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ABSTRACTS

of the

XIX PTCOG MEETING

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A fresh look at old proton dose intercomparisons and current status of proton dosimetry

L. Verhey, University of California at San Francisco.

The recent publication of ICRU Report 49 "Stopping Powers and Ranges for Protons and Alpha Particles" provided the incentive to review proton dosimetry intercomparisons performed at the Harvard Cyclotron Laboratory, particularly a group of experiments done with the Yale water calorimeter in 1990. In these experiments, the water calorimeter, a tissue equivalent (TE) ionization chamber and a fluence-based Faraday cup (FC) calibration of a transfer ion chamber were intercompared. For the TE ion chamber, the W value for protons in air and the proton stopping power ratio from water to air must be known. For the FC fluence-based calibration of a transfer ion chamber, the stopping power in water for the proton calibration beam must be known (requiring knowledge of the proton energy distribution). For the water calorimeter, only the thermal defect for protons in water must be known (assumed to be zero) to obtain absorbed dose in water from the thermal increase measurement.

Using the ICRU-approved value of 35.2 J/C for protons above 1 MeV (consistent with recent higher energy experiments) and the stopping powers in ICRU Report 49, the reanalysis showed agreement between the calorimeter and the ionization chamber determination of dose to within 1% ± 2.5%. On the other hand, doses determined using a fluence-based calibration of an ion chamber with the Faraday cup, are lower than the calorimeter doses by 6% ± 3.5%. Since the water calorimeter is the most direct measurement of absorbed dose in a proton beam and since it now appears to agree with ion chamber measurements using ICRU-approved dosimetric factors, these results indicate a need for a restatement of physical proton dose and RBE for those facilities which rely on a fluence measurement with a Faraday cup.

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Intercomparison of Dosimetry Techniques for Protons.

Jeffrey Siebers, Stanislav Vatnitsky, Dan Miller, Loma Linda University Medical Center

Water calorimetry, ionometry, and Faraday cup dosimetry were intercompared to determine the absorbed dose to water. The Schultz water calorimeter[1] was used in the horizontal beamline with an incident beam energy of 250 MeV. The beam energy at the calibration point was approximately 180 MeV. Ionization values were converted to dose values using an Ngas type protocol. Using the AAPM-16 recommended W value (34.3) and the ICRU 49 stopping power values, the dose as recorded by the ionization chamber and the calorimeter were found to coincide (CAL/ION = 0.999). Faraday cup dosimetry was performed on the eye beam line at several different distances from the 2 cm diameter aperture. Film dosimetry was used to determine the beam area, hence proton fluence. The proton energy was determined by comparing the depth dose profile with those of Berger[2]. The energy distribution was determined using a LAHET Monte Carlo simulation. Using the AAPM-16 W value (34.3) and the ICRU 49 stopping power values, the dose recorded by the ionization chamber and Faraday cup were found to be within error (FC/ION =1.019). Use of other published W values and stopping powers changes the CAL/ION and FC/ION ratios by up to 3%.

1. R. J. Schultz, C. S. Wuu, and M. S.. Weinhous, Medical Physics, 14 5 1987.
2. M. Berger, National Institute of Standards and Technology Report NISTIR 522 6. July 1993.

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Proton Transport in Water

M. J. Berger, NIST, Gaithersburg, MD 20899.

This is a brief review of proton transport calculations carried out at the National Institute of Standards and Technology in collaboration with S. M. Seltzer. Descriptions of this work are available in four publications: 1) Report NISTIR 5113 (1993) describes the proton Monte Carlo program PTRAN. 2) Report NISTIR 5226 (1993) presents results from PTRAN on depth-dose distributions, spectra and LET distributions. 3) Report NISTIR 5221 (1993) deals with cross sections for nonelastic proton interactions with oxygen, and also presents an assessment of the RBE taking into account the presence of secondary charged particles. 4) A report now in press deals with 3-D absorbed dose distributions from proton beams with circular, rectangular or arbitrary cross sections. Reports 1) and 4) include computer programs for use on IBM compatible personal computers, and Fortran source code.

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Monte Carlo Studies of Edge Scattering in Proton Beams

C. S. Mayo[1], B. Gottschalk, M. Wagner, Harvard Cyclotron Laboratory,
Cambridge, Massachusetts 02138, [1]and St. Anne's Hospital, Fall River MA 02722.

Monte Carlo simulations of 250, 160 and 70 MeV proton beams have been carried out to assess the dose contribution of protons scattered from the edge of a brass defining aperture. Protons scattered from the edge of a 2 cm diameter aperture with reduced energy converge on axis and produce a dose maximum. In air the maximum is 68%, 23% or 7% , with respect to energy, larger than primary beam. Behavior of edge scattered protons must be accounted for when setting up a beam line for dosimeter calibration or any beam which presumes a knowledge of the beam energy. Based on simulation results, a protocol for beam line design which minimizes the contribution of edge scattered protons is recommended. A phenomenologic model which describes on axis dose measurements is discussed. Dose in water simulations are made to assess the role of protons scattered from aperture edges in therapy beams. Owing to current practice for field calibration, their effects are negligible.

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Radiobiology of Protons; Summary of session and Panel discussion

Participants: E. Blakely, R. Cherubini, J. Dicello, V. Gregoire, A. Kacperek, B. Kaser-Hotz, M. Kirby, A. Kronenberg, A. Mazal, J. Robertson, H. Suit, L. Verhey
Contributors unable to attend: J. Gueulette, E. Krasavin, M. Urano

The issue of variability in proton RBE (relative biological effectiveness) values was the focus of two panel discussions on radiobiology during PTCOG XIX. In addition to a brief introduction of the major concerns, ten speakers presented brief reviews of their recent biological measurements, several completed in coordinated studies with microdosimetry. Inter-institutional comparisons were also provided. Salient features of the discussions included: 1) evidence for proton RBE dependence on particle residual energy and on the uniformity of the microdosimetric spectra, with RBE values greater than 1.10 at very low, and also at very high proton energies 2) evidence for low-energy protons (< 2 MeV) being more biologically effective than helium ions of the same LET, 3) evidence for enhanced mutagenesis only at very low proton energies, 4) a demonstration that proton microbeam irradiation of feline LGN (lateral geniculate nucleus) is capable of discrete disruption of function in the absence of acute cellular necrosis or observable disruption in surrounding brain regions, and 5) that spontaneous canine and feline tumors can be used as a model for the development of conformal radiotherapy with protons.

