PROTON THERAPY CO OPERATIVE GROUP	Chair Michael Goitein Ph. D Department of Radiation Oncology Massachusetts General Hospital Boston MA 02114 (617) 724 - 9529 (617) 724 - 9532 Fax Goitein@hadron.mgh.harvard.edu	Secretary Janet Sisterson Ph. D. Northeast Proton Therapy Center Massachusetts General Hospital 30 Fruit Street Boston MA 02114 (617) 724 – 1942 (617 724 - 9532 Fax Sisterson@radonc.mgh.harvard.edu

ABSTRACTS

of the

XXXI PTCOG MEETING

Bloomington, Indiana
USA

October 11 - 13 1999

INDEX

Page

Stereotactic Radiosurgery
Modeling Absorbed Dose in Proton Beams. 3
W. D. Newhauser, S. Rosenthal, A. Smith, X. Yan, and H. Paganetti

Small Beam Dosimetry
Physical parameters of small proton beams. 3
B. Gottschalk

Collimator scatter studies in small irradiation fields with a CCD/scintillator system. 4
P. van Luijk, A.A. van 't Veld, H.D. Zelle and J.M. Schippers

Eye Treatments
Proton Therapy For Choroidal Neovascular Membranes In Age-Related Macular Degeneration 4
T. Ciulla, and R. Danis

Proton Radiation therapy (PRT) for pediatric optic pathway gliomas: Comparison with 3D planned conventional photons and a standard photon technique. 4
M. Fuss, E. B. Hug, R. A. Schaefer, M. Nevinny-Stickel, D. W. Miller, J. M. Slater, and J. D. Slater

Radiobiology
Proton irradiated rat retinal digest model: Preclinical bioassay quantifying retinal microvessel radiation changes. 5
J. O. Archambeau, X. W. Mao, P. J. McMillan, V. L. Gouloumet, R. Grove, L. T. Yonemoto, J. D. Slater, and J. M. Slater

Normal tissue complication probability (NTCP) calculations as a means to compare proton and photon plans. 6
M. Fuss, K. Poljanc, E. B. Hug, D. Miller, J. O. Archambeau, J. M. Slater, and J. D. Slater

Gantries and Beam Delivery Systems
The PSI compact gantry judged from the practical experience of using the system. 7
E. Pedroni, H. Blattmann, T. Bohringer, A. Coray, M. Dellert, E. Egger, E. Emmenegger, G. Goitein, M. Grossmann, S. Lin, A. Lomax, B. Rohrer, W Roser, B. Rossi, B. Siegenthaler, O. Stadelmann, HU. Stauble, C. Vetter, and L. Wisser

The 2π + project: an improved compact proton gantry design dedicated to scanning. 7
E. Pedroni

Gantry Design Considerations. 8
J. Flanz, M. Schippers, and S. Bradley

Gantry Studies for the German Heavy Ion Medical Accelerator Project. 8
P.Spiller, A.Dolinski, H.Eickhoff, B.Franczak, B.Langenbeck, T.Haberer, A.Kalimov, E.Malwitz

Practical Design of a 'Riesenrad' Ion Gantry. 8
S. Reimoser

Gantry design and beam delivery system of the new proton therapy facility in PMRC, Tsukuba. 9
Y. Takada, A. Maruhashi, T. Sakae, K. Yasuoka, A. Nohtomi, Y. Akine, T. Okumura, and K. Hasezawa

Page

First position dependent beam gating of the PSI-Gantry during a phantom irradiation: A step towards conformal proton therapy with real time tumor tracking. 9
P. G. Seiler, H. Blattmann, T. Boehringer, and R. K. Muench

Proton Loss Model: a Fast Computational Tool for Radiotherapy Treatment Planning. 10
A. V. Chvetsov and G. A. Sandison

A System for Precision Automated Daily Target Volume Positioning. 10
D. Litzenberg

Posters

Overview of the Proton-Ion Medical Machine Study (PIMMS). 11
S. Reimoser

Response of an imaging plate to clinical proton beams. 11
A. Nohtomi, T. Terunuma, R. Kohno, Y. Takada, Y. Hayakawa, A. Maruhashi, T. Sakae and K. Yasuoka

Proton Dose Distribution Measurement with Screen and CCD-camera. 11
A. Maruhashi, A. Nohtomi and M. Satoh T. Terunuma

2D and 3D dose distribution determination in proton beam radiotherapy with GafChromic™ film detectors. 12
S.O. Troja, E. Egger, A.M. Gueli, A. Kacperek, M. Coco, and R.Musmeci

Chromosomal aberrations detected by Interphase Chromosome Painting in lymphocytes from cancer patients given X-ray or carbon-ion therapy. 12
S. Yamada, M. Durante, R. Lee, K. Ando, H. Tsujii

General Clinical Presentations

Esthesioneuroblastoma : Results of a prospective study of neoadjuvant chemotherapy and proton irradiation. 12
M. M. Fitzek, A. F. Thornton, M. Varvares, J. McIntyre, J. Adams, S. Rosenthal, B. Z. Pilch, M. Joseph, P. Amrein

Follow-up of the 1997 and 1998 patients @ PSI, Villigen, Switzerland. 13
L. Wisser, G. Goitein and Team Radiation medicine

1999 patients from PSI. 13
L. Wisser, G. Goitein and Team Radiation medicine

Proton-beam radiotherapy for early stage lung cancer. 13
D. A. Bush, J. D. Slater, R. Bonnet, G. A. Cheek, R. D. Dunbar, M. Moyers, and J. M. Slater

Proton Beam Therapy for Hepatocellular CarcinomaPreliminary Experience at LLUMC. 14
D. A. Bush, D. J. Hillebrand; J. D. Slater; B. A. Runyon; and J. M .Slater

Modeling Absorbed Dose in Proton Beams.

W. D. Newhauser[1], S. Rosenthal[1], A. Smith[1], X. Yan[2], and H. Paganetti1, [1]Northeast Proton Therapy Center, Massachusetts General Hospital, Boston MA, [2]Harvard Cyclotron Laboratory, Cambridge, MA.

