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ABSTRACTS

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3-D Conformal Treatment Plan for the Nasopharynx Using Multiple Noncoplanar Fields

T.L. Phillips, L.J. Verhey, C. Akazawa, Department of Radiation Oncology, University of California, San Francisco

A thin-section CT scan of a nasopharynx patient from Loma Linda University Medical Center was contoured by Gudrun Munkel, MD from PSI. After dose constraints for targets and normal tissues were defined, the CT scans and contours were converted into AAPM exchange format and made available on the internet. The AAPM files were converted into UMPlan files at UCSF and plans were developed which attempted to satisfy all the constraints. A total of 6 fields were used to irradiate the nodal and initial target volumes to 68.4 Gy and a boost plan with an additional 6 fields was used to boost the final target to 76.8 Gy. More than 90% of all targets received the full prescription dose. Most of the optic chiasm and brainstem/cord were below their constraint doses, although a small portion of each exceeded the defined limit. Approximately 80% of the submandibular glands and 40% were below the dose constraints, although clinically such a plan would probably result in some retained salivary function. Although more complex than most plans delivered at UCSF, such a plan is clearly achievable with current technology. The effort to develop such a plan was estimated as 8 hours to plan (normal 3D planning time would be approximately 2 hours). The treatment delivery would be no more complex than many other head and neck 3D cases treated in our clinic.

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Comparative Treatment Planning for Nasopharyngeal Tumors: Loma Linda University Medical Center Protons

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A nasopharyngeal tumor with lymph node involvement was provided as a test case for developing a three-dimensional treatment plan. Various target and critical structure contours were provided along with the CT information. The first task was to contour CT artifacts and convert the CT numbers to the CT number of water. The large uncertainty associated with this conversion process dictated that no anterior beams be used in regions of the patient containing these artifacts. The complexity of the case suggested that the plan be broken into three adjoining sections. Each section, inferior, middle, and superior was developed as a separate plan. The inferior section of the plan used only two posterior oblique fields to deliver 68.4 CGE to the lymph nodes. The middle section used two pairs of posterior oblique fields with an every-other-day alternating patchwork technique to deliver a dose of 54 CGE. Two more pairs of patched posterior oblique fields delivered an additional 14.4 CGE but were reduced in width to reduce the dose to the parotid glands. The upper section started out using two large lateral beams to deliver 45 CGE. The laterals were then reduced in width but paired with two posterior oblique patch fields to deliver an additional 11.7 CGE. The patch fields were then dropped and an additional 11.7 CGE given through the laterals. Finally, the laterals were reduced again and an additional 8.4 CGE was delivered. In designing the proton beams, several uncertainties were taken into account. These uncertainties included 1 mm for beam range, 3% for CT values, and 2 mm for patient alignment. This procedure ensured that 90% of the

prescribed dose for each beam was placed at the beam edge except when critical structures in the beam path were being blocked. Dose-volume histograms were calculated for several structures. 94% of the high dose target received 90% of its prescribed 76.8 CGE. 97% of the low dose target received 90% of its prescribed 68.4 CGE. 98% of the lymph node volume received 100% of its prescribed 68.4 CGE. None of the brainstem received its limit of 64 CGE at the surface. Only 4% of the total brainstem volume received a dose in excess of 53 CGE. 95% of the sub-mandibular glands received less than 45 CGE. No part of the optic chiasm received more than 40 CGE. A significant portion of the parotid glands received more than their limit of 35 CGE due to the nearness of the targets. This plan was developed assuming that a fraction of the glands' volumes can receive larger than this dose while still preserving some function. Virtually all of the prescribed constraints for the plan were met using the described technique which is treatable using standard technology available today.

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Optimized, Intensity-Modulated Treatment Plan for Standardized Nasopharynx Case Using the Peacock Planning System

L.J. Verhey, Department of Radiation Oncology, University of California, San Francisco and M.P. Carol, NOMOS Corporation, Sewickley, PA

A thin-section CT scan of a nasopharynx patient from Loma Linda University Medical Center was contoured by Gudrun Munkel, MD from PSI. After dose constraints for targets and normal tissues were defined, the CT scans and contours were converted into AAPM exchange format and made available on the internet. The AAPM files were converted into Peacock files at NOMOS and plans were developed which attempted to satisfy all the constraints. The resulting plans were downloaded from NOMOS to UCSF for documentation and verification.

The optimized plans were developed assuming rotational slice-based treatment delivery with the Peacock MIMiC intensity-modulated delivery system. Virtually all dose goals and constraints for the plan were met. 96.5% of the nodal volume, 99.85% of the low dose target volume and 99.93% of the boost volume received 90% or more of the prescribed dose. Except for about 3% of the parotid volume, all normal structures were completely below their stated dose limits. The time required to develop this plan was estimated to be less than one day and the time required to deliver each fraction would be expected to be no more than 20 minutes after patient setup, or approximately 30 minutes total.

Treatments such as this have been delivered to more than 15 patients at Baylor College of Medicine and more recently, at several other sites. At UCSF, we expect to be able to deliver such treatments in the next few months.

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Comparative Study of Proton Therapy and Photon Therapy for Nasopharyngeal Cancer

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The purpose of the study is to demonstrate the advantages of proton therapy and to ascertain its beneficial role in the curative therapy for nasopharyngeal cancer, either as boost treatment for moderately advanced cases or as the major treatment for early cases.

Radiation Therapy has been the primary therapy for nasopharyngeal cancer which is one of the major malignant diseases in Taiwan. Three dimensional treatment planning offers the capability to optimize the dose distribution. Proton therapy provides the high precision and better dose distribution capabilities and has been more widely used for larger treatment fields and various disease sites due to improved design in beam delivery system using rotation gantry and higher energy source using synchrotron. Treatment planning analysis was carried on cases of nasopharyngeal cancer, including those for primary treatment and for recurrent treatment and those treated with proton alone, photon alone, and combined proton and photon. Optional plans were generated in both modalities in each case for comparative study, including dose distribution, dose volume histograms for tumor and normal tissues, tumor control probabilities, complication probabilities, complication free tumor control, follow-up requirement and further adjuvant therapy. A protocol for more effective combination of proton and photon therapy for a major portion of patients with nasopharyngeal cancer is proposed and will be implemented in the treatment of the very common malignant disease in Southeast Asia. The real benefits must be confirmed by good long-term follow-up systems as in many other therapy methods.