After the presentation of new data, the panel held open discussions as to what are the practical limits to precision in RBE determinations, how to deal with particle dose in fields of mixed radiation quality, which biological models are appropriate or necessary for estimating effectiveness or particle doses, and how, or if, changes should be made in the way RBE is incorporated into treatment planning with protons. Limitations introduced by the fact that particle dose responses are likely tissue-specific, that there may be a dissociation between early and late normal tissue responses, and that individual inherent radiosensitivities and technical limitations in biological resolution of small changes in RBE exist were also discussed. Consensus was reached only in the acknowledgment that more research is needed to clarify the clinical significance of these factors, especially in light of the report by at least one institution of a 5%-8% difference in absolute dose calibration between Faraday cup- and ionization chamber-based dosimetry. A proposal was made to organize a team to draft a “standardized” proton radiobiology and physical dosimetry protocol. This protocol will be presented in a future issue of PARTICLES. Anyone wishing to contribute to this effort is welcome to contact E. Blakely (FAX 001-510-486-4475).

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Proton radiotherapy of spontaneous canine and feline tumors as a model for the development of conformal radiotherapy planned at PSI.

B. Kaser-Hotz[1], H. Blattmann[2], G. Munkel[2], E. Egger[2], [1]Veterinary Clinic, University of Zurich, [2]Division of Radiotherapy, Paul Scherrer Institute, Switzerland.

The dynamic proton application technique planned and currently installed at the Paul Scherrer Institute will enable conformation therapy with tailoring of the dose in three dimensions. Patient and organ movement are critical factors in a dynamic system. Uncertainties with dose distribution and dose fall-off may occur.

To study these questions and to gain clinical experience in the dynamic spot scanning dogs and cats with selected, spontaneous tumors will undergo proton radiotherapy next year. Diagnostic work-up, treatment planning, positioning and therapy will be performed in the same manner as for human patients. Animals are studied for acute and late normal tissue reactions and for tumor control. Results are compared to the experiences and references in veterinary radiotherapy. Biologically the selected spontaneous animal tumors behave biologically very similarly to the same tumors in humans but progress at a faster rate, which means that results are available within a shorter period of time.

In order to gain experience and test the practicability in the treatment of pet animal patients at PSI dogs and cats with spontaneous tumors have been treated on the optis beam since March 1993. Due to the limited availability of the beam, the total dose has to be applied within 4 days. Currently pet animal patients are treated twice a day with 5.05 CGE (RBE assumed 1.1 for protons).

Results available from the first pet animal patients treated are presented.

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The Massachusetts General Hospital - Northeast Proton Therapy Center

Alfred Smith, Michael Goitein, Jacob Flanz, Stanley Durlacher and Anne Levine
Northeast Proton Therapy Center, Massachusetts General Hospital, Boston, MA

The decision has been made to construct a new proton therapy center on the campus of the Massachusetts General Hospital in Boston. The Northeast Proton Therapy Center (NPTC) will serve as a regional resource for cancer treatment and affiliations have been formed with major medical centers in Massachusetts and surrounding states. Funding for the NPTC will be provided jointly by the National Cancer Institute and the Massachusetts General Hospital. The need for the NPTC arises primarily from the energy and beam delivery limitations of the 160 MeV Harvard Cyclotron Laboratory (HCL) facility where proton therapy has been successfully carried out for over thirty years. In addition, we believe a hospital-based facility is needed for the conduct of clinical trials of protons versus photon conformal radiation therapy. The NPTC is planned to have two treatment rooms with isocentric gantry capability and one with horizontal beams. We will describe the procurement strategy for the building and equipment; the equipment clinical specifications and their technical ramifications; and the time table for the construction and acceptance of the overall facility. Preliminary architectural concepts for the building will be presented and some insight will be provided into the accelerator, beam transport and beam delivery systems which are likely to be installed in the NPTC.

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Proton Dose Calculations: A Broad Beam Algorithm and A Pencil Beam Algorithm

Linda X. Hong[1], Michael Goitein[1] and Marta Bucciolini[2], [1]Department of Radiation Oncology, Massachusetts General Hospital, [2]University of Florence.

We have developed a broad beam algorithm and a pencil beam algorithm for proton dose calculation. Both algorithms are incorporated into the Axiom treatment planning system.

The broad beam algorithm is based on a ray-tracing model, with good estimate of the lateral penumbra. The dose is determined by the range shortening and beam scattering effects of the beam modifying devices and of the patient. In this algorithm, the penumbra is affected by the thickness, composition and location of the upstream materials and varies with depth within the patient. In particular, the algorithm takes into account the effect of the air gap between the range modifier and the patient.

The pencil beam algorithm calculates the dose at a point-of-interest (POI) by the summation of the dose distribution of individual pencil beams. The off-axis dependence of the pencil beam dose distribution is described by a Gaussian distribution with the standard deviation calculated by adding in quadrature the multiple Coulomb scattering contributions from each beam modifying device and the patient. The central-axis term of the pencil beam dose distribution is related to the measured broad beam central-axis depth dose in the water phantom by an effective depth and inverse square correction. For each POI, the individual pencil beams are sampled on a pencil wheel with its center at the POI. The pencil wheel and the pencil beams on it are POI dependent.

Experiments for several geometries are presented and compared with calculations from the algorithms.

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Proton versus photon treatment planning for prostate cancer.

Michael Lee, Alan Nahum, Steve Webb, Joint Department of Physics, Institute of Cancer Research and The Royal Marsden Hospital, Downs Road, Sutton, Surrey, SM2 5PT, U.K.