Practical proton therapy dose calculations can be improved using a physics-based semi-empirical dose model. Many proton treatment planning programs predict the relative dose distributions in a patient by taking the product of the central-axis percent-depth-dose (CAX PDD) and off-axis ratio (OAR) values. While the OAR values may be computed from a variety of previously available physics models, the CAX PDD values are usually obtained from lookup tables of measured data. Although the latter approach is computationally efficient, a predictive model offers several important advantages. With a physics-based model, one can more efficiently explore the variable space of machine settings in order to find an optimum treatment plan. Examples of the variables that may be optimized are the proton fluence, energy (range), and the width of a range-modulated spread-out Bragg peak (SOBP). In addition, this obviates the need for acquiring and maintaining a large library of lookup tables within the treatment planning system. The latter point is increasingly important in light of the proliferation of beam delivery techniques (e.g., passive spreading, spot or voxel scanning, wobbling), each with distinctive CAX PDDs. Additionally, a realistic model for the measured dose distributions can reasonably be expected to provide insight into the beam delivery system's underlying behavior, e.g., the influence of various machine settings on the delivered dose distributions.

In this work, we show that a wide variety of CAX PDDs, including pristine and spread-out Bragg peaks (SOBP), are accurately described with a physics-based semi-empirical model. The model parameters were determined for each PDD with non-linear least-square-fit methods, including the proximal and distal extents of the modulated peak, the distal falloff width, the slope and ripple in the modulated peak region, etc. This procedure has been tested with a wide variety of PDDs from the Northeast Proton Therapy Facility (Boston) and the Harvard Cyclotron Laboratory (Cambridge). The model includes semi-empirical terms for electronic and protonic buildup that were verified with measurements and Monte Carlo simulations, respectively. The model's accuracy, speed, and simplicity make it well suited as a dose calculation engine for treatment planning, especially for intensity-modulated proton therapy (IMPT) calculations. There is also a role for this model in QA data analysis were the model parameters can be extracted quickly and compared directly with expected (standard) values.

****

Physical parameters of small proton beams.

B. Gottschalk, Harvard Cyclotron Laboratory, 44 Oxford St., Cambridge, MA 02138.

This talk, in the 'Small Beam Dosimetry' session, did not present any new material but tried to summarize the characteristics of small cross-section proton beams. (W.M. Preston and A.M. Koehler at HCL were the first to discuss the subject comprehensively, in 1968. Unfortunately their manuscript was never accepted for publication.) Among the points covered in the present talk: (A) For the smallest lateral penumbra,, beam-modifying material (range modulator and particularly, range shifter) should be placed upstream at or near the effective proton source. (B) In small beams the Bragg peak is suppressed because out-scattering is not fully compensated by in-scattering. In consequence, the design of a range modulator depends on the aperture size. (C) Protons degraded but not fully stopped by the patientspecific collimator can affect the dose distribution significantly, particularly in the proximal region. (D) The transverse penumbra for a given beamline can be predicted accurately by a program (not a Monte Carlo) that takes a second or so on a high-end PC. The paper concludes with a worked problem: design a single-scattered beam of a given transverse size.

Full copies of this talk and/or the 1968 Preston and Koehler manuscript are available on request. (gottshlk@huhepl.harvard.edu)

****

Collimator scatter studies in small irradiation fields with a CCD/scintillator system.

P. van Luijk, A.A. van 't Veld, H.D. Zelle and J.M. Schippers, KVI, Groningen, The Netherlands

Accurate, spatially resolved dosimetry in small radiation fields encounters several problems. Due to the typical size (-5 mm) of standard ionization chambers, profiles of small fields show a decrease in the measured D_{max} and a broadening of the measured dose distribution.

At the KVI radiobiology experiments are performed with field sizes ranging from 2-20 mm. For these fields accurate information on the collimator dependence of the dose-to monitor unit relation was needed. A CCD/scintillator system has been used for dosimetry in these small radiation fields.

We will discuss measurements of the sub-mm spatial resolution of the CCD/scintillator system. A comparison is presented between measurements with the CCD/scintillator system and measurements with a diamond detector.

The very good spatial resolution of the system is a prerequisite a study of the influence of collimator scatter on the homogeneity of irradiation fields. Measurements with the CCD/scintillator system have been done on small apertures (slits), varying from 2 mm to 40 mm. The measurements will be compared to Monte Carlo simulations.

****

Proton Therapy For Choroidal Neovascular Membranes In Age-Related Macular Degeneration

T. Ciulla, and R. Danis, Dept. of Radiation Medicine, Loma Linda University Medical Center, Loma Linda, California.

This study is a prospective, randomized, single blinded, controlled phase III trial to determine the effect of proton beam irradiation on occult subfoveal and juxtafoveal choroidal neovascular membranes (CNVM) in age-related macular degeneration (AMD). Patients with subfoveal CNVM and juxtafoveal occult CNVM not amenable to laser photocoagulation according to the Macular Photocoagulation Study parameters are eligible. Other eligibility criteria include subjective visual acuity impairment of less than six months duration and best corrected visual acuity of less than 20/40 and better than or equal to 20/400. The radiation treatment arm involves a total dose of 16 Gy in two fractions. Masked assessment of angiography and analysis of visual acuity between groups is being performed for the three month, six month and one year visits. Angiography is being evaluated by a masked observer to estimate the area of fluorescein leakage and angiograms will be graded as improved, stable, or worsened compared to baseline.

****

Proton Radiation therapy (PRT) for pediatric optic pathway gliomas: Comparison with 3D planned conventional photons and a standard photon technique.

M. Fuss[1], E. B. Hug [2,3], R. A. Schaefer[2], M. Nevinny-Stickel[2], D. W. Miller2, J.M. Slater[2], and J. D. Slater[2], [1]Dept. of Radiation Oncology, University of Heidelberg, Heidelberg, Germany, Depts. of [2]Radiation Medicine and [3]Pediatrics, Loma Linda University Medical Center, Loma Linda, California

Purpose: Following adequate therapy, excellent long-term survival rates can be achieved for optic pathway gliomas. Therefore, avoidance of treatment related functional and cosmetic sequelae are of utmost importance. The present study compares proton radiation therapy (PRT) with a 3D planned multiport photon and a lateral beam photon technique for localized and extensive optic pathway tumors.

Material and Methods: Between 2/1992 and 11/1997, seven children with optic pathway gliomas underwent PRT. For this study, we computed 3D multiport photon and lateral photon plans based on the same CT data sets and using the same treatment planning software for both, proton and photon planning. Radiation exposure for normal tissue (NT) and discrete organs at risk was quantified based on dose volume histograms for all three plans.