An example of recurrent nasopharyngeal carcinoma recently treated with proton beam for the relapse is reviewed. Photon beam (6MV) would have been used otherwise. A comparison of dose distribution and dose-volume histogram between the proton beam and 6 MV photons clearly shows advantage of proton beams. The patient is now 18 months post re-treatment. Application of hyperbaric oxygen and solcoseryl (growth stimulant from blood) administration greatly improved the commonly seen complications of meningeal irritation and indomitable radiation mucositis following accumulated high dose radiation of nasopharynx.

World-wide experiences in treatment of nasopharyngeal cancer showed that relapse in the primary site of nasopharynx is a significant failure by conventional radiation therapy (20-40%). Higher tumor dose and reduced volume of normal tissues under irradiation by proton beam is probably the important approach to greatly improve the local control of NPC. Therefore a wide application of proton beam in the routine treatment of NPC is foreseen in the near future.

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Fixed Versus Variable Modulation in Proton Beam Therapy of Advanced Nasopharyngeal Cancer: A Comparative Treatment Planning Study.

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We are initiating a trial in patients with advanced nasopharynx cancer (NPC) which is designed to substantially increase the dose delivered to the tumor, and to limit the dose received by adjacent critical normal tissues, relative to conventional X-ray treatment. We anticipate that this will result in improved loco-regional tumor control and reduced treatment-related morbidity. We aim to accomplish this by combining our ability to use modern cross-section imaging studies (CT and MRI) to precisely map the loco-regional tumor extent with the ability of stereotactic fractionated proton beam therapy to conform the dose distribution to the defined target area. In preparing for this trial, we have treated 6 patients with stage T4 NPC to 76.8 CGE in 48 fractions (1.6 Gy BID, with inter-fraction interval $\geq$ 7 hrs). Five patients have loco-regional control of their tumor to date, while one patient had local failure 1 year after completion of treatment. No serious treatment-related complications have been observed.

We plan to treat a total of 10 patients to this level (76.8 CGE), and then progressively escalate the dose to 80 and 83.2 CGE for 10 additional patients at each of the higher dose levels, carefully monitoring toxicity, to assess both local control and treatment-related morbidity.

Current techniques employ customized brass apertures to conform the dose to the tumor profile as seen in the beams-eye view and field-specific compensators to achieve dose conformality to the distal tumor surface. Full dose to the proximal tumor surface is achieved by spreading out the Bragg peak (modulating the beam), to a fixed extent which is determined by the greatest tumor diameter along the beam axis. Unless the tumor is of uniform thickness, employing fixed modulation results in excess radiation to normal tissue overlying thinner portions of the tumor. Variable modulation, however achieved, can vary the amount to which the Bragg peak is spread out as appropriate to variations in tumor thickness throughout the volume of interest. In preparation for this dose escalation study in advanced NPC cancer, we are exploring the use of variable modulation to further reduce the dose delivered to non-target tissues. To this end, we have performed comparative treatment planning for a patient with advanced NPC, to quantitate the advantage of using variable rather than fixed modulation in terms of normal tissue coverage.

A larger tumor volume containing gross tumor and regions of potential microscopic spread, and a smaller tumor volume containing gross tumor only were defined (by GM) on the MGH 3D planning system. Dose-limiting normal structures, including the optic nerves and chiasm, brain stem, cervical spinal cord, and both parotid glands were also defined. Plans were then prepared (by JA), using fixed modulation and variable modulation. A total of 12 individual aperture-compensators were employed, using standard margins
[3 mm motion, 4.5 mm penumbra (90-50%)]. Dose prescribed to the gross tumor was 76.8 CGE, and to the gross tumor plus probable areas of microscopic involvement was 68.8 CGE. Plans were developed to treat both those volumes to the prescribed dose, while limiting dose to the optic nerves and chiasm to $\leq$ 60 CGE, to the surface and center of the brain stem to $\leq$ 64 and 53 CGE, respectively, to the cervical spinal cord $\leq$ 45 CGE, and to the parotid glands to $\leq$ 36 CGE. Plans were compared using the technique of dose-volume histogram (DVH) analysis.

Dose to both the larger and smaller volumes was identical on each plan: the DVHs for each structure could be super-imposed. Minimum doses were 64 and 68 CGE, respectively. Ninety and 80% of the larger and smaller volumes received the prescribed dose, reflecting incorporation of the stated normal tissue dose constraints into the planning process.

Dose to each of the defined normal structures was reduced with variable modulation. Dose to spinal cord and brain stem were reduced substantially, with dose reductions approximating 5 and 10 CGE, respectively, for approximately 60% of each structure. Optic chiasm dose was reduced approximately 2 CGE for the entire structure, while optic nerve doses were reduced by 1 CGE for 50-80% of the volume. Significant sparing of both parotid glands was achieved with both plans, but further dose reduction was evident with the variable plan. Maximum and mean doses to the right and left organs were 45 and 50 CGE and 16-20 CGE, for the variable and fixed modulation plans, respectively.

Tumor coverage should not be compromised with either variable or fixed modulation. The benefit of variable modulation in sparing normal tissue will vary, depending on tumor-normal tissue configuration and technique employed. Further efforts are certainly justified to allow its routine implementation, since substantial normal tissue sparing can indeed be achieved with that technique.

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Comparative Treatment Planning for Nasopharynx Tumors

Alfred Smith, Department of Radiation Oncology, Massachusetts General Hospital, Boston MA

Nasopharynx tumors were selected for the first clinical focus session on comparative treatment planning. The session included the following talks. Case Presentation - Gudrun Munkel; Standardized Data Acquisition and Exchange - Dan Miller; The Clinical Problem and Conventional Strategies for Treatment - Ted Phillips; Proton Strategies for Treatment - Norbert Liebsch; Presentations of Treatment Plans - Mike Moyers, John Munzenrider, Tony Lomax, Lynn Verhey, Fang-Jen Lin, and Joe Deasy. The session ended with a discussion of the clinical presentations led by Al Smith. Proton plans were presented by the speakers from Loma Linda, PSI, and MGH, while UCSF speakers presented a conventional conformal x-ray plan as well as a plan using the Peacock system which provides inverse planning and multi-leaf collimator delivered intensity modulation. The MGH presentation included a proton plan incorporating proximal beam shaping and one using proton intensity modulation. Joe Deasy from the University of Wisconsin presented some novel x-ray plans using inverse calculations and intensity modulation. The speakers generally used dose-volume histograms to summarize their plans.

