| | Chair | Secretary |
|---|---|---|
| **P**ROTON **T**HERAPY **C**O-**O**PERATIVE **G**ROUP | Michael Goitein Ph. D.<br>Department of Radiation Oncology<br>Massachusetts General Hospital<br>Boston MA 02114<br>(617) 724 - 9529<br>(617) 724 - 9532 Fax | Daniel Miller Ph. D.<br>Department of Radiation Medicine<br>Loma Linda University Medical Center<br>Loma Linda CA 92354<br>(909) 824 - 4197<br>(909) 824 - 4083 Fax |

# ABSTRACTS

# of the

# XX PTCOG MEETING

# held in Chester, England
# May 16 - 18 1994

# INDEX

**Proton Dosimetry 2 (relative)**

**General Proton Therapy 2**

**Clinical Applications**

## Updated Design of a Dedicated Proton Therapy Linac

Robert W. Hamm[†], AccSys Technology, Inc., Pleasanton, CA 94566

The use of a conventional 5-band standing wave electron linac structure to accelerate low current proton beams up to 250 MeV for proton therapy was first suggested in 1991. This presentation will review the updated design of such a system, reflecting new choices for the operating frequencies of the linac subsystems to take advantage of commercially available rf power tubes. The low energy sections, consisting of the Radio Frequency Quadrupole (RFQ) and the drift tube linac transition section, both operate at 357 MHz; the main drift tube linac operates at 714 MHz. The 70 MeV beam from the drift tube linac is then injected into a series of conventional side coupled linac cavities operating at 2856 MHz. These 10 short tanks can be turned on and the rf power phased separately to continuously vary the proton beam energy from 70 to 250 MeV. Alternatively, fewer tanks could be used for maximum energies less than 250 MeV.

The use of an RFQ with a very small aperture restricts the pulsed beam current that is accelerated so that a single pulse from this system is never a significant fraction of the total dose given to a patient. The average current capability of such a system is compatible with present scattering techniques of patient treatment. In addition, this system could be adapted to full three dimensional voxel scanning since the final beam energy can be varied on a pulse-to-pulse basis. Finally, the cost of such a system is projected to be less than existing proton therapy accelerator systems.

[†]Presentation made by M. Marc.

*****************************************

## TRITRON, the post-accelerator at the Munich tandem accelerator facility

Jorrit de Boer, Ludwig-Maximilians-Universität München, D-85748 Garching

The accelerator laboratory is jointly operated by the two Munich universities, the Ludwig-Maximilians-Universität and the Technische Universität München. A 14 MV tandem accelerator is being used for basic nuclear research (nuclear reactions, nuclear structure) and for some applications (element analysis and some others). To extend the energy range to the Coulomb barrier for ion beams heavier than nickel a post-accelerator, named TRITRON, has been installed. It is an ambitious new accelerator type using superconducting bending magnets and superconducting acceleration cavities operating at $T \leq 4.5$ K (liquid Helium). All components have been put together in January 1994, and the post-accelerator is at present being tested.

Protons have the longest range for particles accelerated by TRITRON. The maximum energy should reach 70 MeV, and it is planned to install an eye-treatment facility and to perform selected dosimetry studies in collaboration with the radiotherapy group of the University of Regensburg.

The special feature of TRITRON is a spiral orbit with unusually large distances between the turns; $\Delta r$ = 4 cm. This brings the advantage of being able to adjust the magnetic field and its gradient for each of the 12 sectors of each turn individually, leading to strong focusing in the transverse and in the longitudinal direction. High, easily extracted external currents are expected. It requires, however, the acceleration voltage per turn to be sufficiently large to increase the radius by a 4 cm step on each of the 20 revolutions.

The accelerator has a sixfold symmetry: Six superconducting cavities are placed between six pairs of superconducting magnet-sectors. Each magnet has 20 channels. The channels are copper tubes with an inside clearance of 1 cm diameter flanked by superconducting coils.

The six radiofrequency cavities are operated at the fixed frequency of 170 MHz. The cycle time for the projectiles can be 18 to 60 times the radiofrequency period (harmonic number).

The specifications were easily fulfilled by all individual components and in some cases considerably surpassed. Yet it has turned out that many unexpected problems come up with an unconventional accelerator design as the one described here. The crew at present working on the accelerator (P. Schütz, L. Beck, U. Buhl, A. Cazan, M. Högenauer, B. Köppl, H. J. Körner, J. Labedzki, L. Rohrer, H. Seeger, U. Trinks) is confident that these obstacles can be overcome.

A more detailed description (by U. Trinks) of the accelerator can be found in Proceedings of the 13th International Conference on Cyclotrons and their Applications, Vancouver 1992 (Ed. G. Dutto, M.K. Craddock) and in references therein.

**\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\***

### Proton Beam Technology: Slit Scattering and Penumbra

B. Gottschalk, A.M. Koehler, C.S. Mayo* and M.S. Wagner, Harvard Cyclotron Laboratory, Cambridge MA, *St. Anne's Hospital, Fall River MA.

This talk deals with two unrelated aspects of proton beam technology. *Slit scattering* refers to those protons which interact with a collimator or 'slit' but don't stop, coming out degraded. They fall into two classes with very different characteristics: *inners* which entered the slit *inside* the nominal radius and grazed the far corner, and *outers* which entered *outside* the nominal radius but managed to multiple scatter back into the hole. The numbers are not tiny; for 160 MeV protons hitting a 2 cm diameter brass collimator from a 1 m effective source distance, the ratios of inner to 'clean' and outer to 'clean' protons are 7 and 10% respectively. Downstream, inners diverge more or less at the beam cone angle and still have fairly high energy. Outers are more troublesome since they *converge* (at $\approx 6^o$ for brass) with much lower average energy, so a dosimeter is very sensitive to them. In our example we get a 30% dose enhancement a few cm downstream. The net effect in a Faraday cup calibration can be much less if the dosimeter is strategically placed; nevertheless it is clear that calibration beams with apertures must be planned carefully. We have a well tested Monte Carlo which helps in this and can estimate residual correction factors.

The *penumbra* of a proton radiotherapy beam depends on the *amount* of range modifying material (absorber, modulator, bolus), its *position* along the beamline relative to the aperture, any *air gaps* between the aperture and the patient and, of course, the *depth* of the point of interest in the patient. Objects between the effective source and the aperture contribute angular confusion at the aperture in proportion to their distance from the source. Objects at the source contribute none and therefore it is very desirable to arrange matters so that the absorber and/or modulator also act as the first scatterer in a passive beam spreading system. We have a fast (non Monte Carlo) algorithm for calculating penumbra; it has been checked with measurements.

**\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\***

## Medical Facility for Radiation Therapy at JINR (Dubna) Proton Phasotron Beams.

V. M. Abazov, B. V. Astrakhan, Y. G. Budjashov, A. G. Molokanov, C. V. Mytsin, V. K. Poidenko, O. V. Savchenko, V. P. Zorin. JINR, Dubna Russia

The six-compartment clinicophysical facility for radiation therapy with proton, negative pion and neutron beams was realized at the phasotron of the Joint Institute for Nuclear Research in Dubna (Russia) after its conversion. The clinicophysical facility consists of several medical channels: three therapeutic proton beams with energies from 100 to 660 MeV; a negative pion beam with energy up to 80 MeV; a therapeutic neutron beam with the mean energy about 350 MeV and a therapeutic gamma-unit with Co-60 source.

The first treatment room for proton therapy is equipped for proton beam irradiations of large deeply located tumours by the method of rotation scanning. Motion of a patient during irradiation procedures and the Bragg peak position are controlled with a computer.

An original method of oesophagus cancer irradiation was realized. The oesophagus was irradiated with a horizontal proton beam on several floors along its length. The Bragg peak and the tumour were overlapped at each floor under the control of a computer on the basis of information from a miniature silicon detector inserted inside the oesophagus or calculations from X-ray tomographic images, measured immediately before the irradiation run.

The second room is intended for transvaginal cervix utery cancer proton irradiations. The depth-dose distribution is formed by means of the ridge filter. Regional limphatic nodules are irradiated at the gamma-unit.

The third treatment room consists of equipment for stereotactic converging irradiations of small intracranial targets by a "fly-through" method with a narrow proton beam of 660 MeV.