Results: GTV (gross tumor volume) ranged from 3.9 cm^3 to 127.2 cm^3. Conformity index (relation of encompassing isodose to GTV volume) was 2.3 for protons, 2.9 for 3D photons and 7.3 for lateral photons. NT encompassed at different isodose levels was calculated by subtracting GTV volume from the respective isodose volume. The relative increase in relation to NT encompassed by the 95% proton isodose volume was computed. Analysis for small (<20 cm^3) and larger (>80 cm) tumors showed that protons encompassed the smallest volumes of NT at all isodose levels. Comparable conformity and high dose gradient were achieved for proton and 3D photon plans in small tumors. However, with increasing tumor volume and complexity differences became larger. At the 50% isodose level, 3D photons were superior to lateral photons for small tumors, this advantage was equalized for larger tumors. At the lowest isodose level 3D photons encompassed the highest amount of

NT. Analysis of organs at risk showed that PRT reduced doses to the contralateral optic nerve by 48% and 77% compared to 3D photons and lateral photons, respectively. Reductions were also seen for the chiasm (11% and 16%) and pituitary gland (13% and 16%), with differences at clinically relevant tolerance levels. Furthermorereduced dose exposure of both temporal lobes (sparing 39% and 54%) and frontal lobes was achieved with PRT.

Conclusion: PRT offered a high degree of dose conformity to target volumes and steep dose gradients, thus leading to substantial normal tissue sparing in high and low dose areas. It is expected that this will result in decreased long-term toxicity in the maturing child. For small tumors 3D photons were comparable in terms of dose conformity and high dose reduction to normal tissues, but inclusion of higher amounts of tissue at risk in mid and low dose areas may impair long-term results. Lateral photons resulted in inferior dose distribution with high radiation exposure of clinically relevant normal tissues. Data of this study can be applied to most low-grade childhood brain tumors, as the advantageous dose distribution of proton plans may offer reduced normal tissue complication probability whenever tumor

control doses exceed normal tissue tolerance doses.

****

Proton irradiated rat retinal digest model: Preclinical bioassay quantifying retinal microvessel radiation changes.

J. O. Archambeau[1], X. W. Mao[1], P. J. McMillan[2], V. L. Gouloumet[1], R. Grove[1], L. T. Yonemoto[1], J. D. Slater[1], and J. M. Slater[1], [1]Dept. of Radiation Medicine Loma Linda UniversityMedical Center, [2]Dep. of Anatomy, Loma Linda University, Loma Linda, California

Purpose: This study measures the retinal microvessel endothelial/pericyte population changes produced over a twenty-two month period. The objective was to determine if dose schedules used clinically produced severe late changes in normal rat retinal microvessels.

Materials and Methods:

Animals. A total of 52 Sprague Dawley rats were used. The eyes from ten age matched unirradiated rats were used as controls. Single animals were sacrificed monthly beginning at 5 months for those irradiated with 28 Gy and at 10 months for those receiving 8,14 and 20 Gy used clinically and a reference dose of 28 Gy which produced necrosis in rat brain in 100% of the animals.

Irradiation. The eyes of 52 rats were irradiated with a 100 Mev, 8 mm conformal proton beam. The dose schedule was 8, 14, 20 and 28 Gy The selected dose was delivered as a single dose fraction to the left eye and in two equal dose fractions to the right eye.

Retinal Digest Preparation: After autopsy and fixation, the retinas were dissected free and the neurosensory layer; digested away from the microvessels with elastase. The flat mounted retinal network was stained with periodic-acid-Schiff reaction and hematoxylin counterstaining for image analysis.

Parameters. Microvessel length, surface area and population parameters were quantified using image analysis. The DNA distribution was determined using laser scanning cytometry of propidium iodide stained preparations. The 2'bromodeoxyuridine (BrdU) labeling index was determined using immunohistological staining of the retinal preparation.

Results. Progressive, linear endothelial cell loss occurred out to 15 months after 28Gy, and out to 22 months post 20Gy following both single and split dose schedules. The degree of endothelial cell loss was similar for both schedules. The decrease in the slopes of the cell density regression lines compared to controls was progressive achieving significance ($p < 0.01$) at 15 and 22 months. Cell loss was noted following 14 Gy but this loss was not significantly different from control. Cell loss was not observed following 8 Gy dose schedules. The irradiated pericyte cell density was the same as that for unirradiated age-matched controls out to 22 months. The pericyte:endothelial cell ratio decreased progressivelyfollowing irradiation from 1: 1.7 in controls to 1: 0.5 in the 28, 20 and 14 Gy irradiated digests. The progressive endothelial cell loss produced vessel collapse and formation of acellular vascular strands at 15 and 22 months. Foci of stranding were observed at all dose schedule. The endothelial cells were in the quiescent stage of the mitotic cycle as confirmed by the G1/G0 DNA distribution and absence of BrdU DNA labeling.

Discussion. The lack of a difference in endothelial cell density following single and split dose schedules was new and unexpected. It suggests that DNA injury is not repaired following irradiation and the dose response is cumulative. It raises the question that endothelial cells are not proliferative since recovery was noted in the skin and posterior lens capsule. The pericytes, retinal pigmented epithelial cells, middle neuronal layer and the ganglion cells and choroidal vessels appeared intact.

Conclusions.

1. The retinal digest preparation is an excellent bioassay to use to document radiation changes in microvessels.
2. The test dose schedules of 28 Gy single and split dose fractions produces significant endothelial cell loss and microvessel stranding.

3. The 20 Gy split dose schedule proposed for treating large subfoveal neovascular membrane lesions
4. produces significant endothelial cell loss and microvessel stranding.
5. The late occurrence of a time and dose dependent progressive endothelial cell loss in the retinal
6. microvessels characterizes it as a late responding tissue.
7. The lack of difference in the endothelial cell density following single and split dose schedule suggests that there is little DNA repair (rejoining) following split course irradiation.

****

Normal tissue complication probability (NTCP) calculations as a means to compare proton and photon plans.