During the discussion it was pointed out that there remained problems with data transfer between institutions which hampered the comparisons. Also the group lacked a common format for presenting their results which would facilitate the comparison of the different plans. It was decided to develop the ability to display collective DVHs, i.e., everyone's DVH for tumor on a single graph, and likewise for normal tissues, so that direct comparisons might be made. The group also decided to attempt a calculation of tumor control probabilities and normal tissue complication probabilities from the respective DVHs thus providing another method for comparing plans. There will be another session on nasopharynx held at the South Africa meeting with the intent to present additional treatment plans and to use the tools described above to facilitate the plan comparisons.

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Forming Therapeutic Proton and 350 MeV Neutron Beams for Combined Irradiation at the JINR Phasotron

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For extension of the JINR phasotron application for medical purposes a special channel and a treatment room were constructed, which permit a high energy neutron beam to be formed and used for irradiation of the large radioresistant deeply located tumours both independently and in combination with a therapeutic proton beam introduced into the same room. The scheme of formation of these beams is given. For formation of the neutron beam the 660 MeV proton beam is focused on beryllium target 36 cm thick, which is located inside a revolving steel drum together with other targets and a collimator. The neutron beam with mean energy of approximately 350 MeV is purified of target-emitted charged particles by a bending magnet and passes through the collimator of 3.5 m in length in the shielding wall to the treatment room. This room is equipped with a collimating system and a rotational stand with arm-chair for irradiation of a patient. The unused neutron beam is absorbed in a 4 m thick back wall of the room. This channel also permits changing over from a neutron beam to a proton beam in the treatment room either by turning the target drum to install copper target and to decelerate 660 MeV protons down to 250 MeV, or by employing a carbon moderator near accelerator to form 250 MeV proton beam, which is then transported through the same channel (readjusted on new proton energy) to the treatment room. Here the proton beam gives rise to a wide and uniform dose field, which allows 14 narrow, horizontal, independent proton beams to be formed with the aid of special equipment located before patient's arm-chair. This device is provided with a pair of moving collimating plates and additional wedgy perspex absorber for each of 14 horizontal levels. The total maximum height of the irradiated target amounted to 21 cm, permitting large deeply located tumour of complex shape to be scanned along depth during rotational or multifield irradiation. For irradiation with neutrons alone a separate rotational stand is installed in the forepart of the treatment room. Basic characteristics of the beams obtained are given, including its dosimetry, dose distributions, neutron energy and LET spectra, RBE and OER values.

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A Treatment Planning Comparison of Protons Versus Photons in Non-Small Cell Lung Cancer

J. M. Collier, N. Choi, A. Niemierko, Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA

A patient with non-small cell lung cancer in the right hilar region and mediastinum was planned to compare 3 treatment plans. Two targets were drawn on CT: an initial target which included microscopic extension and a boost target for the visible gross disease. The 3 plans were: (1) 50 Gy initial plus 10 Gy boost, all with 10 MV X rays, (2) 50 Gy initial with X rays plus 28 CGE boost with protons, and (3) 50 CGE initial plus 28 CGE boost, all with protons. Thus the purpose of the exercise was to see if a higher dose could be given to a boost target using protons while still keeping normal tissues below tolerance. For this situation the critical structures include the spinal cord, the right, left and whole lung volume, the entire heart as well as the four chambers of the heart contoured separately, the esophagus, and the liver.

In the first planning step the photon plan (1) was optimized by the Niemierko weight optimization technique. The optimization program was presented with 49 ports from 12 directions; the variations on the ports involved apertures which included the entire target or shielded critical organs, and which used different wedges. Only 6 of the 49 weights calculated were significantly different from zero: 5 ports

aimed at the initial target and 1 at the boost target. For (2) the same 5 ports treated the initial target, but the boost photon port was replaced with 2 proton ports to reduce the chance of hot regions from the increased boost dose. Then in (3) the 5 photon ports for the initial target were replaced with protons one for one, giving an all proton treatment.

The treatments were analyzed using Dose-Volume Histograms for the two targets and for the contoured normal tissues. All plans covered the targets adequately with the intended doses as planned. However, the all photon plan (1) does give a hot region; about 8% of the boost target receives 15% more than desired. In (2) a similar hot region is about 10% high. For all protons (3) the boost target dose is within 1% of the intended value. Also the additional proton boost in (2) can be given with little or no additional dose to critical structures except for a short section (~2 cm) of the esophagus, which receives approximately 80 CGE because it lies within the boost target and a small volume (~10%) of the left ventricle, which receives about 50 CGE. The tolerance doses for such small regions are unknown. The all proton treatment (3) reduces the doses to many of the normal organs over (2), and even over (1) except for the esophagus, by 3 to 10 CGE, thus offering the possibility of that much higher dose to parts of the boost target.

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A Treatment Planning Intercomparison of Radiation Therapy Using Spot Scanned Protons and Intensity Modulated Photons

A. Lomax, G. Munkel, T. Bortfeld, C. Dysktra, H. Blattmann, J. Debus.
The Paul Scherrer Institute and DKFZ Heidelberg

In this presentation, we will discuss the preliminary results of a collaborative project between the Paul Scherrer institute and the German Cancer Research Center in Heidelberg, in which a variety of cases with different anatomical sites and clinical indications have been evaluated for radiation treatment using state of the art proton and photon planning techniques. In the case of protons, plans have been made using the PSI planning system, designed specifically for the planning of treatments using the spot scanning method being developed at PSI. For photons, plans have been calculated using a inverse planning technique developed at the DKFZ at Heidelberg. The resulting dose distributions from both methods will be presented and the source and consequences of the differences between the techniques will be discussed.

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Temporal Lobe (TL) Damage Following Surgery and High Dose Photon and Proton Irradiation in 96 Patients Affected by Chordomas and Chondrosarcomas of the Base of the Skull

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Materials and methods:

This study is based on the analysis of 96 patients affected by chordomas and chondrosarcomas of the base of the skull who have been referred to the Massachusetts General Hospital (MGH) Department of Radiation Medicine between 1984 and July 1993 and have been treated, primarily, with the fixed horizontal proton beam of the Harvard Cyclotron Laboratory. Proton doses ranged between 30.6 and 66.2 CGE (average 55.3) while photon doses ranged between 5.4 and 36 CGE (average 12.6 CGE). The mean treatment time in days was 55.3 (range 50-71 days) and primary targets were comprised between 5 and 135 cc (average 43.2 cc). After treatment the patients have been followed from 15 to 131 months with a median and mean time of 41 and 43.8 months respectively.