Radiation therapy was carried out by the medical personnel from the Cancer Research Center (Moscow) and engineering personnel from the JINR (Dubna). Up to April 1994 26 patients with uterus cervix cancer and 5 patients with esophagus cancer were treated.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## A Compact Accelerator for a BNCT Neutron Source

G. Proudfoot, R. McAdams, J. Holmes, T. D. Beynon\*, AEA Technology, Culham, \*Birmingham University, UK

The outline of a 10 mA 3 MeV tandem accelerator design was described. This offers the potential for exploiting the $Li^7(p,n)$ reaction for BNCT. The critical design feature of vacuum insulation allows the accelerator to be reduced to ~2.5m in length as well as enabling use of gas stripping for the high current beam. A solid target, $Li_2O$ has been considered and a moderator based on $D_2O$ designed with additional features to reduce the photon kerma and the thermal neutron flux. The composite system is designed to produce high quality epi-thermal neutrons, and tests of the target concept and moderator are expected to begin at Birmingham in June this year.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## An Accelerator Booster for the Clatterbridge Cyclotron

A J Holmes, G Proudfoot A Kacperek*, AEA Technology, Culham, *Douglas Cyclotron Unit, Clatterbridge.

The prospects for increasing the energy of the Clatterbridge Cyclotron continue to be explored, and over the last 12 months alternatives to the linac concept developed earlier have been considered. One option which retains the basic probe structure and frequency of the cyclotron looks promising both technically and commercially, and this is being developed further.

*****************************************

## Supplement to the Code of Practice for Clinical Proton Dosimetry

S. Vynckier[1], D. E. Bonnett[2], D. T. L. Jones[3], [1]UCL Cliniques Universitaires St-Luc, Brussels, Belgium, [2]Leicester Royal Infirmary NHS Trust, Leicester, United Kingdom, [3]National Accelerator Centre, Faure, South Africa.

**Summary:** The "Code of Practice for Clinical Proton dosimetry" (Vynckier et al, 1991) was published two years ago, but since then new data for mass stopping powers for protons have been reported (ICRU 49, 1993) and consideration has been given to the specification of the absorbed dose in water instead of the original recommendation of absorbed dose in tissue. This supplement summarises the basic recommendations of the original Code of Practice in Table 1 and incorporates the new stopping power data for dose specification.

### Table 1: Basic recommendations of the supplement to the Code of Practice

| | |
|---|---|
| Choice of dosimeter | - Ionisation chamber<br>-<br>- Calorimetry |
| Choice of ionisation Chamber | - TE ionisation chambers<br>- Other thimble ionisation<br>  chambers (IAEA report 277) |
| Choice of cavity gas | - air |
| Proton energy specification | - (Ep)eff or<br>  proton energy spectral information |
| Absorbed dose specification | - water |
| Reference phantom material | - water or acrylic phantom |
| Reference depth | - middle of the SOBP |

The formalism for the determination of the absorbed dose in a clinical proton beam, using an ionisation chamber, was given in the Code of Practice (Vynckier et al, 1991). Following final formula was derived for A-150 ionisation chambers:

**Note added in March 2008: The original article had some form of error in the equations……**

$$D_{water} = M_{corr} \times N_K \times C_p \qquad\qquad 1.$$

where:

$M_{corr}$ is the corrected electrometer reading, $N_K$ is the air-kerma calibration factor and:

$$C_p = A_{wall} \times \left[ (\bar{S}/\rho)_{air}^{water} \right]_p \times k \qquad \qquad 2.$$

In this equation $A_{wall}$ is a chamber dependent factor, $\left[ (\bar{S}/\rho)_{air}^{water} \right]_p$ is a proton-energy dependent factor and k is a constant given by:

$$k = (1-g) \times \frac{(W_{air}/e)_p}{(W_{air}/e)_c} \times \frac{\left[ (\bar{\mu}_{en}/\rho)_{air}^{A150} \right]}{\left[ (\bar{L}/\rho)_{air}^{A150} \right]} = (1-g) \times \frac{(W_{air}/e)_p}{(W_{air}/e)_c} \times k_m \qquad \qquad 3.$$

Using the values listed in Table 2, k equals 0.993.
The air-kerma calibration factor $N_K$ and the exposure calibration factor $N_X$ are related by:

$$N_K = N_X \times (W_{air}/e)_c \times (1-g)^{-1} \qquad \qquad 4.$$

If $N_X$ is still expressed in (roentgen . reading$^{-1}$), then it should be multiplied by 2.58 x 10$^4$ in order to obtain its value in (C . kg$^{-1}$ . reading$^{-1}$). The $N_{gas}$ or $N_{air}$ calibration factor can be obtained from the $N_K$ calibration factor using:

$$N_{gas} = N_{air} = (W_{air}/e)_c \times m_{air}^{-1}$$

$$N_{air} = A_{wall} \times (1-g) \times N_K \times \left[ (\bar{L}/\rho)_{A150}^{air} \right] \times \left[ (\bar{\mu}_{en}/\rho)_{air}^{A150} \right] \qquad \qquad 5.$$

The corrected reading $M_{corr}$ obtained from the actual reading, M by:

$$M_{corr} = M \times \prod_i p_i \qquad \qquad 6.$$

with $\prod_i p_i$ the product of factors (Vynckier et al, 1991) used to correct the electrometer reading to the charge produced in the cavity under standard temperature and pressure conditions.

The parameters listed below in Table 2 are for tissue-equivalent ionisation chambers made of A-150 plastic and filled with air. For other ionisation chambers the values can be found in existing photon dosimetry protocols (AAPM, Task Group 21, 1983, IAEA report 277, 1987, Mijnheer et al, 1986).

**Table 2**: values for the physical parameters

| Parameter | | Value | Reference |
|---|---|---|---|
| $A_{wall}$ | | | Gastorf et al. (1986) |
| | Exradin T1 | 0.992 | |
| | FWT IC18 | 0.991 | |
| | Exradin T2 | 0.985 | |
| | FWT IC17 | 0.983 | |
| g | | 0.003 | Boutillon (1985) |
| $\left(W_{air}/e\right)_c$ | | 33.97 J/C | Boutillon et al. (1987) |
| $\left(W_{air}/e\right)_p$ | | 35.2 J/C | ICRU 31 (1979) |
| $\left[\left(\bar{\mu}_{en}/\rho\right)_{air}^{A\,150}\right]_c$ | | 1.101 | Hubbel (1982) |
| $\left[\left(\bar{L}/\rho\right)_{air}^{A\,150}\right]$ | | 1.145 | AAPM TG21 (1983) |
| $\left[\left(\bar{s}/\rho\right)_{air}^{water}\right]_p$ | | see Table 3 | ICRU 49 (1993) |

**Table 3**: Mass stopping powers for water and air and their ratio (from ICRU 49,1993)

| Proton Energy (MeV) | Mass stopping powers (MeV . cm$^2$ . g$^{-1}$) | | |
|---|---|---|---|
| | water | air | water/air |
| 10 | 45.67 | 40.06 | 1.1400 |
| 20 | 26.07 | 22.94 | 1.1364 |
| 30 | 18.76 | 16.53 | 1.1349 |
| 40 | 14.88 | 13.12 | 1.1341 |
| 50 | 12.45 | 10.99 | 1.1328 |
| 60 | 10.78 | 9.517 | 1.1327 |
| 70 | 9.559 | 8.443 | 1.1322 |
| 80 | 8.625 | 7.620 | 1.1319 |
| 90 | 7.888 | 6.970 | 1.1317 |
| 100 | 7.289 | 6.443 | 1.1313 |
| 125 | 6.192 | 5.475 | 1.1310 |
| 150 | 5.445 | 4.816 | 1.1306 |
| 175 | 4.903 | 4.338 | 1.1302 |
| 200 | 4.492 | 3.976 | 1.1298 |
| 225 | 4.170 | 3.691 | 1.1298 |
| 250 | 3.911 | 3.462 | 1.1297 |
| 275 | 3.698 | 3.275 | 1.1292 |
| 300 | 3.520 | 3.118 | 1.1289 |
| 350 | 3.241 | 2.871 | 1.1289 |
| 400 | 3.032 | 2.687 | 1.1284 |

**Conclusions**

This supplement to the Code of Practice for absorbed dose determinations in proton beams provides amendments to the guidelines and procedures presented in the original Code of Practice. The major amendments are:

1. the adoption of the mass stopping powers for protons published in ICRU 49;
2. specification of the proton absorbed dose in water.