Conformal photon and proton therapy plans for prostate cancer have been compared to assess the usefulness of proton beams for treatment. 2 x-ray plans (3-field and 6-field) and one proton beam only plan (2-field) are made and compared for each of the 20 T3 prostate patients with the aid of the 3D planning system VOXELPLAN. Dose distributions were analyzed and Tumour Control Probability (TCP) and Normal Tissue Complication Probability (NTCP) were computed. The study shows that an improvement in the dose distribution can be achieved by using protons, hence reducing the complication of the treatment. For an equivalent NTCP, the predicted proton TCP (using the current biological models) is only 2-3% greater than the TCP obtained using conformal x-ray therapy.

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Optimized Photons vs Protons

Marcia Urie, Andrzej Niemierko and Alfred R. Smith, Proton Therapy Program, Massachusetts General Hospital and Harvard Cyclotron Laboratory

Photon and proton dose distributions have been compared numerous times over the years. When patient dose distributions have been compared it has usually been done using different beam arrangements, weights, etc. for photons and protons. However, unless the same optimization program is used to arrive at the beam arrangements, the question arises as to whether the differences in the distributions are due to the inherent physical properties of photons and protons or, in part, to the fact that one modality was more optimized than the other. We present a study in which treatment plans were optimized for photons and then the photons were replaced by protons, beam for beam, to calculate proton treatment plans. Such comparisons show differences attributable only to the physical differences between photons and protons. The case selected for these intercomparisons was a patient who presented with a large abdominal, horseshoe-shaped mass surrounding the spinal cord and in close proximity to the right kidney and gut. The first treatment plan for photons (23 MV) used two 120 degree arcs, each having an isocenter on one side of the 'horseshoe'. As described above, this same arrangement was then used for a proton beam treatment with the proton beams compensated. For the second plan, 31 different photon beams, including arcs (without wedges), 4-field box beams, oblique beams, wedged beams and non-coplanar beams were designed for treating the target volume and then used as input to an optimization program along with the prescribed target dose (+/- 2% uniformity) and normal tissue doses (5% at 5 yr complications). The optimization resulted in the selection of 8 beams which had non-negligible beam weights. Both photon (23 MV) and proton dose distributions were calculated. For both the 2-arc and optimized 8-field plans dose volume histograms were calculated for the target volume and normal tissues.

The dose volume histograms for the target volume were equivalent for both photons and protons for both treatment plans. Those for the normal tissues showed dramatic differences between photons and protons, with protons being superior for all normal tissues. For the spinal cord, gut and right kidney, protons showed at least a 10 Gray advantage. The conclusion is that for equivalent (and acceptable) normal tissue complications, protons would permit at least 10 more Gray to be given to the target volume. Future studies will include dose distributions optimized for protons then replaced beam for beam with photons and treatment plans optimized separately for both photons and protons.

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Proton Radiography: A Tool for Quality Control in Proton Therapy

Uwe Schneider, Alexander Tourovsky and Eros Pedroni, Department of Radiation Medicine, Paul Scherrer Institute, 5232 Villigen-PSI, Switzerland

Since radiotherapy with protons is a high precision treatment, it is important to verify the calculated dose distribution and to control the correct positioning of the patient with respect to the beam in order to avoid damage to critical structures or target misses.

Radiographic images of the patient body region to be treated can be taken directly with the proton beam exactly under the geometrical conditions as during treatment (*proton-beams-eye-view-projection*). The control of the patient position can be performed directly on the gantry immediately before and after treatment provided that the beam can be quickly tuned to a higher energy (enough to penetrate the patient) and to a low intensity adequate for diagnostics.

As opposed to photons, the data of radiographic images contain important information (for therapy) on the range of the protons traversing the patient. The range information of transmitted particles (*radiography*) and the range of stopping protons in the patient (*therapy*) can be predicted by the same algorithm in the treatment planning software based on CT images. The radiographic measurements can be compared quantitatively with the predictions, provided that the energy of the beam is will under control and that the radiographic equipment is absolutely calibrated in energy (*energy-calibrated-radiography*). With this method errors in the treatment planning range calculation and in the calibration of the CT slices used for treatment planning can be detected. Calibrated radiographic images contain also information on the range variations due to inhomogeneities in the body (the combined effect of inhomogeneity interfaces parallel to the beam direction and the proton path uncertainty due to multiple scattering). These measurements can be used as a warning for critical situations. The safety margins around the target volume can be determined on the base of such measurements.

Moreover it is possible to use proton radiography or proton tomography for pure diagnostic purposes. Proton images are characterized by a high density resolution with a very low dose to the patient. A disadvantage results from the bad spatial resolution compared to conventional X-ray Images.

For these reasons we prepared and realized experiments for proton radiography and we did study the density and spatial resolution of the images and produced quantitative results for the precision of the positioning and range control.

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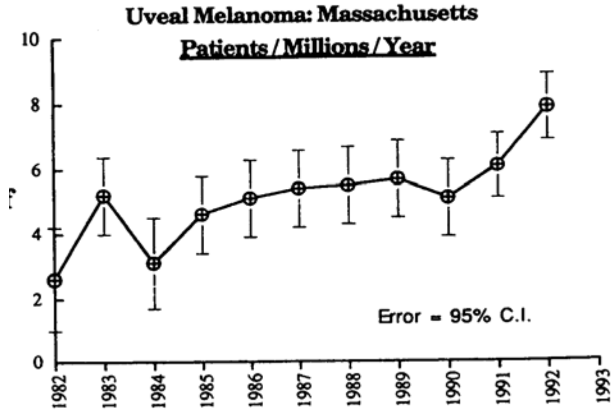
Review of the Harvard Cyclotron experience: Patient statistics.

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

The Harvard Cyclotron Laboratory started treating patients in 1961. Up until September, 1993, 5949 patients have been treated. Our patients can be categorized into three programs: Neurosurgical which began in 1961; Radiation Oncology, Fractionated patients started in 1974 and our Uveal Melanoma program in 1975. Our total, yearly patient load has averaged about 300 over the last 4 years.