To evaluate the incidence of temporal lobe damage, all the available clinical documents of these patients have been re-examined. The clinical symptoms of temporal lobe damage were classified into 4 grades according to the RTOG-EORTC classifications. CT and MRI scans were evaluated for white matter changes. Abnormalities associated with persistent or recurrent tumor, or changes induced in the normal tissues by surgery have been divided by white matter modifications induced by the treatment.

Results:

Ten patients presented TL damage and the diagnosis was made on an MRI scan after the onset of clinical symptoms in 9 cases; in the remaining subject the damage was found on the MRI performed during a regular follow-up examination. Two patients showed bilateral TL damage while in 8 only one temporal lobe showed post irradiation modifications. Three patients underwent surgery to resect the injured area in the temporal lobe and in all of them radionecrosis was pathologically documented. The injured area of white matter in the temporal lobes was always characterized, on the MRI scans, by a generalized increase in the signal intensity on T2 weighted images and was located in the anterior portion of the TL.

The following clinical and pathologic factors have been evaluated to detect an association between TL damage and prognostic factors: age, gender, tumor site (Occipital bone OB, Temporal bone TB, Sphenoid bone SB), histology (Chondroid Chordoma CC, Non Chondroid Chordoma NCC, Intermediate Grade Chondrosarcoma IGCS, Low Grade Chondrosarcoma LGCS), type of presentation, type and number of surgical procedures, primary volume tumor, dose and normal tissue involvement by the tumor prior to radiation therapy. Table 1 reports the incidence of TL damage with respect to the examined clinical and pathologic parameters.

Conclusions:

The rate of TL damage for each of the analyzed baseline variables as well as the significance of each for predicting damage using a univariate (logrank) test have been calculated. Only gender was a significant predictor of damage ($p=0.015$). In a stepwise Cox regression, which included sex as a variable, no other baseline variable significantly improved the prediction of damage.

Table 1 - 10 PATIENTS WITH TL DAMAGE: Clinical and tumor related parameters

				p values
Age	≤ 50	3/64	5%	0.191
	> 50	7/32	22%	
Gender	Males	9/51	18%	0.015
	Females	1/45	2%	
Tumor site	OB	4/41	10%	0.857
	SB	4/26	15%	
	TB	2/28	7%	
Histology	CC	1/17	6%	0.619
	NCC	5/32	16%	
	IGCS	2/28	7%	
	LGCS	2/19	10%	
Type of presentation	Primary t.	7/75	9%	0.513
	Recurrent t.	3/21	14%	
Tumor volume	≥60 cc	4/13	31%	0.176
	<60 cc	6/83	7%	
Intracranial arteries involvement	Absent	4/43	9%	0.689
	1 artery	4/35	11%	
	>1 artery	2/18	11%	
Number of surg. procedures	1	5/64	8%	0.189
	>1	5/32	16%	
Type of surgery	at least 1 craniotomy	6/58	10%	0.980
	non craniotomy	4/38	10%	
Prescribed dose	66.6	3/44	7%	0.304
	> 66.6	7/52	135	

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Paired Gas Flow Ionization Measurements in Proton Beams

M. F. Moyers, S. M. Vatnitsky, and J. V. Siebers, Loma Linda University Medical Center, Loma Linda, CA 92354

Ionization chambers designed for use in radiotherapy are usually filled with air and made of an air or muscle equivalent material. Other filling gasses and wall materials are useful for investigational purposes such as studies of the energy dependence of w-values and chamber effects. Several plastic and magnesium walled chambers were used with air, synthetic air, nitrogen and argon flowing gasses for paired gas flow experiments. Rationale, techniques, and uncertainties associated with these types of measurements were discussed. Using argon as a reference gas, the w value of air was measured and ranged from 32.7 eV/ion

pair for 207 MeV protons to 33.5 eV/ion pair for 22 MeV protons. Using nitrogen as a reference gas, the w value of air ranged from 35.3 eV to 35.5 eV/ion pair over the same range of proton energies, independent of the ion chamber used. The uncertainty in these measurements was estimated at 5.2% at the 2s level. This uncertainty was dominated by the 4.4% uncertainty in the w value of the reference gasses.

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Deduction of the Air W-Value in Proton Beams

J.V. Siebers, S.M. Vatnitsky, D.W. Miller, and M.F. Moyers, Loma Linda University Medical Center, Loma Linda, CA 02354

Calorimetry was used in conjunction with an ionization chamber calibrated in a Co-60 beam to determine the dry air w-value at two proton energies. Absolute dose was measured using the water calorimeter, then ionization measurements were made in the same location. Application of Bragg-Gray relationship for cavity ionization allowed determination of the w-value. In the first beam, the acceleration energy was 250 MeV, and the effective energy at the measurement point was 180 MeV. Three Co-60 reference calibrations were used with a PTW Farmer type ionization chamber. Using an air-kerma calibration from the University of Wisconsin ADCL, a w-value of 34.4 ± 0.6 eV was measured. Using an absorbed-dose-to-water reference calibration from PTW, the w-value was 34.6 ± 0.9 eV. When the calorimeter was used to calibrate the ion chamber in the Co-60 beam, the w-value determined was 34.2 ± 0.5 eV. The uncertainty in these w-values is dominated by the 1.2 percent (one standard deviation) uncertainty in the proton water-to-air stopping power ratio.

The second beam was a range-modulated 155 MeV treatment beam. The measurement point was in the center of the modulation, where the effective beam energy was 65 MeV. Using a Co-60 reference air-kerma calibration, the w-value was measured to be 34.5 ± 0.9 eV. The additional uncertainty in this w-value is due primarily dose uncertainties due to small ripple on the beam modulation.