In addition it is recommended that practical proton dosimetry be based on ionisation chambers and that further work be carried out on the use of calorimeters for the calibration of such chambers.

It is the purpose of this document, together with the original Code of Practice to present a common basis for international proton dosimetry, which will allow to achieve uniformity and facilitate the exchange of clinical information.

**References**

AAPM, task group 21, "A protocol for the determination of the absorbed dose from high-energy photon and electron beams.", Med. Phys. 10, 741-771, 1983.

Boutillon M., "Values of g for photon energies.", CCEMRI report (I)/85-18, Offilib, 1985.

Boutillon M. and Perroche-Roux A. M., "Re-evaluation of the W-value for electrons in dry air.", Phys. Med. Biol. 32, 213-219, 1987.

Gastorf R., Humphries L., Rozenfeld M., "Cylindrical chamber dimensions and the corresponding values of $A_{Wall}$ and $N_{gas}/(N_x.A_{ion})$." Med. Phys., 13, 751-754, 1986.

Hubbell J.H., "Photon mass attenuation and energy absorption coefficients from 1 KeV to 20 MeV.", Int. J. Radiat. Isot., 33, 1269, 1982.

IAEA report 277, "Absorbed dose determination in photon and electron beams.", IAEA Vienna, 1987.

ICRU report 49, "Stopping powers for proton and alpha particles.", Bethesda Maryland, 1993 (in press).

ICRU report 31, "Average energy required to produce an ion pair.", Bethesda Maryland, 1979.

Mijnheer B. J., Aalbers A.H.L., Visser A., Wittkämper F. W., "Consistency and simplicity in the determination of the absorbed dose to water in high-energy photon beams: a new code of practice (NCS report 2).", Radiother. Oncol., 7, 371-384, 1986.

Vynckier S., Bonnett D. E., Jones D. T. L., "Code of practice for clinical proton dosimetry.", Radiother. Oncol., 20, 53-63, 1991.

*****************************************

**Ion-chamber dosimetry in proton beams: $N_W$ versus $N_K$ calibrations**

Joakim Medin[1,3], Pedro Andreo[1,2], Erik Grusell[3], Anders Montelius[4] and Martin Roos[5], [1]Dept. of Medical Radiation Physics, University of Stockholm, Box 602, 171 76 Stockholm, Sweden, [2]Dept. of Radiation Physics, University of Lund, 221 85 Lund, Sweden, [3]Dept. of Oncology, University of Uppsala, 751 21 Uppsala, Sweden, [4]Dept. of Hospital Physics, University Hospital, 751 85 Uppsala, Sweden, [5]Physikalisch-Technische Bundesanstalt, D-3300 Braunschweig, Germany

The use of $N_K$-calibrated ionization chambers in the dosimetry of proton beams is well established. The transfer of $N_K$ to $N_D$, step previous to the determination of absorbed dose to water or tissue is responsible, however, for an important contribution to the final uncertainty in $D_W$ because of the chamber-dependent factors involved in the usually theoretical transfer (mainly through $k_m k_{att}$). Recent

trends in photon bean dosimetry favour the utilization of ion-chambers calibrated in terms of absorbed dose to water, $N_w$, mainly at the quality of $^{60}$Co gamma rays, and the final uncertainty in $D_w$ is considerably reduced. The same quality can be implemented in proton beams.

In the present work we report unexpected results in the determination of absorbed dose in a proton beam with two different cylindrical ion-chambers: an IC-18 and a NE-2571 (Farmer type). Both chambers had been calibrated in terms of $N_K$ at the Swedish Standard Dosimetry Laboratory. In accurate measurements the IC-18 chamber yielded a dose which was 1.2% lower than that obtained with the Farmer chamber. Since the Farmer chamber is well-known for its reliability in different beam qualities another approach was investigated, this time also including two plane-parallel chambers in the study (NACP-II and Roos-FK6) for comparison. Experimental $N_D$-factors using the Farmer chamber as reference were determined in electron beams for the other three chambers, following the procedure commonly used with plane-parallel ion chambers. When applied in a proton beam, all the $N_D$-factors yielded consistent absorbed dose determinations within the experimental uncertainties. This finding questions the use of IC-18 chambers in proton beams when the chamber has been calibrated in terms of $N_K$. This chamber is entirely made of A-150 (wall and central electrode), material known to be highly hygroscopic and with I-value and stopping-powers not closely equivalent to water, and at the same time has a massive central electrode which minimizes the detector air cavity size.

One of the plane-parallel chambers (Roos-FK6) has an absorbed dose to water factor $N_W$ at the quality of $^{60}$Co, provided by the Standard Laboratory in Germany (PTB). The absorbed dose to water in a proton beam was determined using $N_w$ together with a beam quality factor $k_Q$ which contains ratios of quantities at proton and $^{60}$Co beam qualities, mainly stopping-power ratios and W/e values. Using this formalism excellent agreement was found with determinations based on experimental $N_D$, which encourages the implementation of this method in therapeutic proton beams. The use of $N_w$ at $^{60}$Co reduces the final uncertainty in the determination of absorbed dose in proton beams because the contributions from $k_m$ and $k_{att}$ are not involved, systematic uncertainties cancel out in the $k_Q$ factor, and the same physical quality $D_w$ is used from detector calibration to the determination in the user's beam. If the reference quality can be a proton beam, the $k_Q$ factor will practically be unity. Even with $^{60}$Co whenever the product (W/e $s_{med,air}$) is directly available from calorimetry the uncertainty will be decreased even further.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

### Comparative Measurements with Faraday-Cup and Ionization Chamber in an Uncollimated Proton Beam

Erik Grusell[1] , Ulf Isacsson[1], Anders Montelius[2] and Joakim Medin[1,3], [1]Dept. of Oncology, Uppsala University, Sweden, [2]Dept of Hospital Physics, University Hospital, Sweden, [3]Dept of Medical Radiation Physics, Karolinska Institute, Stockholm, Sweden

The Faraday cup (FC) and the ionization chamber (IC) are recommended as detectors for dosimetry in therapy beams of heavy charged particles (protons) both by the American[1] and the European[2] dosimetry protocols. It is recommended that an FC can be used to calibrate an IC. Alternatively the IC can be calibrated in $^{60}$Co. The FC measures the number of particles passing through a collimator with known effective area, and the absorbed dose is obtained as the product of particle fluence and mass stopping power. It is assumed that the particles are near-monoenergetic and that the energy can be determined from range measurements. The main source of error is the scattered particles that lose a considerable fraction of their energy in the collimators. Arrangements with anti-scatter collimators have been used[3] to reduce this effect. Recent reports[4,5] indicate,          however, that this problem may be difficult to solve.

Also, our own measurements demonstrate this problem.

In order to achieve a useful beam of near-monoenergetic particles, we used a single scatterer and no collimation. In our comparison we determined the total number of particles in the beam in two ways: with the FC and with a $^{60}$Co calibrated, plane parallel IC. We used 173 MeV protons (determined by range measurement) at the synchrocyclotron at the Svedberg Laboratory in Uppsala. The FC was placed close to the scatterer and detected all protons in the beam. The IC was placed at a large distance from the scatterer and was used both to measure the fluence at the centre of the beam and to scan the beam profile so that the total number of particles in the beam could be obtained. The two methods agreed within the estimated error ±3.8%. Measurements were also made in a collimated beam, where the IC gave a value 19 % higher than that obtained with the FC.

l. AAPM report No. 16. Protocol for heavy charged particle therapy beam dosimetry. AAPM, New York, 1986.
2. Vynckier S., Bonnett D. F. and Jones, D. T. L. Code of practice for clinical proton beam dosimetry. Radiotherapy and Oncology, 20, 53-63, 1991.
3. Verhey L. J., Koehler A. M., McDonald J. M., Goitein M., Ma I-C., Schneider R. J. and Wagner, M. The determination of absorbed dose in a proton beam for purposes of charged-particle radiation therapy. Radiation Research. 79, 34-54, 1979.
4. Verhey L. J., A fresh look at old proton dose intercomparisons and current status of proton dosimetry. Abstract, XIX PTCOG, Cambridge, Mass., 1993.
5. Delacroix S., Bridier A., Mazal A., et al. Proton dosimetry comparison involving ionometry and calorimetry. Ms submitted to Int. J. Rad. Onc. Biol. Phys. Appeared in Rapport technique of Centre de Protontherapie d'Orsay, 1993.