More recently, we have been investigating the geographical referral patterns of our patients, keeping in mind that any current or planned proton facilities must depend on a continuous flow of referrals. Our



largest group of patients has been in the uveal melanoma category, with some 1870 patients treated through December 1992; 1744 (93%), of which have come from the United States. We have found that approximately 90% of these patients have come from within a 1200 mile radius from the Cyclotron. Noticeable exceptions are the north-central and western states.

The six states bordering Massachusetts (i.e. Maine, New Hampshire, Vermont, New York, Connecticut and Rhode Island), have provided a rather steady supply of uveal patients since 1984, averaging about 1.8 patients, per million population, per year. In Massachusetts, in more recent years, we have reached 6 patients, per million population, per year (see graph). This number is the currently accepted incidence rate of uveal melanoma in the United States, indicating a possible saturation of the state's patient population.

Finally, analysis has also been made of our chordoma/chondrosarcoma patient-referral pattern. We have treated 314 through December, 1992; 238 (76%), of which have come from the United States. Most of the country has been represented, with the greatest concentration living in Massachusetts (33 patients).

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The PSI Proton Unit for Medical Applications: A Status Report

E. Pedroni, H. Blattmann, T. Böhringer, A. Coray, S. Lin, A. Lomax, G. Munkel, S. Scheib, U. Schneider, A. Tourovsky (on leave from ITEP Moscow) Paul Scherrer Institute, CH-5232 Villigen-PSI, Switzerland

The realization of the 200 MeV proton therapy facility at PSI is coming close to its completion. The installation of the PSI compact gantry is proceeding almost on schedule. We are now mounting the magnets on the gantry support. The patient table has been delivered and the computer dedicated to the steering of the gantry motors is being installed. An extended anti-collision system is also being designed under the supervision of the concerned official authorities. The first beam through the gantry is planned for March 1994. On the gantry we will mount a retractable support used for taking X-ray pictures of the patient at the isocenter at an angle of 90° with respect to the beam. The same mechanics will also be used to insert boxes (containing the detectors for proton radiography) in the beam in front and behind the patient. Patient transporters (the special carriage system used to carry the patient lying in his couch between preparation-, positioning- and treatment rooms) and the two "top-rot supports" (used to rotate the patient couch for head treatments in the horizontal plane) have been ordered from Schär Engineering, the Swiss company in charge of the mechanical realization of our gantry.

We have started the work necessary for the installation of a dedicated CT in the medical pavilion. The table of the CT will be modified in such a way as to permit the coupling of the patient couch on the CT table using the same mechanism as for the gantry. The same CT unit will be used for treatment planning, for the positioning of the patients before irradiation (with scout view images) and for dosimetry.

The thesis work of S. Scheib on treatment planning will be completed in December of this year. The thesis work of U. Schneider on proton radiography (see 2nd report to this conference) will be submitted in spring 1994. Other important issues at PSI are the intercomparison of photon and proton treatment plans (in collaboration with the DKFZ of Heidelberg) and the development of a fast Monte Carlo code for the simulation of treatment plans in complex anatomical sites (collaboration with ITEP Moscow).

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Status of the Particle Therapy Facilities at the National Accelerator Centre

D. T. L. Jones, A. N. Schreuder and J. E. Symons, National Accelerator Centre, P O Box 72, Faure, 7131, South Africa

The p(66)/Be isocentric neutron therapy facility at the NAC has been operating routinely since the beginning of 1989. The beam characteristics are very similar to those of x-rays from a 8 MV linear accelerator. In order to most efficiently accommodate the other major NAC activities (radioisotope production and physics research) neutron therapy is given in 3 fractions per week on Tuesdays, Wednesdays and Thursdays. A total of 515 patients had undergone neutron therapy up to 30 September 1993.

A 200 MeV horizontal beam proton therapy facility is now in use and the first patient was treated on 10 September 1993. Feedback systems which operate on multiwire and quadrant ionization chambers ensure position stability and beam symmetry respectively. A stereophotogrammetric patient positioning system utilizes the images obtained by television cameras of reflective markers on the patient for precise (<1 mm) automatic patient set-up and movement monitoring on the treatment chair. The horizontal beam is being used initially for plateau crossfire irradiations on Fridays only for the treatment of intracranial lesions. A progressive expansion of this facility is planned to accommodate spread out Bragg peak therapy and later fractionated large-field treatments. A further treatment room is available for an additional proton beam configuration such as an isocentric gantry. Facilities for intraoperative proton therapy are also available.

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Update on the Development of the Eye Proton Therapy Project at TRIUMF

G. Lam, S. Atkins, E. Blackmore, E. El-Khatib, M. Nicolic, U. Oelfke, K. Paton, T. Pickles, J. Rootman and J. Vincent, TRIUMF, University of B. C., Vancouver, Canada.

The eye therapy project is part of the on-going TRIUMF particle therapy program that started with pion therapy in 1974 and is the first (funded) phase of a general proton therapy proposal that includes a large field facility. The target date for first eye treatment is June, 1994.

The eye proton channel was previously used as a neutron channel for neutron radiobiology studies at different neutron energies and has a variable energy range of 70-120 MeV with a maximum proton range of about 10 cm. Hence the eye treatment chair is designed with seven degrees of translational and rotational modes of motion to cover a wider range than necessary for the eye treatments such that some head and neck sites can be treated as well. The other equipment, such as the range modulator, the eye fixation table and the head immobilization devices are similar to those used in other eye facilities.

The expected beam availability will be about 35 weeks per year and the number of patients will be about 40 per year from the western provinces of Canada. RBE values will be measured with a spatial resolution of about 3 mm using an in vitro system with cells suspended in gelatin. For treatment planning, the Clatterbridge version of the program EYE is installed together with the graphic package obtained from PSI. We plan to pursue some minor developments such as (i) automated treatment planning using systematic search in fixation angles and (ii) the use of a single “universal” range modulator using variable speed control.

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Osteo- and Chondrogenic Tumors Of The Axial Skeleton: Results Of Combined Proton And Photon Radiation Therapy

Eugen B. Hug, John E. Munzenrider, and Norbert J. Liebsch, Dept. of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, and Harvard Cyclotron Laboratory, Cambridge, Massachusetts.