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Absorbed Dose to Water Calibration for Proton Beams

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Comparison of the absorbed dose-to-water, determined from ionometry measurements based on the three different reference calibrations, was performed in a 155 MeV range-modulated proton beam. A PTW chamber with three independently determined calibration factors ($N_{w,g}$, $N_{w,p}$, N_x) was employed. The factors $N_{w,g}$ and N_x are traceable to NIST, the $N_{w,g}$ calibration factor was obtained from the PTW-Freiburg. In method 1 we used the beam quality correction factor based upon the ^{60}Co reference beam (k_{Qc}) in conjunction with the absorbed dose to water ^{60}Co calibration factor $N_{w,g}$. In method 2 we used the proton absorbed dose to water calibration factor $N_{w,p}$ in conjunction with the beam quality correction factor k_{Qp}. The 250 MeV proton beam was selected as the reference to determine the calibration factor $N_{w,p}$ and the Schulz water calorimeter as the absolute dose standard was employed. In method 3 we used the AAPM Report 16 approach and calculated N_{gas} the ^{60}Co gas cavity calibration factor with the AAPM TG-21 protocol. Absorbed doses to water obtained with the three methods agreed within 2% when ionization chamber dosimetry data were analyzed using the proton w-value for air from the AAPM

Report 16 and the ICRU 49 proton stopping powers. The combined systematic uncertainty of the k_{Qp} method (method 2) is 2% at one standard deviation, whereas uncertainty of methods 1 and 3 is 4.7%. Use of the proton calibrated reference ionization chamber, in conjunction with the beam quality correction factor k_{Qp}, reduced the systematic uncertainty of the absorbed dose determination by a factor of two.

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A Comparison between Water Calorimetry and Ionometry in the Clinical 85 MeV Proton Beam at Louvain-la-Neuve.

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The importance of clinical proton beam therapy increased significantly during the last decade and in this respect, the request for accurate dosimetry of proton beams. Recently water was recommended as reference material for absorbed dose specification (1). Therefore water calorimetry became extremely important in order to obtain correct information for dosimetry in proton beams. In a collaboration between the Standard Dosimetry Laboratory of Gent in Belgium and the Proton and Neutron Therapy Centre of the Clinique Universitaires St- Luc, UCL at Louvain-la-Neuve in Belgium, a comparison study between water calorimetry and ionisation chamber dosimetry was undertaken. Calorimetry was performed using the temperature stabilised, sealed water calorimeter of Gent (2,3). The absorbed dose determination was preceded with a relative response study of the water calorimeter in a 85 MeV proton beam using different chemical water systems. This investigation, combined with theoretical model calculations, showed that the heat defect could be understood and treated the same way as for high energy photon beam dosimetry. Therefore the pure water and the hydrogen saturated water systems, both showing a zero heat defect, could be used to determine dose to water. Ionisation chamber dosimetry was performed applying the protocol of the European Clinical Heavy Particle Dosimetry Group (ECHED) (1). The ratio of the calorimetrically to the ionometrically determined dose resulting from this comparison was found to be 0.974 ± 0.009, which is in close agreement with the ratio of 0.978, found by the water calorimetry measurements at Loma Linda (4). Measurements performed with five different types of ionisation chambers yielded doses deviating no more than 1.1% from each other. Variation of the dose response as a function of the ion chamber wall thickness was observed, indicating that a small part of the above-mentioned discrepancy could possibly be attributed to chamber dependent effects. If confirmed, these effects could be included in the ionisation chamber dosimetry formalism.

(1) S. Vynckier, D. E. Bonnett, D.T.L. Jones : A Supplement to the code of practice for clinical proton dosimetry., Radiotherapy and Oncology, 32, 174-179 , 1994. (2) J. Seuntjens Comparative study of ion chamber dosimetry and water calorimetry in medium energy X-ray beams. Ph. D. Thesis University of Gent (1991). (3) J. Seuntjens, H. Palmans, F. Verhaegen, J-M. Denis, S. Vynckier and H. Thierens : Water calorimetry for clinical proton beams. Proceeding of the NPL calorimetry workshop, NPL, Teddington, UK, 12-14 October 1994. (4) S. M. Vatnitsky and J. V. Siebers : Comparison of water calorimeter with reference ionization chamber dosimetry in high photon and proton beams. Proceeding of the NPL calorimetry workshop, NPL, Teddington, UK, 12-14 October 1994.

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Proton Dosimetry at TRIUMF: Experimental Profiles and PTRAN MC Calculations

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Depth dose profiles of 70 MeV protons in water were measured with four different detectors and compared to Monte Carlo (MC) calculations based on the PTRAN code [1]. The sensitivity and expected spatial resolution in depth of the detectors used, i.e., the optical silicon diode BPW34, the silicon diode 1N4007, the Markus parallel plate chamber and a PTW diamond detector are listed in Table 1. The spatial resolution is determined by the water-equivalent linear detector extension, s, probing the Bragg peak. The low spatial resolution of the diode 1N4007 (s = 2 mm) results because in our setup the pn-junction could not be directed perpendicular to the incoming beam.

Table 1 : Detectors

Detector	Bias (Volt)	Sensitive Vol. (mm^3)	Linear Ext.: s (mm H_2O)	Sensitivity nC/Gy
BPW34	-	1.5	0.4	140-250
Markus PPC	+300	50.0	0.002	1-2
1N4007	-	0.5	2.0	20-30
Diamond	+100	2.1	0.6	200-225

For the comparison of the detectors the following three characteristics of the raw Bragg peak were recorded for each measurement: i) the distal penumbra P_D (distance between 90 % and 10 % isodose), ii) the width $w_{1/2}$ of the Bragg peak (distance between distal and proximal 50 % isodose) and iii) the ratio of peak to entrance dose *P/E* (where the entrance dose refers to a water-equivalent depth of 12 mm). The results obtained for these quantities, shown in Table 2 are based on 27 scans, the indicated errors refer to one standard deviation.

Table 2 : Raw Bragg Peak Characteristics

Detector	$w_{1/2}$	P_D (mm)	P/E (z=12mm)
BPW34	4.00 ± 0.06	1.14 ± 0.07	4.04 ± 0.17
Markus	4.12 ± 0.21	1.02 ± 0.01	3.90 ± 0.06
1N4007	7.13 ± 0.44	1.66 ± 0.03	3.41 ± 0.11
Diamond	4.97 ± 0.37	1.26 ± 0.15	3.60 ± 0.14

The Markus chamber and the optical diode were found to agree fairly well for the distal penumbra and the width of the Bragg peak. For the peak to entrance ratios, the optical diode showed a slight enhancement of 3-4 % with respect to the parallel plate chamber, a phenomenon already observed in ref. [2]. The quite different results with the 1N4007 diode can be explained by the poor spatial resolution of the detection system.