******************************************

## ISS Alanine Dosimetry at PSI Therapy Proton Beam Facility

C. de Angelis, P. Fattibene, S. Onori, Istituto Superiore di Sanita', Rome, Italy, F. d'Errico, DCMN, Pisa University and INFN, Sezlone Pisa, Pisa, Italy, E. Egger, Paul Scherrer Institute, Willigen, Switzerland, I. Janovsky, Nuclear Research Institute, Prague, Check Republic

ESR/alanine dosimetry is based on the quantitative detection by Electron Spin Resonance (ESR) technique, of the stable free radicals induced by radiation in the polycrystalline amminoacid alanine. The Istituto Superiore di Sanita' (ISS) in Rome, has been deeply involved in the subject since the beginning and has contributed to its development and achievement. The ISS alanine based dosimeters are solid pellets (cylinder, 5 mm in diameter and 1 to 10 mm in length) obtained by pressing a blend of alanine (80% by weight) and paraffin (20% by weight) (1). Because of its many favorable properties, ISS alanine dosimetry is a very well established and recognised method of dose assessment for gamma, bremsstrahlung, and electron beams, at the industrial as well as at the therapy level. Among others, high precision, nearly tissue equivalence, absence of energy dependence in a wide range, absence of fading at room storage conditions, non destructive read-out procedures, suggest the use of ISS alanine dosimetry also for dose assessment in proton beams. Nowadays also alanine-polyethylene films are available from the Nuclear Research Institute (NRI) in Prague (3), which are potential candidates to be used in the strong gradient heavy particle beams. The aim of the present work was to test ISS alanine dosimeters and NRI films for proton beam dosimetry. As a first step, the parameters under consideration were: dose effect relationship, relative effectiveness (RE), and energy dependence.

The test was performed at Paul Scherrer Institute (PSI) with a 65 MeV proton beam. Reference

dosimetry at PSI was provided by a Markus type parallel plate chamber. The measurements were performed partly in an unmodulated beam and partly in a spread out Bragg peak. The dose rate was about 0.75 Gy/s. The field size was 34 x 34 mm$^2$. As for alanine dosimeters, in the present work 2 mm thick pellets and 0.2 mm thick films were used. Alanine dosimeters were inserted in a properly designed solid water (WT1) phantom.

RESULTS:

Dose dependence and relative effectiveness

For this measurement 4 dosimeters were lodged in the WT1 phantom at the middle position of the spread out peak.

The dose dependence resulted linear in the (5-100)Gy range.

Doses were evaluated by the cobalt-60 calibration curve and were compared to PSI nominal doses. By this way the RE to cobalt-60 was assessed to be 1 for each dose in the (5-l00)Gy range.

Energy dependence

Different measurements were planned to study energy dependence. In a first experiment three pellets were located at 11, 18, and 26 mm deep in a WT1 phantom on the spread out Bragg peak. A similar measurement was carried out with three LiF TLD. Alanine results (fig. 1) do not show any energy dependence in the tested range, while TLs underestimate the dose at the deepest position.

In a second experiment alanine pellets were stacked up to 30 mm in the modulated beam and the dose profile was reconstructed (fig. 2). Because of the nearly tissue equivalence of the ISS dosimeter, the profile needed just to be scaled according to the density ratio to water. Further improvement could be attained if dosimeter density could be reduced from the present 1.16 g/cm$^3$ to a value closer to 1 g/cm$^3$ by choosing a new dosimeter design.
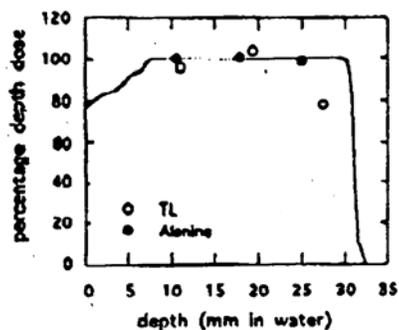


Fig. 1 Comparison of dose evaluation by alanine pellets and TL detectors on a modulated Bragg peak. TLs show a significant dependence on energy at the end of the spread out peak.
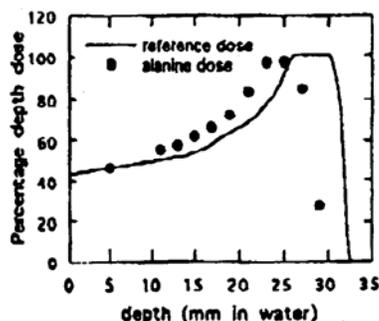
Fig. 2 Effect of density on a modulated beam profile reconstruction by a pile of alanine pellets. Depth is referred to water for the reference system and to alanine for the alanine measurement

The last result was confirmed by further irradiation of pellets in an unmodulated peak (Fig. 3). The profile is described very well if the proper averages of reference doses are considered on the dosimeter length.
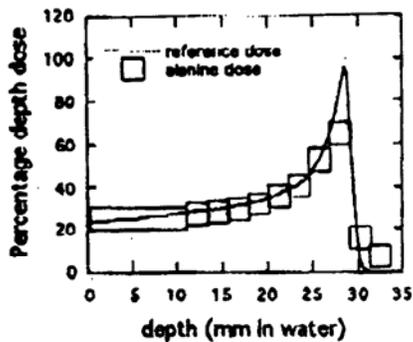
Fig. 3 Profile of dose reconstructed by a stack of alanine pellets. The transversal dimension of the rectangles represents the dimension of alanine pellets referred to water.
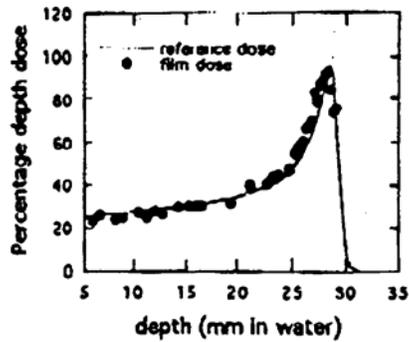
Fig. 4  Profile of dose reconstructed by a stack of thin alanine-polyethyline films.

Finally films (15 x l5 mm$^2$) were stacked in the WT1 phantom in order to evaluate the dose profile with a better resolution (Fig. 4).  It is evident that alanine films can provide very resolved measurements where other dosimeters give only an average value.  Measurements are underway to study the dose profile in the tail of the Bragg peak, where resolution can be of great help.

REFERENCES:
(1) A. Bartolotta, P.L. lndovina, S. Onori, A. Rosati,  *Dosimetry for Co-60 Gamma-rays with Alanine*, Prot. Rad. Dos., 1984, 9, pp. 277-281.
(2) P. Fattibene, S. Onori, *ESR/Alanine Dosimetry*, TERA 94/1 TRA11 (January 1994).

(3) I. Janovsky, "Progress in Alanine Film/CSR Dosimetry", Proc. Int. Symp. on *High Dos. Radiat. Processing*, (IAEA, Vienna, l990), IAEA-SM 314/47, 1991, pp. 173-188.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

### Superheated Drop ( Bubble ) Detector Tests with Proton Therapy Beams

F. d'Errico[1], E. Egger[2], [1]DCMN Universatà degli Studi di Pisa and INFN Sezione di Pisa, 1 - 56100 Pisa, [2]Division of Radiation Medicine, PSI, CH - 5232 Villigen - PSI

Superheated drop (bubble) detectors (1) consist in a uniform emulsions of superheated halocarbon droplets dispersed in compliant gels or polymers.  They operate like bubble chambers, long used in high energy physics: primary or secondary charged particles nucleate the phase transition of the superheated drops generating visible bubbles.  Drops are kept in superheated state, therefore, they are continuously sensitive.  The bubbles they generate upon irradiation provide a measure of the incident particle fluence.  Several devices based on this technology have been developed for radiation protection dosimetry, as they detect neutrons with a dose equivalent response which is quite flat over the thermal to 66 MeV energy range (2).

