 1997 a total of 191 patients (2462 fields) had been treated (mainly for intracranial conditions) on the fixed horizontal 200 MeV proton therapy facility. The facility incorporates an innovative automatic patient positioning system. Of the treatments scheduled 94% have been successfully completed. Conventionally fractionated treatments are now possible with the implementation of the new beam schedule which includes proton treatments on four days per week. PROG treatment protocols will shortly be implemented while a protocol for AVM treatments is under development. Two new fixed beam lines for proton therapy are presently being designed (30 deg. and 90 deg. to the vertical) for an existing unused treatment vault. Magnets and other components from a dismantled physics experiment will be utilized. Spot scanning systems will probably be developed for both beam lines. The anticipated completion date for the new facilities is 2000.

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Stereotactic proton beam therapy of AVMs: results of the first three years.

R. P. Levy[1,2], R. W.M. Schulte[1], K. A. Frankel[1,2], Y. I. Luchin[1], G. K. Steinberg[2], M. P. Marks[3], J. D. Slater[1], and J. M. Slater[1], [1]Department of Radiation Medicine, Loma Linda University Medical Center, Loma Linda, CA; [2]Departments of Neurosurgery and [3]Radiology, Stanford University Medical Center, Stanford, CA

A multi-institutional collaborative AVM program has been established at the Loma Linda University Medical Center Proton Facility. Between December of 1993 and December of 1996, sixty-two patients with 67 inoperable AVMs were accepted for the treatment protocol after evaluation by the multi-institutional protocol team. Fifty-nine AVMs were assessed as Grade III or greater (Spetzler-Martin classification). Fifty-eight AVMs were located in eloquent areas. Treatment plans, usually with the 80% isodose surface covering more than 90% of the AVM target, were developed in a collaborative fashion. Twenty-five medium-size targets (10 - 25 cc) or small targets in critical locations were treated in two days to a dose of 25 + 0.2 GyE (mean + SD). Thirty-five patients with very large and complex AVMs or AVMs with prior radiosurgery treatment received a dose of 19.9 + 0.8 GyE (mean + SD) in two days. A transient focal seizure occurred in one patient, and transient worsening of neurological symptoms was observed in another patient. The remaining 60 patients tolerated the proton treatment without any side effects. Thirty-three patients (53.2%) have been followed with serial MRI scans. White matter changes in the brain surrounding the AVM were detected in 13 patients (39.4%). Two patients developed new neurological symptoms and required treatment with steroids. Ten patients followed with MRI were found to have a significant reduction of flow through the AVM nidus. Angiographic follow, which is planned at three years after treatment, is in progress.

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Proton Treatment Facility at NCC, Kashiwa, Japan: A Progress Report.

T. Ogino, S. Murayama, N. Moriyama, H. Ikeda, S. Yoshida and S. Ebihara, National Cancer Center Hospital East, Kashiwa, JAPAN

The project of proton treatment facility at the National Cancer Center Hospital East (NCC, Kashiwa), JAPAN, is proceeding on schedule. The prime contractor of the building was Tokyu Construction Co.. Building construction started in May, 1996, and completed at the end of March, 1997. The prime contractor of the equipment is Sumitomo Heavy Industries Ltd.. Equipment manufacturing has proceeded very well, and the most of them has already been installed into the building. This facility is primarily medically dedicated. Therefore, the building is connected with the hospital building through passageway.

235 MeV isochronous cyclotron, which is the same as that of NPTC was installed. Energy selection system (ESS) reduces the 235 MeV beam extracted from the accelerator to 190, 150 and 110 MeV. There are two isocentrically rotating gantry treatment rooms. Manufactured parts of a gantry are assembled and a test run was performed at the works. Accuracy of isocenter (+/-1 mm), accuracy of stop angle (+/-0.5 degree), rotational speed (1 rpm), etc. were confirmed. Assembled gantries were decomposed at the works, and re-assembled at the hospital. Caterpillar-driven relatively rotational floor (caterpillar tread), which enables us to access to a patient at arbitrary gantry angle, was originally developed. Patient enclosure of the gantry, part of fixed horizontal beam delivery system, patient positioning system, CT & simulator, MRI, bolus and collimator fabrication machines were already installed into the building.