Purpose: Tumors of the axial skeleton are at high risk for local failure due to difficulties in achieving total surgical resection and tolerance of critical normal tissues limiting the options of conventional photon therapy. This study reviews our experience of using combined high dose proton and photon radiation therapy.

Material and Methods: Between Dec. 1980 and Sept. 1992 47 patients were treated at the Massachusetts General Hospital and Harvard Cyclotron Laboratory for primary or recurrent chordomas and chondrosarcomas of the thoracic and lower spine (Group I, 20 patients), osteogenic sarcomas (Group II, 15 patients) and giant cell tumors, osteo- or chondroblastomas (Group III, 12 patients).The base of skull was involved in 12 patients (group II and III only), C-spine in 7, T-spine in 5, L-spine in 7, and sacrum and coccyx in 16 patients. Age at diagnosis ranged from 8 to 76 years. The mean follow-up period was 3.2 years (0.5 - 11.3 years). Radiation treatment was given postoperatively in 23 patients, pre- and postoperatively in 17 patients, and 7 patients received radiation therapy as definitive treatment modality following biopsy only. The proton radiation component was delivered using a 160 MeV proton beam and the photon component employing megavoltage photons up to 23 MV energy with 1.8 - 2.0 CGE per fraction, once a day (CGE = Cobalt Gray Equivalent) Total external beam target dose ranged from 55.3 CGE to 82.0 CGE with mean target doses of 73.9 CGE (group I), 69.8 CGE (group II) and 61.8 CGE (group III).

Results: Group I (chordomas and chondrosarcomas): Five of 20 patients (25%) recurred locally, and two of those 5 patients developed distant metastasis, resulting in one death from disease (5%). Five year actuarial local control and overall survival rates for all 20 patients were 60% and 75%, respectively. All failures occurred in 14 patients with chordomas.

Group II (osteogenic sarcomas): All patients except one received adjuvant chemotherapy. Three of 15 patients (20%) never achieved local control and died within 6 months of completion of radiation treatment. Only one of the 12 patients who were locally controlled for more than 6 months developed distant metastasis, and another patient failed locally, yielding a 5-year local control rate of 60% for 15 patients. Overall, four patients (27%) developed distant metastasis; three patients succumbed to their disease, and one patient was salvaged by chemotherapy, resulting in overall survival of 44%.

Group III (giant cell tumors, osteo- and chondroblastomas): One of 8 patients with giant cell tumor failed locally, one patient distantly, and all patients are currently alive. Three of 4 patients with osteo- or chondroblastoma are alive and well. One patient suffered local recurrence and died of disease. Local control rate and overall survival for this group of 12 patients was 76% and 88%.

In the majority of cases radiotherapy was well tolerated. However, two patients with large base of skull tumors developed retinopathy, and two patients with sacral tumors have bowel problems after extensive surgery and postoperative irradiation.

Conclusion: Combining the special physical characteristics of proton beam irradiation with photon therapy, optimized by 3-D treatment planning, allows the delivery of higher doses to the target, yielding improved long term local control of tumors of the axial skeleton, while respecting normal tissue constraints.

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The Effect of High-Dose Irradiation on Local Control and Liver Function in Hepatoma

Hirohiko Tsujii, Hiroshi Tsuji, Toshiyuki Okumura, Yasushi Matsuzaki, Naomi Tanaka, Toshiaki Ohsuga., Proton Medical Research Center (PMRC), University of Tsukuba, Japan

The incidence of primary hepatocellular carcinoma (hepatoma) is high among Asian countries, and it is the third cause of death in men in Japan. Because of frequent association of liver cirrhosis and advanced stage when diagnosed, the resectability of hepatoma is low, approximately 15-30%. Accordingly, 5 year survival rate is low, 31% for operated cases and < 5% in overall cases. For treatment of unresectable hepatoma, there are two major modalities commonly performed, transarterial chemoembolization (TAE) and percutaneous ethanol injection (PEI). Conventional radiotherapy, however, has been applied only exceptionally.

At PMRC we have performed high-dose proton beam radiotherapy in 72 patients with hepatoma with curative intent. The liver function of these patients was classified as good in 27, moderate in 30 and poor in 15 patients. They were treated with a total dose of 60-88 Gy in 16-30 fx over 6-8 weeks. In order to avoid unnecessary irradiation to the surrounding liver tissues, we have developed a respiration-gated irradiation system (ReGIS) using a strain gauze semiconductor detector. In-field local tumor control was obtained in 84.7% and for those irradiated with TDF >170 it was 91.2%. The 3 year survival rate was 38% for all patients and 47% for those with moderate to good liver function. Radiation induced complications were observed in 7 patients (hepatic dysfunction 3, GI tract ulcer 3, pleuritis 1), but none of these became fatal. In conclusion, proton beam radiotherapy has proven of potential advantage in treatment of hepatoma.

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A Clinical Protocol for Proton Beam Radiotherapy of Hepatoma.

Hirohiko Tsujii[1], Hiroshi Tsuji[1], Toshiyuki Okumura[1], Yasushi Matsuzaki[1], Naomi Tanaka[1] Toshiaki Ohsuga[1], Tada-aki Miyamoto[2], Hirotoshi Kato[2], [1]The Institute of Clinical Medicine, University of Tsukuba, Japan [2]National Institute of Radiological Sciences, Japan

At Proton Medical Research Center (PMRC) a phase I-II clinical trial of proton beam radiotherapy in hepatoma has taken place since 1983. So far our judgement is that proton beam radiotherapy given with or without transarterial chemoembolization (TAE) has potential benefit for this type of tumor. Based upon this, we have started a clinical trial to evaluate the efficacy of high-dose proton beam radiotherapy alone in treatment of hepatoma. The patients eligible in this trial are those with biopsy-proven tumors, no prior treatment, 2-5 cm in tumor diameter, moderate to good liver function, and performance status ≥70. Treatment techniques include the implantation of radio-opaque Ir seeds at the tumor edge, every day field localization with a localize-and-verify system, immobilization using an universal half-body cast, and the use of respiration-gated irradiation system (ReGIS). The target volume is set at 5 mm around the tumor boundary and the total tumor dose is 78 Gy/20 fx/6 wks or 72 Gy/16 fx/5 wks depending upon machine schedule. So far, 7 patients entered in the trial, of whom 5 patients have already shown complete disappearance of tumors which was confirmed by CT scans as well as targeted biopsies. In no patients radiation-induced adverse effects are noted.