Passive, integrating dosemeters have been employed successfully in the assessment of neutron leakage from medical X-ray accelerators (3).          We used such detectors to measure the exposure of

our OPTIS patients to neutron contamination.  Quantitative measurements of this neutron dose were performed irradiating the detectors on a Rando phantom using a mean size proton collimator.  We simulated the treatment of a tumor located in the left eye.  The dosemeters were positioned in correspondence to the left and right temple., the thyroid and behind the head on the beam axis.  The phantom received a proton dose of 54.54 Gy in 4 fractions.  Measured neutron doses (expressed in mSv) were 16.5 on the left temple, 6 on the right one, 1.8 on the thyroid and 1 behind the head. Further measurements of the stray neutron field away from the proton beam were consistent with data previously gathered by means of standard neutron rem-counters. Various bubble detectors (i.e. suspensions of different superheated liquids) were tested for the 3D dosimetry of our 65 MeV protons.  We irradiated the detectors with a raw Bragg peak and found out that some show  the full proton tracks and visualize the depth - dose distribution with a higher density of bubble formation corresponding to the Bragg peak.  Since the detectors are tissue equivalent, the only correction that appears necessary is for the 1.28 g/ccm density.

   Other detectors require a high ionization density to trigger the drop vaporization.  These detect only the heavy charged particles from proton - nucleus interactions, as was confirmed by the absence of bubbles at depths where protons had less than 20 MeV. The currently available spatial resolution is ~0.5 mm.  Therefore, this system may be used for direct visualization of proton beam penetration or divergence in tissue, as well as for verification of treatment plans with complex 3D geometries.  Among the techniques tested so far for 3D imaging of the bubble distributions, best results were achieved from nuclear magnetic resonance (4).

   At the present stage, bubbles gradually diffuse into the whole volume of the detector.  Our hope is to realise a detector where the bubbles stay in place and to develop an algorithm for the MRI in order to achieve quantitative 3D Imaging of the dose distribution.

 (1) Apfel R.E., *The Superheated Drop Detector*, Nucl. Instrum. Methods, 162, 603-608, (1979)
(2) d'Errico F. and Alberts W.G., *Superheated Drop (Bubble) Detectors and Their Compliance with ICRP-60.*  Radiat. Prot. Dosim. (1994), In press
(3) Nath R., Meigooni A.S., King R., Smolen S. and d'Errico F., *Superheated Drop Detectors for Determination of Neutron Dose Equivalent to Patients Undergoing High Energy X-Ray and Electron Radiotherapy.*  Medical Physics 20(3), 781-787, (1993)
(4) d'Errico F., Nath R. and Apfel R.E., *Superheated Drop Detectors for the Three Dimensional Dosimetry of Brachytherapy Sources.*  In: Proc. International Congress on Advanced Diagnostic Modalities and New Irradiating Techniques in Radiotherapy. Perugia, Italy, March 9 -11, 1994, 401-405

**************************************

## MR Imaging of proton dose distributions in Fricke gels

J.N.H Brunt, A. Kacperek, J.A. Eagle, J.E. Shaw and G.P. Lawrence, CCO, Wirral UK

We have investigated MRI-interrogated Fricke gel techniques to visualize and analyze proton dose distributions from a 62 MeV cyclotron used for treatment of ocular melanomas.  Gel-filled phantoms of various configurations were irradiated using unmodulated, partially and fully modulated proton beams with collimation and wedging appropriate to either calibration or treatment simulation experiments.  MR imaging at 0.5 T employed a sequence providing images of T1 values.  Multiple phantoms (including ones for dose calibration, T1 reference and spatial resolution) were imaged in the same scan.  Calibration (relationship of 1/T1 to dose) was smoothly curvilinear up to 80 Gy.  The scans demonstrated the following: Bragg peak from unmodulated beam, plateaux of spatial dose distributions from partial and full

modulation, effect of collimation and wedging, limitations imposed by ion diffusion. MRI-interrogated Fricke dosimetry is a promising technique for rapid non-invasive demonstration of the 3-dimensional distributions of proton radiation dose in configurations emulating treatment situations.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## ITEP and Proton Dosimetry Intercomparisons.
V. Kostjuchenko, Institute for Theoretical and Experimental Physics, Moscow.

The ITEP synchrotron has a well pronounced pulse structure; the instantaneous dose rate can be as high as $7 \times 10^6$ Gy/s. This dose rate is ca. 3 orders of magnitude higher than those at other proton clinical centers where commercial ionization chambers calibrated against a Co-60 source are successfully used. At ITEP, the standard dosimetry is based on the activation method employing the $^{12}C(p,pn)^{11}C$ monitor reaction. Therefore, comparisons of dose between ITEP and other centers are possible only by means of passive dosimeters.

Since 1992 ITEP has participated in a number of projects involving dosimetry intercomparisons, both within Russia and abroad. In Russia, comparisons were made between three active accelerators used for proton therapy, namely the ITEP synchrotron, the JINR(\*) phasotron and the LINP(\*\*) phasotron. The work was conducted by specialists from the Russian standards laboratory at the Central Scientific Institute for X-Rays and Radiology (St. Petersburg, Russia). LiF thermoluminescent detectors were used in the measurements.

In 1992, the National Cancer Institute (USA) started a study on dosimetry properties of alanine as a material for passive detectors in dosimetry intercomparisons. The research is being carried out at ITEP and the National Institute of Standards and Technology (USA) using the NIST detectors and measuring equipment.

Some preliminary data from this work combined with the data from all-Russian intercomparisons are presented below to help assess the status of absolute dosimetry measurements at the ITEP clinical beam and investigate the potentialities of standard dosimetry at ITEP.

Table. Results of intercomparisons between the ITEP clinical beam and some otheractive proton clinical centers.

| Institutions | Geometry of Measurements | | Dosimeter Used |
|---|---|---|---|
| | Entrance Region | SOBP | $^{12}C$ activation method at ITEP |
| ITEP/JINR | 0.992 | 1.033 | TLD (St. Petersburg) |
| | - | 0.968 | Alanine (NIST) |
| ITEP/LINP | 1.043 | - | TLD (St. Petersburg) |
| ITEP/LLUMC (\*\*\*) | 1.006 | 0.950 | Alanine (NIST) |
| ITEP/TSL | 1.029 | - | Faraday cup (TSL) |

Data obtained from comparison of the flux measurements taken with a Faraday cup (The Svedberg Laboratory, Uppsala, Sweden) and by the $^{12}C$ activation method (ITEP) are also included in the table.

These preliminary results show that absolute dosimetry at ITEP does not differ from absolute measurements at other centers by more than 5%. The measurements

taken in a monoenergetic beam, where it is possible to compare those directly with ^{11}C activation measurements prove that the accuracy of the ITEP standard activation dosimetry meets the requirements formulated in international dosimetry protocols.

*       Joint Institute for Nuclear Research, Dubna, Russia
**      Leningrad Institute for Nuclear Problems, St. Petersburg, Russia
***     Loma Linda University Medical Center, Loma Linda, CA, USA

**************************************

## Estimates of Neutron Dose to Patients receiving Proton Beam Treatment at HCL

Andreas M. Koehler, Xiaowei Yan and Alicea Maas*, Harvard Cyclotron Laboratory, Cambridge MA, *Dept. of Rad. Oncology, Massachusetts General Hospital, Boston MA.

Neutron dose to patients has been estimated in two ways. Commercial dosimeter badges have been placed close to 150 patients during treatment.  The neutron dose readings, based on track etch techniques, show a mean value of about 0.7  mrem per proton rad, but with much scatter. To understand the situation better, a set of Bonner Spheres has been used to collect data at a few locations for one treatment configuration, using a cylinder of lucite to simulate a patient. The data from each location have been analyzed to estimate the neutron energy spectrum and derive a properly weighted dose equivalent. The spectra varies only moderately so that measurements of the dose distribution elsewhere in the treatment room could be carried out using a single 10-inch sphere calibrated against the full set at these benchmark locations. The resulting map of dose equivalent in mrem/rad is shown here and is consistent with the personal dosimeter data.