Accurate setting and adjustment of each equipment is now on going. For the gantries, test run is being carried out. The software for control, safety, network and treatment planning are now under development.

We are expecting to start, testing the extracted beam in the autumn of 1997, and treating patients in the latter half of 1998.

In Japan, incidence of eye melanoma, chordoma and skull base sarcoma is quite low. In contrast, that of lung cancer and liver cancer is increasing. For liver cancer (hepatocellular carcinoma), encouraging results by proton therapy are reported from Proton Medical Research Center (PMRC) of Tsukuba, Japan. For lung cancer, we are conducting a trial of mass-screening to find out early lung cancer patients using helical scanning CT. Its' preliminary results revealed that a lot of candidates for proton therapy were found, and some part of them had no lymph node metastasis by operation. One of the distinguished characteristics of our hospital is quite large number of head and neck cancer patients is being treated. Therefore, we are planning to do, for a start, dose escalating phase I/II clinical trial for cancer of the liver, lung and head & neck.

Fig. 1 cyclotron and part of beam transport line

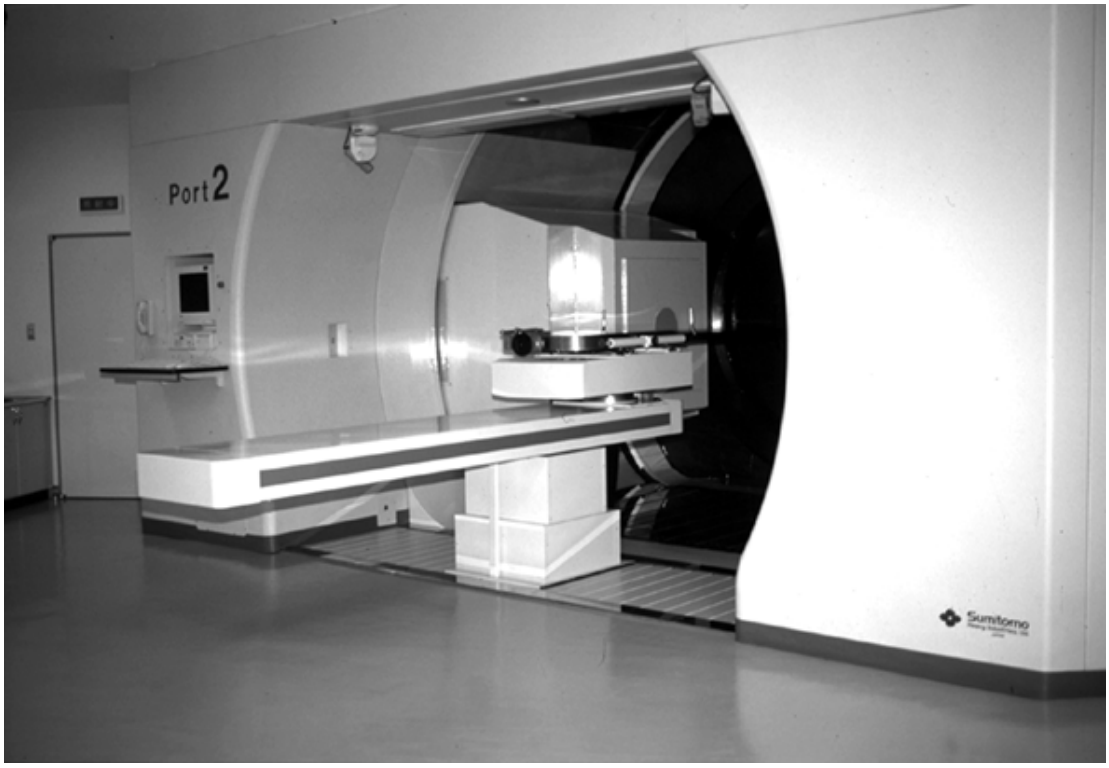

Fig. 2 Gantry treatment room

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Proton Therapy System for National Cancer Center.