M. Fuss[1], K. Poljanc[2,4], E. B. Hug2,3, D. Miller[2], J.O. Archambeau[2], J. M. Slater[2], and J. D. Slater[2], [1]Dept. of Radiation Oncology, University of Heidelberg, Heidelberg, Germany, [2]Depts. of Radiation Medicine and [3]Pediatrics, Loma Linda University Medical Center, Loma Linda, California, and [4]Atomic Institute of the Austrian Universities, Technical University of Vienna, Vienna, Austria

Purpose: Calculation of normal tissue complication probabilities (NTCP) for proton radiation therapy (PRT) and two photon radiation therapy techniques for cranial irradiation of childhood optic nerve gliomas. Evaluation of usefulness for comparison of treatment plans and clinical appropriateness of the calculated NTCP values.

Methods and Materials: Proton, 3D photon, and a standard photon radiation treatment plans were calculated on seven CT data sets of children treated previously for optic nerve glioma with PRT. Dosevolume histograms (DVH) were computed and were used to calculate NTCP. Empirical and estimated clinical data were implemented for complication endpoints such as necrosis, blindness, and cognitive impairment.

Results: Calculated NTCP depended strongly on tumor volume and the normal tissue volume exposed to high radiation doses. Higher degree of dose conformity and steeper dose gradient of the used treatment planning techniques correlated with reduced complication probabilities. Mid- and low-dose volumes were slightly influential. With regard to the chosen deterministic complication endpoints, PRT was superior to 3D photons; conventional photons were calculated to have the highest complication probabilities. Differences, favoring PRT over both photon techniques in calculated NTCP might reach clinical significance for cognitive impairment, a frequently observed toxicity. Calculated NTCP values were dependent on implemented clinical data with higher TD_5 and TD_{50} used resulting in decreasing complication probabilities.

Conclusion: Calculation of NTCP can be used for ranking of treatment plans and modalities. The present study calculated reduced complication probabilities for proton plans compared to two photon treatment techniques. Assumed clinical data implemented into the NTCP calculation model can result in overestimation of NTCP when compared to reported follow-up data. Therefore, the calculated percentage of complication probabilities might be more of a figure of merit than a real predictive value and requires comparison as to clinical experience. Differences in calculated NTCP are highest for complications occurring frequently after moderate doses, such as cognitive impairment.

****

The PSI compact gantry judged from the practical experience of using the system.

E. Pedroni, H. Blattmann, T. Bohringer, A. Coray, M. Dellert, E. Egger, E. Emmenegger, G. Goitein, M. Grossmann, S. Lin, A. Lomax, B. Rohrer, W. Roser, B. Rossi, B. Siegenthaler, O. Stadelmann, H. U. Stauble, C. Vetter, and L. Wisser, Paul Scherrer Institute, Switzerland

In this presentation we report on our practical experience of using the PSI gantry and we focus the attention on those points which deserve improvements, especially for a possible future commercial design for a hospital-based facility.

- Beam properties: precision and stability of the beam position, possibilities for automatic online corrections.
- Changing shape of the beam with sweeper position and gantry angle (better shaping of the spot using scattering foils). Need for a new range shifter for larger spot sizes.
- Achieved parallelism of the swept beam, need for higher-order multipole correction elements in the beam?
- Missing diagnostics elements in the beam line.
- Mechanical aspects: eccentric system, access to patient during treatment with beam from below the horizontal plane, patient rescue in this position in case of power failure.
- Limitations of the present "top-rot" system: angles and distance from the nozzle. Time needed for changing the support.
- Patient positioning with dedicated transporter. Use CT scout view outside of treatment room. Installation of a digital amplifier on the gantry.

****

The 2π+ project: an improved compact proton gantry design dedicated to scanning.

E. Pedroni, Paul Scherrer Institute, Switzerland

Based on the experience of having developed the first proton gantry for proton scanning in the world, PSI is now studying a new improved design for a compact gantry dedicated to proton beam scanning.

- We will present the new combined arrangement of the gantry rotation with patient table, which should allow an easy permanent access around the patient table without compromising too much the freedom to apply the beam on the patient from almost any direction (more than a 2π solid angle).
- The scanning will be performed inside the gap of the 90° bending magnet as before. The third axis of scanning will be scanned with the patient table. The improvement with respect to first gantry comes here by performing the table motion together with the protection enclosure of the nozzle. In this way we will avoid any relative motion of the patient couch with respect to the nozzle and we will have a moving support for collimators and compensators, to be used on top of scanning as an option for compatibility with the passive scattering systems.
- The system shall be in the first place compatible with the present scanning system, but we plan to include in the design many options for future developments, like fast energy variations ahead of the gantry, utilisation of beam intensity modulation, and a second faster lateral magnetic scanning inside the gap of the 90° degrees bending magnets (large fields as a superposition of partially scanned fields in combination with the movement of the patient table). More attention will be paid also to the possibilities for changing rapidly the spot size.

****

Gantry Design Considerations.

J. Flanz[1], M. Schippers[2], and S. Bradley[1], [1]Massachusetts General Hospital, Northeast Proton Therapy Center, Boston MA, [2]KVI, Groenegin, The Netherlands

In the past several years innovative Gantries have been built for particle therapy. Designs range from the Neutron Therapy Facility at Harper, the Koehler/Loma Linda Corkscrew, the PSI 'Compact' Gantry, and the 'Large Throw' Gantries at MGH. Each facility applied its own criteria and priorities in the choice of a Gantry system. It appears that achievement of all clinically desirable features may not be compatible with the construction of a compact system - one defined as smaller than a larger system. This opinion is partly subjective depending upon the desired clinical parameters. A parameter search is done identifying, the clinical, beam optics, mechanical and building factors which combine to produce a Gantry. Advantages and disadvantages or different geometries are discussed for both Gantries already built and some that have not yet been considered. There is a tendency to patent each new design, and we try to show that there is a systematic approach to many Gantry possibilities and parameterization which makes identifying a system for the needs of a particular facility more straightforward than may have been thought. Finally existing Gantries properties are analyzed and some comments are offered regarding considerations that may be useful in the design of future Gantries.

****

Gantry Studies for the German Heavy Ion Medical Accelerator Project.

P. Spiller, A. Dolinski, H. Eickhoff, B. Franczak, B. Langenbeck, T. Haberer, A. Kalimov, E. Malwitz, and M. Pavlovic, GSI, Darmstadt, Germany

GSI, as an experienced accelerator institute, is responsible for the design of the planned heavy ion medical accelerator facility in Heidelberg, Germany. Main parts of the overall layout of the treatment complex are two heavy ion gantries. The aspects of different possible Gantry layouts have been compared and an ion optical system for a rotation angle independent focusing has been defined.