**************************************

14
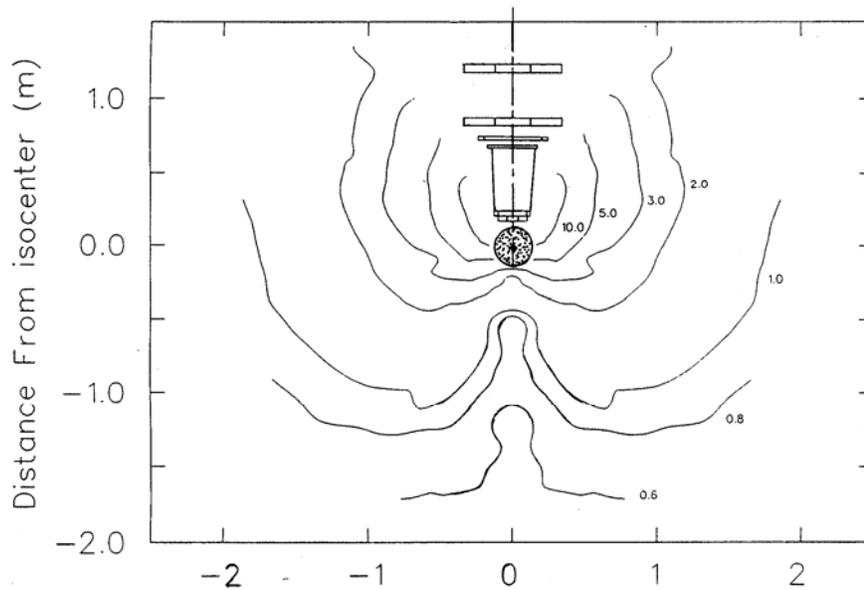
# Comparison of Different Detectors for the Determination of Bragg Peak.

N. Brassart[1], M. Heintz[2], J. Hérault[1], D. Flühs[2], U. Quast[2], J. M. Gabillat[1],
W. Sauerwein[2], P. Chauvel[1], (1) Centre Antoine-Lacassagne - Cyclotron Biomédical, NICE - France,
(2) Universitätsklinikum Essen, ESSEN - Germany

High precision constitutes a formal request for the treatment of uveal melanoma and particularly for those located at the posterior pole of the eye, close to critical structures as optic disc, macula and optic nerve, as far as the treatment aims to both cure the tumor and conserve a useful vision. This requires a very accurate determination of the Bragg peak and of the range value. But it is of general knowledge that the instruments used disrupt the measure according to their own detecting systems.

It is therefore of major interest to study the shape of the Bragg peak and spread- out Bragg peak and to compare the value of the distal 90% isodose range obtained through different detectors. The measurements were performed with the photosensitive diodes currently used in Nice, scintillators tested in Essen with photons and electrons, plane parallel chamber and extrapolation plane parallel chamber from PTW. Cylindrical chambers generally used for dose measurements have also been tested: FWT 0.1 cc, X Radin 0.05 cc and 0.5 cc. As expected the displacement of the effective point of measurement varies from one detector to another as well as the shape and characteristics of the Bragg peak. The results obtained from photo-diodes are in complete agreement with those from plane parallel chambers and scintillator. In comparison, the results obtained from cylindrical ionization chambers have to be carefully interpreted, important discrepancies remaining after all the corrections, as shown on the figure.
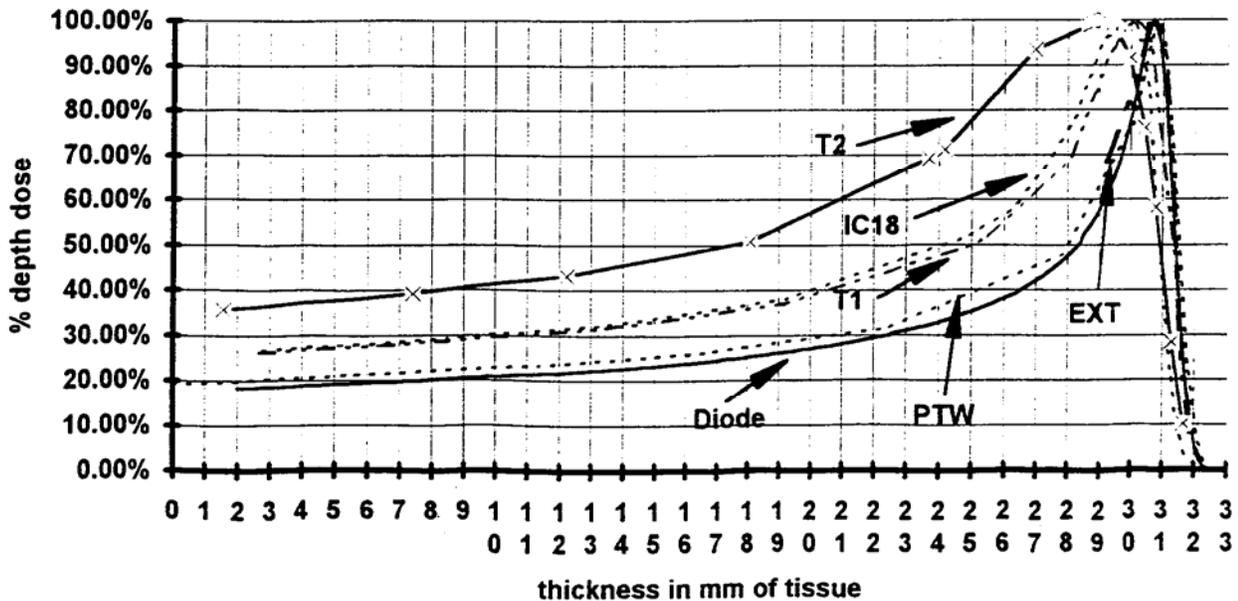
| | PTW ion chamber | Extrapolation ion chamber | Diode | Scintillator NE 102A | XRadin T2 (0.5cc) | XRadin T1 (0.05cc) | FWTIC18 (0.1cc) |
|---|---|---|---|---|---|---|---|
| Range 90% mm | 31.1 | 31.1 | 31 | 31.1 | 30 | 30.7 | 30.4 |
| Fall off (90-10) % mm | 0.9 | 0.8 | 0.8 | 0.9 | 1.6 | 1.2 | 1 |
| width half max | 3.6 | | 3.3 | 2.6 | 13.5 | 6.3 | 6.8 |

**************************************

## Activation Method of Dosimetry: Its State of the Art and Perspectives.

D. Nichiporov, Institute for Theoretical and Experimental Physics, Moscow, Russia.

Because of highly pronounced pulse structure of the proton beam at the ITEP clinical facility in Moscow commercially available ionization chambers can not be used for standard dosimetry there. An activation method based on the $^{12}C(p,pn)^{11}C$ nuclear monitor reaction was established as a standard method of dosimetry at the ITEP clinical beam.

Knowing the activity, A induced in an irradiated target, one can determine the fluence of the beam, F according to the formula;

$$F=A/(\sigma N \lambda),$$

where $\sigma$ is the reaction's cross section, N is the number of Carbon atoms in the target, and $\lambda$ is the decay constant of the $^{11}C$ isotope. The absorbed dose can then be determined as

$$D=1.602 \times 10^{-8} \times F \times S_M,$$

where $S_M$ is the stopping power of the material in which the dose is measured. Activity is induced by the beam in carbon containing targets made of scintillating polystyrene, and is measured with a low activity counting unit designed and developed at ITEP. The block diagram of the unit is shown in fig 1.

The unit employs a method of beta-gamma coincidences to measure activity of the target. For pure positron emitters such as $^{11}C$ isotope, the activity can be determined as

$$A=N_\gamma \times N_\beta / N_c,$$

where $N_\gamma$, $N_\beta$ and $N_c$ are the numbers of counts in the $\beta$, $\gamma$ and coincidence channels, respectively.

To ensure the accuracy of measurements, the unit requires a calibration source of a well-known activity to be measured prior to the measurements of samples. The accuracy of the $^{22}Na$ calibration source that is used at ITEP for this purpose, is guaranteed within ±3%. Taking into account all relevant sources of uncertainty, we have;

1. Activity of the calibration source         ±3 %
2. Cross section of the monitor reaction       ±3 %

3. Counting statistics          $\pm 2\,\%$
4. Concentration of Carbon atoms      $\pm 1\,\%$
5. Knowledge of tissue's stopping power    $\pm 0.9\%$
6. Other          less than $\pm 1\%$ in total.

As a result, the overall uncertainty of the activation method is $\pm 4.9\%$. This means that even at the present stage the activation method meets the requirements set forward by international dosimetry protocols and deserves to be included into their updated versions. The analysis of uncertainties and their sources shows that the most promising ways to increase the accuracy of dose determination are (i) to use a calibration source of higher accuracy ($\pm 2\,\%$), and (ii) to obtain cross section data with a $\pm 2\,\%$ uncertainty. This would increase the overall accuracy of the activation method up to $\pm 3.7\,\%$.