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A Poor Man's Faraday Cup

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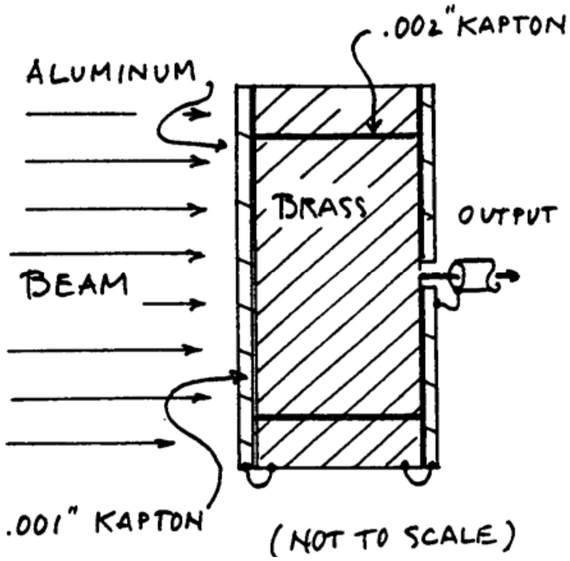
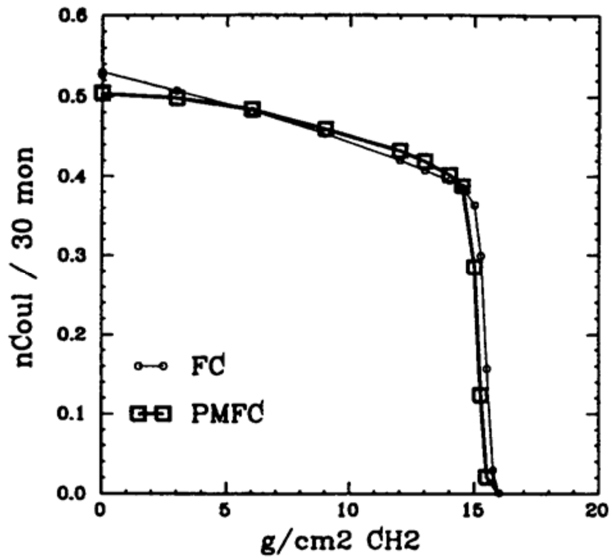
A Poor Man's Faraday cup (PMFC) can be made by covering a brass block with a thin insulator and covering that with a grounded shield. Trapped air should be excluded, particularly in front, to avoid ionization. The assembly should be snug but free of excessive pressure on the insulator, which causes long term drift. For fully contained beams the PMFC





agrees with our 'real' Faraday cup (FC) to ≈1% and we use it as an absolute monitor where the FC will not fit. Range curves (see graph) for the FC and PMFC are slightly different, perhaps due to different outscattering in the two geometries. We are also testing a variant meant to be used in a uniform flood beam (see sketch). Only 0.002″ of Kapton separates the stopping block from the surrounding brass, so protons scattered in should compensate those scattered out. Such a 'defined area' Faraday cup would act as a self contained proton fluxmeter.

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Dosimetry of Small Proton Beams with a Radiochromic Film

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The suitability of using radiochromic film (GAF) for dose distribution measurements in small proton beams with energy of 120 MeV was studied. GAF films were irradiated in plastic phantoms with collimated proton beams (field size from 0.5 x 0.5 cm to 5 x 5 cm) and films were tilted to the beam axis. The measured doses delivered to the films were varied between 300 and 400 Gy. A comparison of dose distributions measured with GAF films and other detectors (parallel plate ionization chamber, diamond detector, LiF detectors and radiographic films) was performed. The results show that GAF films can be used for dose distribution measurements in modulated beams. Depth dose measurements in monoenergetic beams were found to be affected in the Bragg peak region.

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Quantitative Studies for Proton Dose Monitoring with PET

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In order to investigate the feasibility of ‘in situ’ proton dosimetry with PET first experimental studies were performed at TRIUMF. A lucite $C_5H_8O_2$ phantom was irradiated with protons of energies of 62 MeV and 110 MeV. The absorbed doses in the phantom ranged from approximately 2 Gy to 85 Gy. The induced e^+-activity in the phantom was then analyzed about 20 minutes after the irradiation with a Siemens ECAT 953b PET scanner at the UBC hospital.

At first dynamical PET scans were performed. Their analysis showed that at the time of the scan almost the entire activity was due to the decay of ^{11}C, which was mainly produced by neutron knockout from ^{12}C. Contributions from ^{13}N and ^{15}O were found to be negligible. Static PET scans were used to analyse the spatial distribution of the induced activity. The spatial activity profile was obtained in an axial field of view of 10.46 cm divided into 31 slices of 3.375 mm. For the depth activity profiles the relative activity was found to drop to 50% of its maximum value approximately 6 mm before the position of the corresponding Bragg peak at both energies. For the proton energy of 110 MeV an almost flat depth activity curve was observed.

Furthermore, a model calculation for the induced activity was performed. The calculation uses the relevant data for ^{11}C production cross sections and takes into account the smearing of the activity profiles due to the range spectrum of the emitted positrons. The model for the corresponding proton flux is based on p-stopping power data and includes as well the effects of energy straggling and inelastic nuclear interactions. The results from this model calculation were found to be in fairly good agreement with the experimental data obtained in our phantom studies.