Detailed studies were made on the most critical components and the mechanical structure as well. Mechanical tolerances were fixed, taking into account the capabilities of the raster scan system developed at GSI, and the properties of the ion optical system. Structure designs and analysis were performed by means of finite element programs and mechanical stress and deformations were evaluated. The effect of temperature variations and other reasons for misalignments of optical elements on the beam position in the ISO center was investigated.

Furthermore, the field properties and the dynamic behaviour of the most critical beam guiding elements, as e.g. the last 90 degree bending magnet were investigated in detail. The set-up and test of a prototype of the final beam guiding system, including the huge 90 degree dipole, is planned for 2001 at GSI.

****

Practical Design of a 'Riesenrad' Ion Gantry.

S. Reimoser, CERN, ST Division, CH 1211 Geneva-23 and Institute for Building Construction and Industrial Building, Vienna University of Technology, Karlsplatz 13, A-1040 Vienna

The benefit of hadron therapy can be maximised by offering the possibility to deliver the particle beam from any direction in space towards the patient with the help of a gantry. For carbon ions, their increased beam rigidity (magnetic) yields considerable structural difficulties and has so far prevented a practical realisation of an ion gantry. The concept of a 'Riesenrad' ion gantry promises to provide an effective and efficient solution. The basic idea is to deflect the ion beam with a single 90° dipole, which rotates around the incoming beam axis, and direct it towards the eccentrically positioned patient cabin. Inside the cabin similar conditions as exist in a classical iso-centric treatment room prevail. The practical design of such a Riesenrad gantry, its structural principles and its function are presented. The underlying beam optics and its integration into the mechanical structure are explained. Aspects of safety, flexibility and ergonomics are discussed. Based on the calculated mechanical deflections, a beam and gantry-alignment system to guarantee the specified accuracy is presented.

****

Gantry design and beam delivery system of the new proton therapy facility in PMRC, Tsukuba.

Y. Takada[1], A. Maruhashi[2], T. Sakae[2], K. Yasuoka[3], A. Nohtomi[1], Y. Akine[2], T. Okumura[2], and K. Hasezawa[2], [1]Institute of Applied Physics, University of Tsukuba [2]Institute of Clinical Medicine, University of Tsukuba, [3]Institute of Basic Medical Sciences, University of Tsukuba

Proton Medical Research Center, University of Tsukuba, is now constructing a new facility dedicated to proton therapy and related researches inside the University campus. We will install a 250 MeV proton synchrotron and two rotating gantries for therapy together with two fixed horizontal beam ports for basic researches. The gantries are isocentric type and have a single bending plane. The structure of the gantry is a cylinder on which beam line elements, a nozzle, and patient alignment devices are mounted. A treatment cage is inserted around the isocenter, and rotated in the direction opposite to the gantry rotation to keep its same position in space at any gantry angle. Since it has a floor made of caterpillars, staff can freely access the patient placed at the isocenter.

Since our main targets are the moving organs in the abdominal and thorax region, we employ a well-establish method for beam delivery. The nozzle has a dual-ring double scattering system to obtain the uniform lateral field. The first scatterer is a binary type. Thickness of the scatterer can be changed depending on the energy of the incident protons. Up to twelve second scatterers can be mounted on the two rotating tables with a blank position on each table. Two tables are placed near to each other in the beam direction. Each table can be rotated to locate the right second scatterer for the selected energy. Each table can be moved with a stroke of 20 cm in beam direction for fine adjustment of the fluence flatness at the isocenter. A binary range compensator and a table mounting upto twelve bar ridge filters are installed on the nozzle structure. A multi-leaf collimator is used to define the shape of the irradiation field coarsely. A bolus and a patient aperture collimator are used to define the distal and lateral shape of the irradiation field, respectively, to conform the distal and lateral boundary of target volume. Two dose monitors and a beam flatness monitor are installed to monitor the dose and flatness of the beam. In the gantry beam line and the nozzle, there remains spaces for a pair of scanning magnet for future installation.

Since the thickness of the first scatterer and the second scatterer can be changed during the interval between the consecutive spills, it will be possible to form a spread-out Bragg peak by dynamically changing the beam energy and by controlling the dose for the proton range without using the bar ridge filter in the future.

We mounted two sets of X-ray imaging system on the gantry for patient alignment. One of the X-ray source is placed inside the nozzle, mounted on the movable table and can be moved to the beam line position. An X-ray Image Intensifier is mounted on the gantry and is extracted to the counter position of the X-ray source in the axial direction when used. The set can be used at any gantry angle. Another set of X-ray system is also mounted on the gantry. An X-ray source and the X-ray I.I. are placed orthogonal to the other set. They are extracted from the home position to the right position in the axial direction of the gantry. The set is only used at the location where the X-ray source is at the uppermost position. The two sets of the X-ray system are used to align the patient precisely. We can make a nearly-simultaneous exposure in orthogonal directions.

****

First position dependent beam gating of the PSI-Gantry during a phantom irradiation: A step towards conformal proton therapy with real time tumor tracking.

P. G. Seiler, H. Blattmann, T. Boehringer, and R. K. Muench, Life Science Department, Paul Scherrer Institute PSI, CH 5232 Villigen-PSI, Switzerland

Organ motion creates severe difficulties in the precision radiotherapy of tumors in the chest and the abdomen. To overcome these problems, a novel magnetic tracking method is being developed at PSI (project TULOC). It shall enable the real time tumor tracking with high resolution in time and space during radiotherapy. In a first phase this method shall be used for tumor-position dependent beam gating. The goal of a second R&D phase is the fast adaptation of the irradiation pattern to the tumor motion in a feed-back loop.

The proper functioning of the magnetic tracking has been demonstrated recently. We simulated a moving tumor by putting an X-ray film in a phantom moving on our patient table by the help of a computer controlled device, and recorded the dose deposition in the film. The gating of the proton beam with our system re-established the sharp dose distribution seen before in a motionless film. This is world-wide the first gating of a precision irradiation with a sensor which can be placed within or close to a tumor.

****

Proton Loss Model: a Fast Computational Tool for Radiotherapy Treatment Planning.