\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*
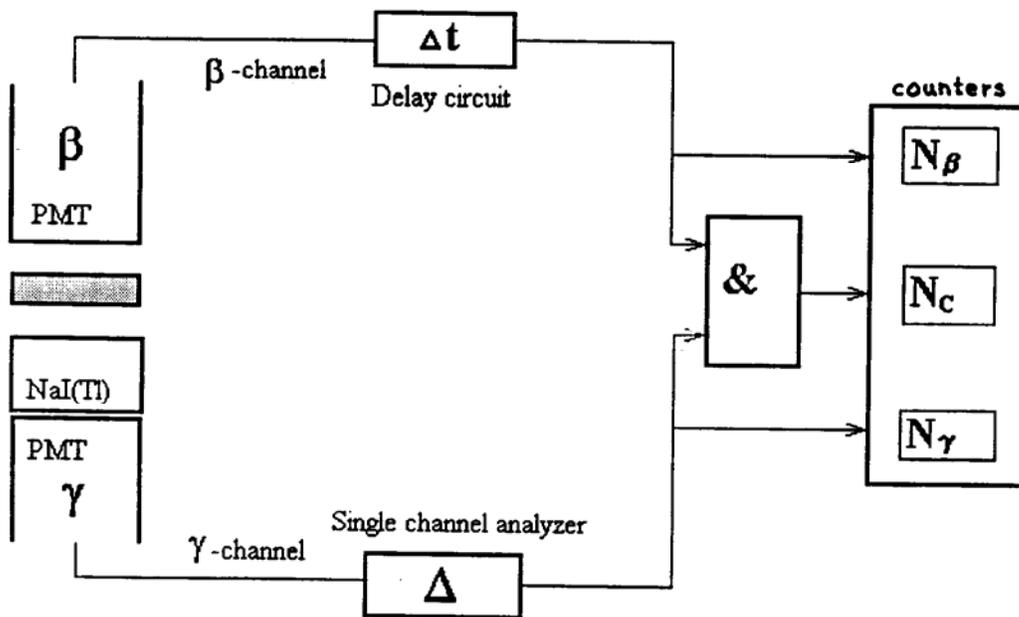
**World Wide Proton Therapy Experience: Where are we now in 1994?**
J. M. Sisterson, Harvard Cyclotron Laboratory, Harvard University, Cambridge MA 02138

There are now 16 operating proton therapy centers in the world; four in the USA, six in Europe, three in Russia, two in Japan and one in South Africa. At eight centers, the accelerator is a cyclotron, at five, a synchrocyclotron, and at three, a synchrotron. At six centers, the maximum proton energy is < 100 MeV. Six centers can provide proton beams with variable energy and six centers can deliver proton beams with diameters > 10 cms.

The cumulative patient total number of patients treated with proton beams since the 1950's is shown

in Figure 1. For the calendar year 1992, it was estimated that 1526 patients were treated with proton beams. The percentage number of patients treated at each operating center in 1992 is shown in Figure 2. Actual patient numbers were not available for Moscow, Dubna, St. Petersburg and Louvain-la-Neuve, but reasonable estimates have been used.

At those centers reporting patient data by site in 1992, a total of 1336 patients were treated. 56.4% of those patients were treated for uveal melanoma, 15% for prostate cancer and 4.5% for chordoma or chondrosarcoma. No other category accounted for more than 3% of patients. These numbers would be different if the experiences of Moscow, Dubna, St. Petersburg and Louvain-la-Neuve could be included, but can serve as an indicator of the type of sites that are being treated with proton beams at this time.
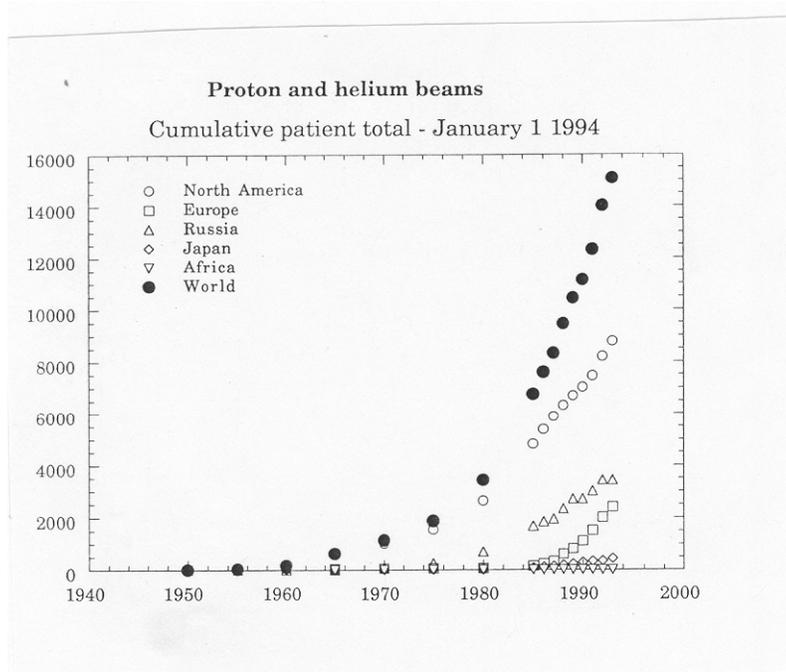


Fig. 1
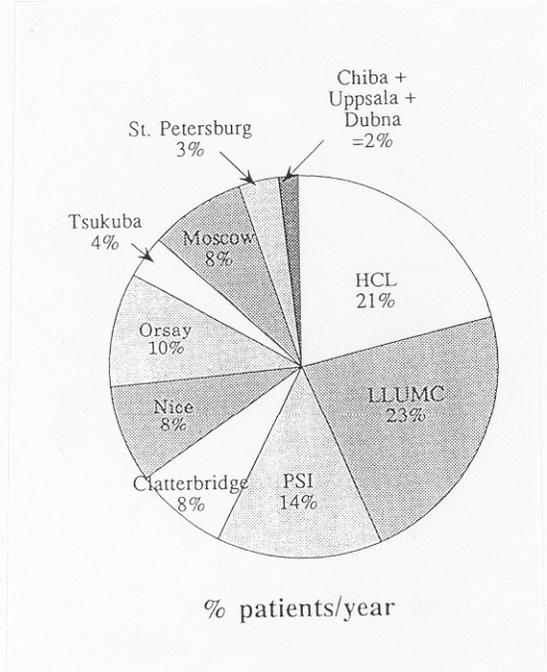


Fig. 2: Year = **1992**:
100% = 1526 patients

*****************************************

### DVH analysis of the rectum, treated by combined photon and proton for the uterine cervix at PMRC, Tsukuba.

J. E. Mizoe[1], H. Tsujii[2], H. Tsuji[2], T. Okumura[2], Y. Matsuoka[1], T. Inada[2], A. Maruhashi[2], Y. Hayakawa[2], Y. Takada[2] and J. Tada[2], [1]Division of Radiation Medicine, National Institute of Radiological Sciences (NlRS), Japan, [2]Proton Medical Research Center (PMRC). University of Tsukuba, Japan.

DVHs of the rectum of 23 patients who were treated by proton beams of PMRC at the University of Tsukuba between October 1983 and December 1991 for their uterine cervical cancer were analyzed. Patients were treated with a combination of          proton therapy for their uterine cervix and X-ray

18

therapy by 10 MeV Linac for the whole pelvis. RBE value of the proton was assumed as 1.1 and average total dose of the proton was 63.9 Gy/19 fractions with average fraction dose of 3.36 Gy. Average dose of combined X-ray therapy was 45.5 Gy/25 fractions with average fraction dose of 1.82 Gy. In X-ray therapy, average dose of 22.4 Gy was irradiated for the uterine cervix without central shield, and this dose was assumed as homogeneous rectal dose from the X-ray therapy. Two patients showed grade 2 late rectal complication which needed surgical intervention and these DVHs were considered having late rectal complication. The dose-complication probability equation by logistic model, calculated at 40% partial volume of DVHs and by 16 Gy bin size, is followed,

$$P=1-1/(1+EXP(-11.7086+0.194669*D(Gy)))$$

In this equation, 5% probability dose is 45.0 Gy and 50% probability dose is 60.1 Gy. This dose seems to be higher than reported dose of rectal complication. Immobilization of inner organ and assessment of RBE value will be needed.