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250 MeV Superconducting Isochronous Cyclotron for Proton Therapy

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In the winter of 1993 the National Superconducting Cyclotron Laboratory conducted an intensive design study of a 250 MeV Superconducting Isochronous Cyclotron for proton therapy and in February submitted a proposal to the National Science Foundation requesting funding for construction of a prototype cyclotron based on this design. (An official response from this proposal has not been received, but informal contacts indicate that funding is unlikely based on mismatch with the perceived mission of the National Science Foundation.) The design study included all sensitive features, i.e. the superconducting coil, the cyclotron central region, the radio frequency system, and the beam extraction system. Such a cyclotron should achieve extraction efficiencies of more than 99% with intensity at any level desired by the medical user, and with a beam emittance (normalized) of approximately 0.1 pi millimeter-milliradians and an energy spread of l/4000. The excellent extraction efficiency and the self shielding characteristics of the cyclotron yoke can be combined with use of close-in shielding at the range shifter to greatly reduce building shielding and space requirements. All the essential features of the design have been tested and verified in earlier MSU cyclotrons giving a high level of confidence in performance projections. (An isochronous superconducting cyclotron built at the NSCL and now in routine use at Detroit’s Harper Hospital delivered neutron beams for 2800 fields and 141 patients in the first nine months of 1993.*)

*Fast Neutron Therapy at Harper Hospital: A Progress Report, R.L. Maughan et al, Proceedings of the International Symposium on Hadron Therapy, Como, Italy, Oct. 1993.

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Intensity measurements and upgrade paths for the Loma Linda accelerator

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More than two years have passed since Loma Linda treated the first cancer patient with the world's first proton accelerator dedicated to radiation therapy. Since that time, over 600 patients have completed treatments and the facility currently treats more than 30 patients per day. With a typical intensity of 3×10^{10} per pulse and 27 pulses per minute, dose rates of 90 - 100 cGy/min are easily achieved on a 20 cm diameter field. In most cases, patient treatment times are two minutes; much less than the patient alignment time required before each treatment. Nevertheless, there is considerable medical interest in treating field sizes up to 40 cm in diameter without decreasing dose rate or increasing treatment times. This will require an intensity increase from the accelerator which can be achieved with an improved injector. In this paper, we present beam measurements relevant to intensity studies and propose an injector modification for any intensity upgrade. We show that nearly all intensity losses can be ascribed to the large momentum spread of the injected beam and occur at the injection energy of 2 MeV. In addition, optimum beam characteristics for the new injector are discussed based upon the momentum acceptance and space charge limits of the Loma Linda synchrotron.

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Integrating Control System Components for Proton Therapy

Richard Leath, Maxwell Labs, Richmond, CA

A high-performance, safe, and reliable control system is critical to a hospital-based proton therapy system. To minimize development and maintenance costs, it's important to reuse existing software where appropriate and utilize industry-standard hardware throughout. We have selected a commercial software package and a standard hardware architecture as the foundation of the control system. Accelerator commissioning software will be adapted from existing mature codes. The user interface will be modelled on the radio-therapy systems developed by Varian. Considerable effort will be dedicated to insuring that all new and reused software meets the FDA requirements for a clinical medical device.

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Corkscrew Versus "Big Gantry"

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An ion-optical design of a new in-plane gantry is presented. Beam spreading by scanning or scattering is performed at the entrance to the gantry, and the maximum field at isocenter is 40 cm x 25 cm. The last dipole (135-degree) has to have a relatively large gap (20 cm), although there is a transverse-beam "cross-over" in the middle of this magnet. A multipole set of coils can be placed at the position of the cross-over and another, set inside one of the quadrupoles. By correcting the "flatness" of the field with these multipoles one can utilize a larger portion of the beam from a double scatterer, or, simply use a single scatterer. The system is non-dispersive. The following is a comparison between a Corkscrew gantry (3.5 m throw) and the new design (with 1.5 m throw.) The estimates of floor space and volume in the following table are made by assuming a shielding-wall thickness of 1.5 meter.

	Corkscrew	New gantry
Floor space (w. shield)	85 m^2	92 m^2
O.D. of shielding	14.2 m	10.5 m
Gross volume (w. shield)	685 m^3	620 m^3
Time constant	2.1 sec	5.0 sec
Magnet weight	18 tons	55 tons
Magnet power	190 kw	320 kw
Eff. source distance	3.0 m	∞ and 4 m
Flatness correction	None	Multipoles
Energy loss in scatterer	~40 MeV	~2 MeV
Energy modulation	"simple"	Formidable
Scanning (30, 1000 Hz)	Formidable	"simple"

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Determination of the Isocenter for a Proton Ring Gantry

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The majority of commercial electron / x-ray accelerator gantries use a slewing ring bearing to mount a rotating treatment head to a stationary stand. The world's first proton gantry uses a rotating external ring to which is mounted a fixed treatment nozzle with a movable snout that extends close to the center of rotation. A method to determine the size, shape, and virtual center location of radiotherapy gantry isocenters will be described and a comparison of the characteristics of the proton treatment unit to slewing ring based electron / x-ray treatment units will be given.

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Feasibility Study for a Hospital Based Hadron-Therapy Facility for Italy

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The "Progetto ADROTERAPIA" is a feasibility study for a hospital-based hadron-therapy facility for Italy. The name *hadron-therapy* has been introduced to indicate *collectively* the use of beams of particles made of quarks, i. e. protons, neutrons and light ions. The accelerator is a H^- synchrotron capable of providing 60-250 MeV proton beams with an intensity of 10-20 nA. Two extraction channels will be available, which can be operated simultaneously and independently; the possibility of proton acceleration is also being considered. The injector is an RFQ + DTL structure with the capability of producing positron emitting radionuclides for PET diagnostics and thermal and epithermal neutrons for Boron Neutron Capture Therapy via the Be(p,n) reaction. The injector energy into the synchrotron is 11 MeV. The design includes the possibility of implementing, as a future development, acceleration of light ions up to $^{16}O^{8+}$ with energies up to 400 MeV/u with minor upgradings of the ring and the addition of a second injector.

The main advantages of accelerating H^- are: 1) the simplicity of the ejection system (stripping foil) which makes it possible to have a number of independent extraction ports at a low cost; 2) the extremely small transverse emittances (of the order of 0.1 p mm mrad), nearly equal in the two planes, of the extracted beams which can be obtained with a small stripping target. This allows the design of lighter and cheaper isocentric gantries as compared to conventional units, due to the smaller required aperture of the magnets.