A. V. Chvetsov[1] and G. A. Sandison[1,2], [1]Dept. of Medical Physics, Tom Baker Cancer Centre, and [2]Dept. of Oncology, University of Calgary, 1331-29 Street N.W., Alberta, Canada T2N 4N2

We present an analytical proton transport model called the proton loss (PL) model which can be applied as a fast computational tool in problems relevant to radiation dosimetry and treatment planning. The PL model includes the most important physical processes affecting the form of the proton dose distributions; multiple scattering and energy loss as well as pathlength straggling and inelastic nuclear reactions.

Multiple scattering of charged particles from nuclei and energy loss to atomic electrons are processes in which there are great number interactions resulting in small deflections or energy transfers, respectively. For protons, these processes approach the diffusional limit where scattering and energy loss probability densities become Gaussian. This particularly simple distribution is computationally useful since only knowledge of the mean values, variances and any cross-correlation coefficients are required. Our PL model uses the Fermi-Eyges (FE) diffusional multiple scattering theory and Gaussian theory of energy straggling.

In order to model the effect of energy straggling on range straggling we consider an elemental pencil beam as a superposition of monoenergetic pencil beams, which have slightly different ranges of penetration. The contribution of every monoenergetic pencil beam to the elemental beam is defined by depth dependent weights calculated using the diffusional theory of energy straggling. For every monoenergetic beam, we introduce a generalization of the FE equation, labeled the PL equation. Unlike the FE equation, this equation models inelastic nuclear reactions as a depth dependent absorption and pathlength straggling as a quasi absorption.

We have tested the PL model for proton pencil beams with energies of interest for radiation therapy (50-250 MeV) incident normally upon water. The PL model predicts both radial and depth-dose distributions from a proton pencil beam in close agreement with PTRAN Monte Carlo simulations and measurements.

****

A System for Precision Automated Daily Target Volume Positioning.

D. Litzenberg, University of Michigan Medical Center, Dept. of Radiation Oncology, Ann Arbor, MI

While computer-controlled accelerators and digital radiography systems promise the potential for precise daily evaluation and correction of patient setup, little progress has been made in the integration of these components. As a result, online setup adjustments remain a cumbersome task, limited in accuracy and speed. In order to address these issues, a modular control system is being developed and implemented to integrate the sub-systems of a "target-of-the-day" patient setup system. Components have been developed to measure patient position and correct this position using a computer-controlled treatment couch with six degrees of freedom (tilt and roll capability have been integrated within a standard linac treatment couch). The control system is based on an interactive client/server model and will allow components to be integrated in a semi-automated fashion from within an in-house Computer Controlled Radiotherapy System (CCRS). Redundant position feedback systems within the treatment couch allow for precise computer-controlled setup. The repositioning accuracy is limited not by the repositioning system (approximately 1 mm translation and 0.03 degrees rotation) but by the tools used to measure setup error. The overall target volume positioning accuracy is ± 0.2 cm in each translation and ± 1.0 degrees in each rotation. This system is being evaluated for daily localization of the target volume in a clinical liver protocol and a prostate protocol. A third protocol for fractionated treatments of acoustic neuromas is being developed.

****

Overview of the Proton-Ion Medical Machine Study (PIMMS).

S. Reimoser, on behalf of PIMMS Group* *Full-time members: L. Badano[1], M. Benedikt[2], P.J. Bryant[2] (Study Leader), M. Crescenti[1], P. Holy[3], A. Maier[2,4], M. Pullia[1], S. Reimoser[2], S. Rossi[1], Part-time member: P. Knaus[1,2], [1]TERA Foundation, via Puccini. 11, 1-28 100 Novara, [2]CERN, CH 1211 Geneva 23, [3]Oncology-2000 Foundation, Na Morani 4, CZ-12808 Prague 2. [4]Med-AUSTRON, c/o RIZ, Prof. Dr. Stephan Korenstr.10, A-2700 Wr. Neustadt.

The Proton-Ion Medical Machine Study (PIMMS) was set up following an agreement between MedAUSTRON (Austria) and the TERA Foundation (Italy) to join their resources in the design of a medical synchrotron that could later be adapted to individual national needs. CERN agreed to host this collaboration inside its PS Division and to contribute to the study. The group has worked in contact with GSI (Germany) and was later joined by Onkologie 2000 (Czech Republic). The work is expected to finish by 2000. The agreed aim of the study was to investigate and design a generic facility that would allow the direct clinical comparison of protons and carbon ions for cancer treatment. The ring, transfer lines and gantries form a closely integrated design that contains many new features to ensure a stable and controllable particle spill at the patient. Emphasis has also been laid on the architectural integration of the accelerator complex into the overall facility

****

Response of an imaging plate to clinical proton beams.

A. Nohtomi, T. Terunuma, R. Kohno, Y. Takada, Y. Hayakawa, A. Maruhashi, T. Sakae and K. Yasuoka, Proton Medical Research Center (PMRC), University of Tsukuba, Tsukuba, Japan

For an application to the dose-distribution measurement, response of an imaging plate (IP) has been studied with proton beams, which are routinely utilized for the radiation therapy. The upper limit of measurable proton dose by an IP system is almost controlled by the readout range of scanner used. Within this limit, reasonable linear response of an EP to proton dose to water is maintained. Fading curves are neither so sensitive to a small change of room temperature nor to a certain variation of proton dose (0.0108 - 0.132 Gy). Reproducibility of the PSL intensity is fairly good if both the fading characteristics and the lot-dependence of the sensitivity of each IP are taken into account carefully. Stopping power dependence of IP response has been measured at different positions in a Bragg curve. Tolerance of IP to radiation damage by proton irradiation has been examined.

****

Proton Dose Distribution Measurement with Screen and CCD-camera.

A. Maruhashi, A. Nohtomi and M. Satoh T. Terunuma, Proton Medical Research Center(PMRC), Tsukuba University, Oho 1-1 (in KEK), Tsukuba, 305-0801 Japan

In PMRC, dose distributions on the axis of proton beam and on the lines perpendicular to that in the water phantom have been measured by scanning Si semiconductor detector, under the same condition of a beam delivery system including bolus and patient collimator as that of patient treatment.