The diamond detector results were found to deviate from the results for the parallel plate chamber and the optical diode. The Bragg peak obtained with the diamond detector is characterized by a broadened width and a reduced ratio of peak to entrance dose. These deviations can, at least partially, attributed to an observed dose rate dependence of the diamond detector response, also seen with photons in ref. [3].

In order to determine the primary energy spectrum of the TRIUMF 70 MeV proton beam and to quantify the effects of nozzle and collimator scattering our experimental depth dose curves were

compared to MC calculations with the PTRAN code. For each simulated profile a series of 13 monoenergetic Bragg peaks with energies ranging from 67 to 73 MeV was folded with a Gaussian energy spectrum, whose width varied between 0 and 1.5 MeV. By comparing the results of these calculations with the experimental data, the width of the primary energy spectrum was determined to be approximately 0.35 MeV. The contribution of nozzle and collimator scattering to the entrance dose was estimated to be as high as 16 %.

[1] M. J. Berger, NIST-Report NISTIR 5113 (1993) [2] A. M. Koehler, Radiation Research Suppl. 7, 53 - 63 (1967) [3] P. W. Hoban et al., Phys. Med. Biol. 39, 1219 (1994)

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Tests of a Multilayer Faraday Cup

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Encouraged by the performance of the "poor man's Faraday Cup" an insulated block of brass surrounded by a shield, no vacuum) we have constructed a Multi Layer Faraday Cup (MLFC) for use as a proton range spectrometer at 160 MeV. 66 copper sheets each 102 x 102 x 0.534 mm are held together in an aluminum frame with two 0.000254 mm Kapton insulating foils between each sheet. The middle 64 sheets are brought to a 64 channel current integrator via miniature teflon-insulated coaxial cables. The outermost sheets are passive shields. The array of integrators (previously calibrated to 0.1%) is read via RS-232 by a scanning ADC under control of a laptop PC.

When exposed to a small well centered beam the MLFC exhibits a sharp, reproducible peak containing 80% of the total charge, corresponding to protons stopping by multiple Coulomb interactions. A single measurement (about 4 nCoul in the peak channel) takes about 5 seconds and the precision and stability are such that changes in range of about 0.1 mm H_2O equivalent can be detected. The measured range in copper (corrected for Kapton) is 26.12 g/cm^2 corresponding to 158.8 MeV, in excellent agreement with previous measurements in aluminum using the "real" Faraday cup (NFC). The total charge per monitor detected by the MLFC is 3.6% less than that detected by the NFC. Since the MLFC is 2% Kapton by stopping power it appears that only about 1.4% of the charge is redistributed by secondary electrons from Kapton to copper and vice versa. Furthermore the 20 ± 1% of the detected charge in the "nuclear buildup" region of the spectrum is in good agreement with the 20.7% probability of an inelastic nuclear interaction listed by Janni (1966).

The MLFC has also been tested as a fluence (proton/cm^2) meter in a uniform "flood" beam using a 7.6 x 7.6 cm brass area-defining aperture. An ordinary FC with a defining aperture would suffer a large error because protons interacting with the collimator, but not stopping in it, render its effective area uncertain. Because such protons are degraded the MLFC can discriminate against them. We have compared the fluence measured by the MLFC with the fluence measured in the same beam by a small ion chamber calibrated with the NFC. The comparison is complicated and to date the two methods only agree to a few percent. Once the discrepancy is understood one will be able to use the MLFC in any clinical beam to calibrate a dosimeter, rather than having to use a real Faraday cup in a specially designed beam.

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Clinical Implications of Alternative TCP Models for Nonuniform Dose Distributions

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Several tumor control probability (TCP) models for nonuniform dose distributions were compared, including:

(a) a logistic/inter-patient-heterogeneity model,
(b)a probit/inter-patient-heterogeneity model,
(c) a Poisson/radioresistant-strain/identical-patients model,
(d) a Poisson/inter-patient-heterogeneity model
(e) a Poisson/intra-tumor- and inter-patient-heterogeneity model.

The models were analyzed in terms of the probability of controlling a single tumor voxel (the voxel control probability, or VCP), as a function of voxel volume and dose. Alternatively, the VCP surface can be thought of as the effect of a small cold spot. The models based on the Poisson equation which include inter-patient heterogeneity ((d) and (e)) have VCP surfaces (VCP as a function of dose and volume) which have a threshold 'waterfall' shape: below the waterfall (in dose), VCP is nearly zero. The threshold dose decreases with decreasing voxel volume. However, models (a), (b), and (c) all show a high probability of controlling a voxel (VCP > 50%) with very low dose (e.g., 1 Gy) if the voxel is small (smaller than about 10^{-3} of the tumor volume). Model (c) does not have the waterfall shape at low volumes due to the assumption of patient uniformity and a neglect of the effect of the clonogens which are more radiosensitive (and more numerous). Models (a) and (b) deviate from the waterfall shape at low volumes due to numerical differences between the functions used and the Poisson function. Hence, the Poisson models which include inter-patient heterogeneities ((d) and (e)) are more sensitive to the effects of small cold spots than the other models considered.

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The Calibration of CT-Units to Proton Stopping Power for Proton Therapy Treatment Planning

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Computer tomographic scans are used to correct for tissue inhomogeneities in proton radiotherapy treatment planning. In order to guarantee a precise treatment, it is important to obtain the relationship between CT Hounsfield units and proton stopping powers, which is the basic input for radiotherapy planning systems considering tissue heterogeneities. A method is described to determine improved calibrations for real biological tissue (a stoichiometric calibration) based on measurements using tissue equivalent materials. The precision of this stoichiometric calibration and the usually used tissue substitute calibration (listed in the table) is determined by a comparison of calculated proton radiographic images based on these calibrations and measured radiographs of a biological sample. It has been found that the stoichiometric calibration is more precise than the tissue substitute calibration.

Calibration	Maximum deviation [%]	RMS deviation [%]	Number of pixel corresponding to deviations > 2 % [%]	Number of pixel corresponding to deviations > 3 % [%]
Tissue substitute Mylar/Melinex/P.T.F.E.	19.2	4.2	43.8	37.2
Tissue substitute B110/SB5	10.3	2.1	32.4	16.0
Stoichiometric	8.8	1.3	11.6	3.9

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Pencil-Beam Dose Calculations for Skull-Base Tumors: Dose Inhomogeneity within the Target Volume.