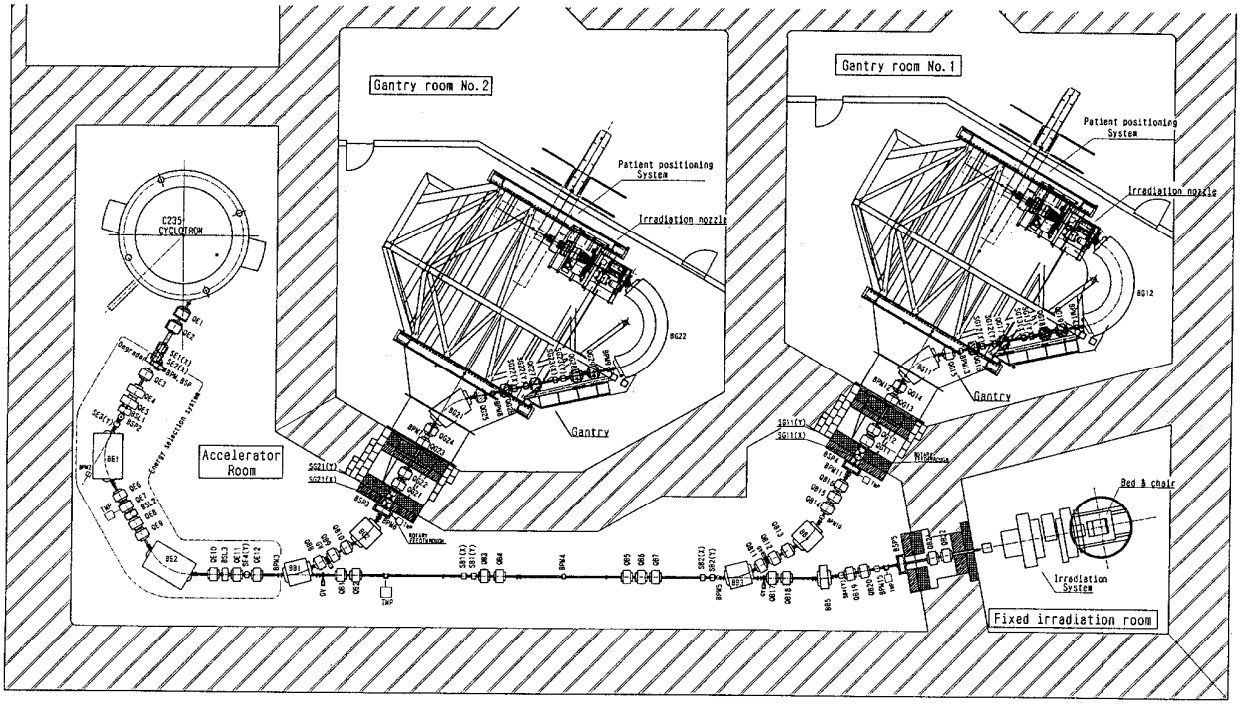
T. Tachikawa, Y. Hayashi, H. Nonaka, M. Sano, S. Hara and T. Satoh, Sumitomo Heavy Industries, Ltd., Niihama, Ehime 792, Japan

A cyclotron-based proton therapy system has been installed in National Cancer Center Hospital East (NCC, Kashiwa). The system is mainly composed of the 235 MeV cyclotron, two isocentric gantries, one fixed horizontal irradiation port and 6-axes patient positioners.

The 235 MeV cyclotron has been developed by SHI/IBA collaboration. The first machine for NPTC was manufactured by IBA and protons of enough intensity (>300nA) was successfully extracted. The field mapping of the second machine for NCC was done at SHI factory. The agreement with NPTC machine was very good and the mapping was finished within 1.5 months, which promises a short delivery time.

Being different from NPTC system, the proton energy is adjusted only by four steps (235, 190, 150 and 110 MeV) with the energy selection system for the purpose of easy adjustment of beam transport system. Fine adjustment of energy is done by the 0.5 mm step binary absorbers in the nozzle.

The double scattering system with dual-ring second scatterer is equipped in the nozzles of one gantry and fixed port. The wobbling system is equipped in the nozzle of the other gantry. The formation of SOBP is made by the 15 sets of ridge filters after the second scatterer.



NCC Proton Therapy System General Layout

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