The purpose of this measurement is to verify that the width of high dose region (90%-95% to maximum on beam axis in the target volume in general) given by SOBP beam is coincident to that of planned target region as a result of the treatment planning. Now, we test the two dimensional dose distribution detector usable in water in place of the present detection system. For this purpose, a system composed of intensifying screen used for X-ray radiography and CCD camera was used. The screen stood vertically in water phantom was set to the axis of proton beam as 1) at small angle to mainly measure intensity distributions of its scintillation light on depth and 2) perpendicularly to measure 2-D light intensity distribution at given depth. In latter case, a miller set at 45 degrees to the proton beam direction was attached to the distal edge of the water phantom. Characteristics of the screen about efficiency converting the absorbed dose to light intensity were investigated on the basis of dose measured by Si semiconductor detector. We show LET dependency of light intensity generated from the screen and relationships between dose distributions by silicon dosimeter and light intensity distributions by the screen as experimental and analytical results on a poster.

****

2D and 3D dose distribution determination in proton beam radiotherapy with Gaf ChromicTM film detectors.

S. O. Troja[1,2], E. Egger[3], A. M. Gueli[1,2], A. Kacperek[4], M. Coco[1], and R.Musmeci[1], [1]Dipartimento di Fisica dell'Universita, Corso Italia 57, 95129, Catania, Italy, [2]Istituto Nazionale di Fisica Nucleare -Sezione di Catania, Corso Italia 57, 95129, Catania, Italy, [3]Division of Radiation Medicine, Paul Scherrer Institute, Villigen-PSI, Switzerland, [4]Clatterbridge Centre of Oncology, Bebington, U.K.

The results obtained using radiochromic (MD-55 GafChromicTM) film for the 2D and 3D dosimetric reconstruction of the dose delivered by a proton beam under the real conditions of a programme of radiotherapy treatment for ocular tumours were reported. Standard microdensitometric measurements were used to determine the variation in film optical density (O.D.) vs dose. Calibration curves were obtained by least-square fitting of the experimental OD values using a second order polynomial. This allows conversion of O.D. to dose. With this procedure it was possible to determine the distribution of the dose delivered by the proton beam in a phantom composed of layers of GafChromicTM film, with high surface spatial resolution and, through sections, the complete mapping of the dose delivered to a volume subjected to irradiation, as in a course of radiotherapy treatment.

****

Chromosomal aberrations detected by Interphase Chromosome Painting in lymphocytes from cancer patients given X-ray or carbon-ion therapy.

S. Yamada[1], M. Durante[2], R. Lee [3], K. Ando[3], H. Tsujii[1]; [1]Research Center of Charged Particle Therapy, [3]International Space Radiation Laboratory, National Institute of Radiological Sciences Chiba, Japan, [2]Department of Physics, University 'Federico II', Italy

The purpose of this study is to investigate the normal tissue damage caused by X-ray or carbon-ion therapy. We measured chromosomal aberrations in peripheral blood lymphocytes before, during and after the radiation treatment by using the novel technique of Interphase Chromosome Painting. Premature chromosome condensation (PCC) was induced in stimulated lymphocytes by incubation in calyculin A, and slides were hybridized in situ with whole-chromosome DNA probes specific for human chromosome 2 and 4 (FISH). Chromosome aberrations increased as tumor dose and were dependent on field size and tumor position. Initial slope of aberration during radiotherapy increased with an increase in the field size. Aberrations decreased several months after the radiotherapy, although still remained higher than pretreatment. Chromosome aberration yields were lower for patients treated with carbonions than X-rays. These results suggest that Interphase Chromosome Painting (PCC+FISH) is an efficient tool for biodosimetry of radiation treatment and carbon-ions induce a lower level of cytogenetic damage in lymphocytes than X-rays.

****

Esthesioneuroblastoma : Results of a prospective study of neoadjuvant chemotherapy and proton irradiation.

M. M. Fitzek, A. F. Thornton, M. Varvares, J. McIntyre, J. Adams, S. Rosenthal, B. Z. Pilch, M. Joseph, P. Amrein. Departments of Radiation Oncology, Hematology and Oncology, Massachusetts General Hospital, Harvard Medical School; Departments of ENT Surgery and Pathology, Massachusetts Eye and Ear Infirmary, Harvard Medical School.

Purpose: We report the results of a prospective study in malignant neuroendocrine tumors of the paranasal sinuses incorporating multimodality treatment with high dose proton/photon radiotherapy.

Material and Methods: Nineteen patients with Esthesioneuroblastoma (ENB) or Neuroendocrine carcinomas (NEC) were treated between 1992 and 1998 on a prospective study incorporating proton/photon radiotherapy for paranasal sinus malignancies. Four patients had Kadish stage B disease, 15 patients Kadish stage C disease. Male to Female relationship was 14:5, median age 44 years. After histological confirmation of diagnosis, patients received chemotherapy with 2 courses of Cisplatinum and Etoposide followed by high dose proton/photon radiotherapy to 69.2 Cobalt-Gray-Equivalent (CGE) in 1.6 - 1.8 CGE per fraction twice daily in a concomitant boost schedule. If there was less than a partial response to chemotherapy, surgical resection was recommended prior to radiotherapy. Following radiotherapy, two further courses of chemotherapy were given to responders.

Results: Of the 19 patients, 15 are alive with a median follow-up of 39 months (range 15 to 84 months). Four patients have died 8 to 47 months after diagnosis (median 18 months), all from disseminated disease. Actuarial 5-year survival is 74%. Two local recurrences have been observed thus far, both salvaged by surgery. Acute toxicity of chemotherapy was tolerable with no

patient sustaining more than Grade 2 hematologic toxicity. Thirteen patients showed a partial or complete response to chemotherapy. Failure to respond was associated with a higher death rate. Radiotherapy was completed after a median treatment time of 38 days with one patient requiring a break of 4 days because of unrelated illness. One patient developed unilateral visual loss after the first course of chemotherapy; otherwise, eye preservation as well as visual preservation was achieved in all patients. Three patients developed radiation induced damage to the frontal lobe by MRI criteria. Two patients showed soft tissue/bone necrosis in the region of the frontal sinus and the ethmoid plate; one of them required surgical repair of a cerebrospinal fluid leak.

Conclusion: Neoadjuvant chemotherapy and high dose proton/photon radiotherapy is a highly successful treatment approach for ENB/NEC. Radical surgery is reserved for non-responders. Due to the precision of delivery of radiation with stereotactic setup and protons the visual apparatus could be preserved in all patients. Toxicities are acceptable in light of the dismal outcome of less aggressive therapy.