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The purpose of this paper is to evaluate a pencil-beam dose calculation algorithm for protons and heavier charged particles in complex patient geometries defined by CT data and to compare isodose distributions calculated with the new technique to those calculated with conventional algorithms in selected patients with skull-base tumors.

Pencil-beam calculations agreed well with Monte Carlo calculations in the patient geometries. The pencil-beam algorithm correctly predicted several multiple-scattering effects which are not modeled by conventional ray-tracing calculations. These include
(1) the widening of the penumbra as a function of beam penetration, (2) the degradation in the sharpness of the dose gradient at the end of the particle range in highly heterogeneous regions, and (3) the appearance of hot and cold dose regions in the shadow of complex heterogeneities. As a result of these effects, the treatment plan comparisons for skull-base tumors showed that for plans which delivered a significant fraction of the total dose through anterior or anterior-oblique fields, the dose distribution within the target exhibited inhomogeneities (of the order of a few percent) not predicted by ray-tracing calculations. This information may indicate that for some patients it may be advantageous to prescribe proton doses to a slightly lower isodose level (e.g., the 95% isodose surface) than is commonly done.

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PEREGRINE: An All-Particle Monte Carlo Code for Radiation Therapy

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PEREGRINE is a new Monte Carlo transport code developed at Lawrence Livermore National Laboratory for the specific purpose of modeling the effects of radiation therapy. It transports neutrons, photons, electrons, positrons, and heavy charged-particles, including protons, deuterons, tritons, helium-3, and alpha particles. This talk describes the PEREGRINE transport code and some preliminary results for clinically relevant materials and radiation sources.

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Proton Dose Distribution Measurement by Imaging Plate

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Radiographic emulsion usually suffers from poor LET dependence for measurement of dose for charged particles. Imaging plate on the other hand has much better LET dependence than emulsion. The dose dependence of the Imaging Plate (commercially obtained from FUJI Film Co. Ltd., which utilizes optically stimulated photo emission of insulator) was nearly linear and dose distribution of unmodified proton Bragg curve was comparable with the original Bragg curve measured in water phantom.

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Proton Beamline Design Programs for the IBM PC under DOS/Windows

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We have recently converted some generally useful Fortran programs from the VAX/VMS platform to PC/DOS and are planning to make them freely available, including source code. They are LOOKUP, a general purpose interactive proton "desk calculator", NEU, a program to design double scattering systems with upstream modulator and GMC, a general purpose proton beamline Monte Carlo. They rely on Fortran modules for range/energy calculations and multiple scattering which may be useful in themselves. A high-end 486 or Pentium processor with 8 Meg of RAM is required. The technical graphics program Axum is required for hard copy and Microsoft Fortran PowerStation is required to work with the source files. The new versions use graphics instructions and allocatable arrays and are therefore not compatible with VAX Fortran.

LOOKUP solves problems ranging from simple lookup of range/energy tables for various materials to multiple scattering to the design of "sandwich" scatterers (energy loss and multiple scattering both specified) to the calculation of lateral penumbra expected in various proton radiotherapy setups. NEU will design a double scattering system for a flat dose field given incident energy, throw (first scatterer to isocenter distance), desired field size, depth and modulation. It uses scaling relations to reduce the

calculation to a minute or so in most cases, and produces detailed recipes for the upstream modulator and contoured second scatterer.

GMC tracks protons through scatterers and apertures. At present it is mainly set up for slit scattering and uses only proton slowing down and multiple scattering (no nuclear interactions).

We are planning to distribute compressed (ZIP) files for these programs via an anonymous FTP account at HUHEPL.HARVARD.EDU . Each such "distribution" will be preceded by an E-mail broadcast to all persons on the distribution list. If you missed the signups at PTCOG you are invited to send me an E-mail message at GOTTSHLK@HUHEPL.HARVARD.EDU. Please indicate whether you have a recent version of PKUNZIP and whether you have access to FTP.

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Energy Spectra in the NAC Proton Therapy Beam: Preliminary Results

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Proton elastic scattering has been used to measure proton spectra in the 200 MeV clinical beam at the National Accelerator Centre (NAC). For the measurements made to date a hydrogenous scatterer (3mm thick, 30 mm diameter polyethylene) is located at the treatment isocentre. Two shielded scintillator detector DE,E telescopes (plastic, NaI) are placed symmetrically about the beam axis subtending an angle of 87.20 at the isocentre. The scattered and recoil proton energies at this angle are 100 MeV (relativistic kinematics). Multiparameter data acquisition is used to determine the coincidence summed spectrum. Background coincidences, which are measured by replacing the polyethylene with a graphite scatterer, are negligible. By imposing appropriate software kinematic and time windows, random coincidences and events due to nuclear reactions in the scatterers and in the detectors are eliminated. The spectra were obtained using a 20 mm diameter collimator and have a monoenergetic peak and a very small (~5%) low-energy component, but broadening of the peak due to insertion of the beam modification components is observed. Further measurements are planned under a variety of different irradiation conditions and at various positions on and off the beam axis.

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Conformal Proton Tomotherapy Using Distal-Edge Tracking

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It is proposed to deliver proton therapy in a "tomotherapy" geometry; that is, by moving an intensity-modulated slit proton beam around the patient in a helical pattern. In addition, it is proposed that, when many proton fields are used from many directions, the usual method of range-modulating across the tumor using spread-out-Bragg-peaks is unnecessary and suboptimal. Instead, 'distal-edge-tracking' should be used, whereby the proton pencil-beam Bragg peak always matches (nearly) the distal edge of the target volume. The depressed dose to the center of a target volume from a single slit beam would be filled-in by intensity modulated cross-firing beams. For targets with nearly circular target cross-sections, uniform doses can be achieved by simply using a uniform incident slit beam which has an optimal length which is less than the diameter of the target disk. For more complex shapes, intensity modulation can be

used to reduce dose variations in the target. A difficult nasopharynx case was simulated and compared with photon tomotherapy. Very steep falloff on all sides of the tumor is achieved using protons (90-50% dose falloff typically approx 0.5 cm). The photon tomotherapy plan is able to achieve as steep a dose falloff only over a fraction of the tumor surface. Distal-edge-tracking, compared to range-modulating across the tumor volume, places more of the Bragg-peak buildup within the tumor and therefore decreases integral dose to normal tissues. Possible designs for delivering proton tomotherapy include non-rotating gantry/rotating-patient designs. Proton tomotherapy would allow for the delivery of extremely complex dose distributions without use of difficult-to-verify noncoplanar fields or uncertain field abutments.