The facility, which is expected to treat at least 1000 patients per year, will have:
- two treatment rooms equipped with an isocentric gantry capable of transporting protons up to 220 MeV;
- one treatment room equipped with one horizontal beam and one vertical beam pointing downward;
- one room equipped with two horizontal beam lines, one for eye irradiations and one mainly devoted to head and neck treatments
- one room with one horizontal beam for experimental activities with both protons and light ions (dosimetry, radiobiology, etc.);
- one room devoted to future light ion treatments;
- two smaller rooms served by the 11 MeV proton beam from the injector., one for the production of positron emitting radionuclides for PET uses, the other for neutron production for BNCT.

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Plans for a 60 MeV proton eye-treatment facility at Munich University

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The two Munich Universities (Technische Universität München, TUM, and Ludwig-Maximilians-Universität, LMU) have been operating an accelerator for nuclear research since 1970. The tandem Van de Graaff attains a maximum voltage of 14 MV and can thus accelerate protons to 28 MeV maximum energy. An upgrading project which is nearing completion consists of a separated-orbit alternating-gradient cyclotron, named TRITRON, which uses the tandem accelerator as an injector. It employs superconducting magnets for deflection on a 20-turn spiral and six super conducting cavities for acceleration.

The TRITRON was conceived to post-accelerate heavy ions stripped to high charge states after leaving the tandem. For most medical applications the range of these heavy ions is, however, too small. The maximum proton energy expected out of the TRITRON is 64 MeV, sufficient to treat melanomas of the eye in the same manner as is done at several existing facilities. The combined accelerator system is scheduled to operate in spring 1994, and reliable routine operation is expected a year later.

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H^- minus Test Program at the ITEP Synchrotron

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Lately, ITEP concept of designing new proton therapy facilities has been reported and discussed a number of times at various international meetings. The basic feature of the project proposed and being realized in Moscow at the moment, is the use of a synchrotron accelerating H^-minus ions for generation of external medical proton beams.

Concerning their parameters, the proton beams produced in such a way are ideal for medical purpose. All the dose delivery systems are being optimized and simplified, their cost is reduced. At the same time, the project contains many new ideas and solutions which, naturally, cause a number of motivated and unmotivated objections from opponents. For experimental verification of the project basic technical solutions and for demonstration of its advantages, an experimental program has been developed and is underway in ITEP for the acceleration of H^-minus ions in the ITEP U-10 synchrotron, and for their extraction by charge exchange in a small foil. Besides the general task of generating the H^-minus ions and accelerating them in the synchrotron, a number of issues are of relevance: the vacuum system, the design of the extraction system, the choice of the parameters for the internal beam during the extraction, slow and fast bumps for driving the beam onto the target, feedback stabilization of the external beam, influence of magnetic field ripple, choice and design of the system for external beam intensity measurement, experimental study of magnetic stripping and particle losses in the residual gas, and measurement of the external beam parameters such as the emittance, the stability of beam intensity and the time structure.

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Certain Considerations on the Accelerator Choice for Proton Therapy.

K. K. Onosovsky, V. S. Khoroshkov, Institute of Theoretical and Experimental Physics, Moscow, Russia

Recent appearance and start of realization of a big number of PTF projects based on specialized medical accelerators, has revealed a number of approaches to designing these accelerators. Despite the variety of the accelerator types proposed (synchrotrons, cyclotrons, linacs), all of them have one common characteristic feature. In the greater part of the projects, the authors try to use the almost 40-year experience of proton therapy acquired at “physical” accelerators, which is natural. At the same time, this experience is being transferred not only to the design of the PTF “medical” equipment, but also to the concept of designing the accelerator itself, which is wrong, from our point of view. As a rule the point is made at the choice of the simplest technical solutions from the viewpoint of accelerator experts.

With such an approach, the ability of radiologically inoptimized proton beams to compete with electron beams, seems doubtful.

The report presents the review of the proton therapy use of the accelerators built for other purposes. Data is presented on the accelerators which were built specially for medical and biological purposes. Analysis of their advantages and disadvantages is carried out.

New approach is proposed to designing accelerators specifically for proton therapy. The essence of the approach is that the simplicity, low cost and dimensions of the accelerator should not be the decisive factors in its choice and designing. The choice of the accelerator and of its parameters is made after, and on the basis of the choice of the optimum, simple, and relatively cheap dose monitoring and delivery systems, and also in view of widening the possibilities of forming dose fields of various configurations.

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Simple Comparison of Two Simulated Treatment Plans Using Photon and Proton Beams

L. Wielopolski, R. Beers, M. Collier*, M. Moyers*, Brookhaven National Laboratory, Medical Department, *Loma Linda University, Medical Center

Two simple treatment plans, using photon and proton beams, were performed for two simulated cases of tumor around the spinal cord. Two simple cylindrical configurations were considered with the following dimensions: outer contour diameter 25 cm, tumor diameter 10 cm, spinal cord diameter 1.5 cm, all cylinders being concentric in one case and spine cord together with tumor offset by 5 cm in the second case. A second case with the dimensions of 15, 8, 2.5, and 3 cm respectively was also analyzed. The photon and proton treatment plans consisted of full arc rotation and three beams, one lateral and AP-PA distal to the tumor, respectively.

Although, qualitatively, the treatment plan using proton beams appears to be superior to that using photons, it is difficult to compare these results using simple treatment planning systems. The accuracy of treatment planning systems needs to be improved in order to obtain a valid dose volume histogram (DVH). With improvements in the delivery of photon beams and attempt to escalate the dose fractionation DVH will play a major role in evaluating treatment plans. However, the number of beams required to obtain dose uniformity within the target area, interfering sensitive organs, quality of matching the fields, and time required to deliver the treatment will be additional factors that will dictate the quality of the treatment. Thus reliable 3-D treatment planning systems will play a major role in evaluating the efficacy of these two cancer treatment modalities.

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