****

Follow-up of the 1997 and 1998 patients @ PSI, Villigen, Switzerland.

L. Wisser, G. Goitein and Team Radiation medicine, PSI, Switzerland

In the two first years of operation at PSI, we treated 19 patients. 4 suffered from a meningioma, 4 low grade gliomas, 3 cordomas/chondrosarcomas of the base of the skull, 4 sarcomas (trunc and extremities), 2 sacral cordomas and 2 cases of metastases. The volumes of the PTV's were between 22 and 3900cc. Doses delivered were between 30 and 72 CGE. 13 cases with follow ups between 8 and 24 months show no signs of progression. 5 patients died from generalization without local progression at the treated site. 1 patient lost in follow-up.

Side-effects were very mild in general (hair-loss, erythema). 1 patient developed a brain necrosis in the 54CGE-region (vascular reasons?). 1(-2) patients with radiation induced tumor necrosis.

****

1999 patients from PSI.

L. Wisser, G. Goitein and Team Radiation medicine, PSI, Switzerland

Until October 1999, we treated 3 chondrosarcomas (2 base of skull, 1 T8), 1 cordoma (C5), 4 meningiomas (one of them with multiple foci), 1 preirradiated, recurrent esthesioneuroblastoma, 1 preirradiated, recurrent basaloma (invading the base of skull), 1 sarcoma (C5), 1 malignant neurofibroma and 1 low grade glioma. Volumes ranged from 22 up to 1100cc, doses from 50 to 74CGE. Until the end of our beam-period (Christmas) we are planning to treat 22 patients.

****

Proton-beam radiotherapy for early stage lung cancer.

D. A. Bush[1], J. D. Slater[1], R. Bonnet[2], G. A. Cheek [2], R. D. Dunbar[3], M. Moyers[1], J. M. Slater[1], [1]Depts. of Radiation Medicine, [2]Diagnostic Radiology, and [3]Pulmonary Medicine, Loma Linda University Medical Center, 11234 Anderson Street, Loma Linda, California 92354

Study Objective: A prospective study was undertaken to assess the efficacy and toxicity of conformal proton beam radiotherapy for early stage, medically inoperable non-small cell lung cancer.

Design: Eligible patients had clinical stage I - IIIa non-small cell lung cancer who were not candidates for surgical resection for medical reasons or patient refusal. Patients with adequate cardiopulmonary function received 45 gray (Gy) to the mediastinum and gross tumor volume with photons with a concurrent proton boost to the gross tumor volume of an additional 28.8 cobalt gray equivalent (CGE). Total tumor dose was 73.8 CGE given over five weeks. Patients with poor

cardiopulmonary function received proton beam radiotherapy to the gross tumor volume only with 51 CGE given in 10 fractions over a two-week course.

Results: Thirty-seven patients were treated on the study from July 1994, to March 1998. Clinical staging of patients was as follows, Stage I - 27 patients, Stage II - 2 patients, Stage IIIa - 8 patients. Eighteen patients received a combination of protons and x-rays, while 19 patients received proton beamradiation only. Follow-up on evaluable patients ranges from 3-45 months with a median of 14 months. Two patients in the proton and photon arm developed pneumonitis that resolved with oral steroids, otherwise no significant toxicities were encountered. The actuarial disease-free survival at two years for the entire group was 63%, for Stage I patient's disease-free survival at two years was 86%. Local disease control was 87%.

Conclusion: Preliminary results from this study indicate that proton beam radiotherapy can safely be used in this group of patients. Disease-free survival and local control appear to be good and compare favorably to published reports utilizing conventional photon irradiation.

****

Proton Beam Therapy for Hepatocellular Carcinoma Preliminary Experience at LLUMC.

D. A. Bush, D. J. Hillebrand; J. D. Slater; B. A. Runyon; and J. M.Slater, Loma Linda University Medical Center, Dept. of Radiation Medicine and Transplantation Institute, Loma Linda, CA

Objective: A perspective study was undertaken to access the efficacy and toxicity of proton beam radiotherapy in patients with localized hepatocellular carcinoma.

Methods: Eligible patients had a diagnosis of hepatocellular carcinoma. Clinical stage was T1-T3, NO, MO. Patients with cirrhosis must have compensated liver disease, with a Child-Pugh score of 9 or less. All patients were either surgically unresectable or refused surgical intervention. Proton beam radiotherapy was delivered to the gross tumor volume (GTV) with an additional 1 cm. margin. Patients received a total of 63 Cobalt Gray Equivalent in 15 equally divided fractions. Follow-up included monthly evaluations in radiation medicine, and hepatology clinics, monthly blood work with liver function tests, and abdominal CT scan every 3 months for the first year.

Results: A total of 20 tumors in 16 patients have been treated to date. The average age is 64 years (44-82). Fourteen tumors in 12 patients were evaluable with at least 3 months of follow-up. Median follow-up is 10 months (3-16). Ten patients had solitary tumors, while 2 patients had two separate intrahepatic tumors. Average tumor size was 5 x 4.8 cm. (1-10 cm.). Eight of 12 patients had elevated AFP levels, with the average level prior to treatment being 270 (4-1580). Hepatic toxicity was monitored in all patients according to the common toxicity criteria. The only hepatic toxicity encountered was a decreased albumin level in two patients (grade 2). Two patients experienced grade 2 GI toxicity in whom bowel was immediately adjacent to the treated portion of the liver. The average AFP level following treatment was 58 (4-519), representing a 78% decrease from pre-treatment values. None of the 14 treated tumors have shown radiographic progression. Eight of the 14 tumors have demonstrated a partial response, with the remaining 6 being stable. One patient has recurred with multiple liver nodules, and is receiving no further therapy. Two patients have had evidence of new, solitary tumors in other segments of the liver, and both are being treated with proton beam. No patient has demonstrated recurrent tumor outside of the liver. No patient deaths have occurred.

Conclusion: Proton beam radiotherapy appears to have limited hepatic toxicity when used as primary treatment for localized hepatocellular carcinoma. Most patients demonstrate tumor response with either decreasing AFPs or radiographic tumor reduction. Our preliminary data seem to confirm the prior experience reported from Japan.

****