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Shielding Calculations for Proton Medical Accelerators

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Medium energy proton medical accelerators produce intense secondary neutron radiation from beam interaction with accelerator components (especially magnets), beam delivery devices (collimators) and the patient. The neutron dose equivalent which the personnel and the general public is exposed to must be reduced under the limits imposed by ICRP 60 through appropriate shielding design. For this reason the transmission curves for neutrons through ordinary concrete were computed by two Monte Carlo codes, FLUKA and LCS.

Neutrons were produced by 100 MeV, 250 MeV and 400 MeV protons striking thick copper, iron and tissue targets. Calculations were made for slab thicknesses from 0 to 400 cm with FLUKA and from 0 to 180 cm with LCS, for both forward (0-50 deg) and lateral (50-90 deg) shielding, in 10 deg angular bins. The necessary shielding thickness can be computed by source term and attenuation length obtained by fitting the results of the Monte Carlo simulations with an exponential function. The present results are in concordance with literature data (calculated and experimental). These results were used for the shielding calculations (walls, ceilings and floors) for the National Centre for Oncological Hadrontherapy to be built in Italy with proper hypotheses on the proton current, beam loss factors, duty factors, occupancy factors and use factors of the shield. A dose equivalent limit of 1 mSv per year in the areas where public have access and of 2 mSv per year for the personnel were also assumed. The results are compatible with Monte Carlo simulations of the complete geometry of the facility. An assessment has also been made of the shielding for the NPTC to be built in Boston under four different hypotheses: 250 MeV protons striking a thick copper target, 50% of 250 MeV protons striking a thick copper target and 50% a tissue target, 250 MeV and 100 MeV protons striking a thick copper target, 50% of 250 MeV and 100 MeV protons striking a thick copper target and 50% a tissue target. The assumptions made for the two facilities and the results of the calculations are compared.

The access mazes to the isocentric gantry room and to the horizontal beam treatment room were designed by LCS by optimizing the length and section of their legs and their wall thicknesses with the dose equivalent limit of 2 mSv per year, fixed in the areas accessed by personnel. The annual neutron dose equivalent at the maze access resulted at 6.0E-1 mSv and 3.74 mSv for the gantry and the fixed horizontal beam rooms, respectively, and is below 1 mSv beyond the maze walls.

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Radiation Shielding Measurements for 200 MeV Protons.

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Neutron dose equivalent radiation levels resulting from stopping 200 MeV protons were measured outside concrete shielding walls that varied in thickness from 0 to 3 meters. Measurements were made at a distance of 4.5 m, between 0 and 90 degrees, with moderated neutron REM counters, modified moderated REM counters (after Birattari et al), and low pressure TE proportional counters. Proton stopping materials of Copper and water were used. Derived source strength and attenuation length parameters are presented and compared to literature reports and parameters used in recent facility designs.

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Status Report on the Texas Regional Medical Technology Center

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The TNRLC is collaborating with the University of Texas Southwestern Medical Center at Dallas on a new design project. The SSC linear accelerator and its related assets will be incorporated into a world-class medical center dedicated to providing proton-beam radiation therapy for cancer patients. The Department of Energy has provided funds for this project to the State of Texas, subject to the completion of an environmental assessment. The linac will be used to inject beam into a proton synchrotron, which will provide protons at energies up to 350 MeV. A unique feature of the facility will be the capability to enhance the precision of the radiation therapy through the use of proton radiography. The design goals, performance specifications, and conceptual design will be discussed.
(See Particles 16 for a more recent report).

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Pilot Study of Carbon IONS at HIMAC (CHIBA)

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A pilot study of heavy charged particles with HIMAC (Heavy Ion Medical Accelerator in Chiba) for advanced H&N cancer has been carried out from June 1994 at NIRS (National Institute of Radiological Sciences). As of the beginning of August 1994, three patients were treated by 290 MeV carbon ions which have maximum range of 16.0 cm. The patients had adenocarcinoma of the cheek mucosa, squamous cell carcinoma of the ethmoid sinus and adenoid cystic carcinoma of the sublingual gland. Patients were immobilized by individual head couch and thermosplint facial shell. Individual collimators and bolus were also prepared for each port. Dose fractionation for the initial pilot study group was 48.6 GyE/18 fractions/6 weeks, which would be equivalent to standard fractionation of 60.0 Gy/30 fractions/6 weeks with photons. This dose fractionation was considered to be 20% lower than 75 GyE/37.5 fractions/7.5 weeks, which is estimated to be maximum tolerance dose for advanced H&N cancers. HIMAC worked well and there was no major trouble, causing any treatment delay.

Acute skin reactions of 3 patients were 2 cases of bright erythema with patchy moist desquamation and one of dull erythema, which were evaluated as equivalent reaction with irradiated dose. Acute mucosa reactions appeared to have less reaction than predicted mucositis. Tumor reactions of three patients were partial reaction (PR) at the end of treatment and complete remission (CR) after 6 months of treatment.

From October 1994, we started to treat patients with advanced H&N cancer with 10% high than previous dose and new candidates of pilot study with non small cell lung cancer, brain tumor and carcinoma of the tongue were entered into pilot study. At the end of February 1995, a total of 21 patients were treated by carbon ions.

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Acoustic Pulse Generated in a Patient During Pulsed Proton Beam Irradiation.

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Acoustic pulse was sensed by a hydrophone attached to a hepatic cancer patient irradiated by pulsed proton beam of approximately 0.3 cGy/pulse. The pulsed proton beam stops within 2 ns where pulse duration is 50 ns. These periods are much shorter than 0.1 microsecond in which the sound travels 0.16 mm inside the patient body with the velocity of 1600 m/s. The acoustic pulse generation is due to expansion of the tissue by instantaneous heat deposit of pulsed proton beam from synchrotron (less than 1 part par million degrees Celsius when dose rate is 0.3 cGy). We have carried out phantom experiment using degassed water with the results of coincidence with the theoretical expectation (J. Tada Y. Hayakawa et al, Med. Phys vol. 18(6), 1100-1104,1991).

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