*****************************************

### Analysis of Dose-Volume Histograms of Patients with Chordomas of the Cervical Spine and Base of Skull.

Patrick E. Hanssens, Marcia M. Urie, Andrzej Niemierko, Jimmy Efird, John E. Munzenrider, Dept. of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.

Purpose : Non-homogeneous dose distributions may result if critical normal structures abut a target volume, the prescribed dose is greater than the defined tolerance doses for those structures, and a plan is developed which limits the dose to be received by those structures. In such situations, a significant portion of the target may receive a dose lower than that prescribed. The physical characteristics of the 160 MeV proton beam of the Harvard Cyclotron, and conformal radiotherapy techniques combining that beam with high-energy X-rays at MGH in treating skull base tumors to varying dose levels produce dose distributions with dose-gradients ranging from the dose constraining levels of adjacent normal structures up to the prescribed dose. Generally accepted guidelines for dose specification may be difficult to apply in such dose distributions. This study describes the results of dose-volume histogram analysis of tumors abutting critical normal structures treated with combined high dose proton beam radiation with 3D treatment planning.

Material and Methods : Dose-Volume Histograms of 125 patients with chordomas of the Cervical Spine (CS : 25) and the Base of Skull (BOS : 100) who received combined photon and proton beam radiation with 3D treatment planning were analyzed. Doses are expressed in CGE (Cobalt Gray Equivalent) assuming a relative biologic effectiveness (RBE) for protons of 1.1. The prescribed dose (PD) was 66.6 CGE for 37 pts (BOS : 33, CS : 4), 68.4 CGE for 32 pts (BOS : 25, CS : 7), 70.2 CGE for 22 pts (BOS : 16, CS : 6) and 72 CGE for 34 pts (BOS : 26, CS : 8). The doses were delivered in daily fractions of 1.8 CGE, 5 fractions a week. The mean photon component was 16.2 Gy (0-48.6) and the mean proton component was 52.7 CGE (21.6-68.4). Normal tissue constraints (NTC's) were 53 CGE to the center of the spinal cord (SC) and brain stem (BS) , 64 CGE to the surface of the SC and BS and 60 CGE to the optic nerves and chiasm. If the tumor abutted a optic nerve, the NTC for that optic nerve was 64 CGE. For each patient, we calculated the percentage of the tumor volume that received the prescribed dose (VPD), the maximum dose and the dose delivered to 100%, 95%, 90%, 80%, 70%, 60%, 50%, 40%, 30%, 20%, 10% and 5% of the tumor volume. Patients were then divided in groups based on the location of their tumor and the PD, and for each group we calculated the average VPD and average DVH.

Results : The average DVH's for each group are shown in figures 1a and 1b. The average VPD's and (standard deviation) for each group are shown in the table below.

| Site | Prescribed Dose | | | |
|---|---|---|---|---|
| | 66.6 CGE | 68.4 CGE | 70.2 CGE | 72 CGE |
| Base of Skull | 57% (18) | 55% (22) | 54% (19) | 44% (19) |
| Cervical Spine | 81% (18) | 54% (21) | 44% (21) | 62% (12) |

Conclusion : Normal tissue dose constraints lower than the prescribed dose may induce a dose inhomogeneity within the tumor volume. For the same NTC's, the percentage of the tumor which receives the prescribed dose (VPD) decreases as the PD increases. There is a wide range of VPD for the same PD depending upon the configuration of the tumor with respect to the normal tissues. The NTC's determine the lowest dose within the tumor and the configuration determines the volume effects. The importance of the dose-inhomogeneity for local control will depend upon the dose-response of these tumors. This needs to be reported and taken into account when designing and evaluating dose-escalation studies, not only for these proton treated patients but in all trials where non uniform radiation of the tumor is delivered.
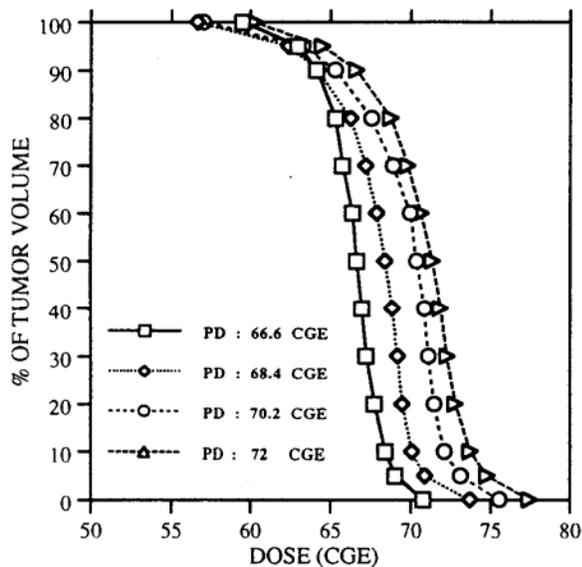


Fig.1a : average DVH for Chordoma of Base of Skull    Fig.1b : average DVH for Chordoma of Cervical Spine
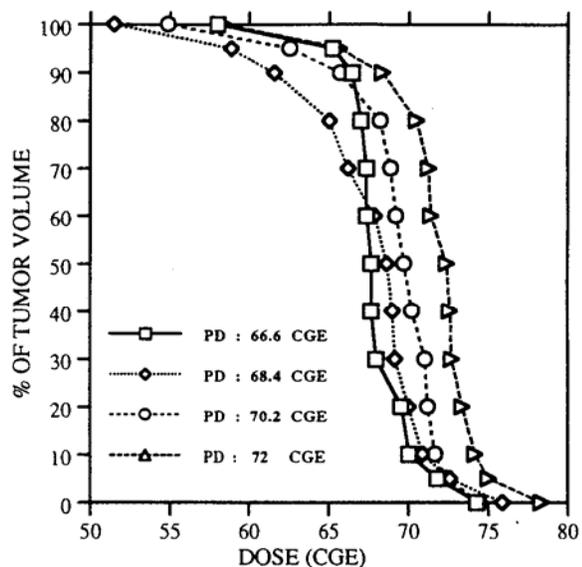
**************************************

**HIMAC Clinical Plans and Protocols for Heavy Ion Therapy**
H. Tsujii, K. Morita, J. Mizoe, T. Miyamoto, M. Mukai, T. Nakano, S. Morita, National Institute for Radiological Sciences(NIRS), Chiba, Japan

At NIRS the HIMAC (Heavy-Ion Medical Accelerator in Chiba) project was started in 1984, and construction of the building and installation of all facilities were completed at the end of 1993.  This is the first heavy ion synchrotron complex dedicated to medical use in a hospital environment.  The aim of the HIMAC project is to establish therapeutic advantage of heavy ion beams in cancer treatment.  The major part of the accelerator consists of two-ring synchrotron, two ion sources, RFQ linac, Alvarez linac, and

20

high-energy beam transport system.  There are three treatment rooms (vertical, horizontal, and vertical and horizontal beams), as well as rooms  for physics and radiobiological studies.  In the initial pilot study, the phase I/II clinical trails will be taken place for treatment of head and neck, CNS and lung tumors, and the first patient will be treated at the end of June using carbon ions.  As irradiation technique developes, other tumor sites including the liver, uterine cervix, bladder and prostate will be evaluated for possible candidates for heavy ion therapy.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## The Implantation of the Fractionated Treatment of Intra-Cranial Malignancies at C.P.O.

J.L. Habrand, C, Haie, S. Helfre, C. Lenir, D. Pontvert, L. Schwartz, A. Mazal, Centre de Protonthérapie d'Orsay 91406 . ORSAY . France

In December 1993, the first intra-cranial malignancy was treated at C.P.O.  The patient, a 28 year-old gentleman, with a medulloblastoma, presented with residual disease in the posterior fossa, after surgery. Following an initial course of conventional radiation to the entire CNS + boost to the posterior fossa up to 55 Gy, he received additional protons confined to visible tumor through a singe posterior approach using a compensator.  Dose was 10 CGE in 5 fractions (RBE 1.1).

Following this case, a preliminary pilot study is going to be initiated with 2 goals:
  1/ validating the positioning, the treatment planning and the treatment reproducibility in clinical situations;
  2/ testing inocuity and efficacy of a dose escalated from 10 to 15 % relative to conventional radiation.

Two end-points have been selected:
  1/ delayed damages to the brain and adjacent structures;
  2/ local control at 5 years.  Selected tumors for this study will be characterized by their aggressiveness (survival $\leq$ 5 years). This will include a wide variety of tumors seen in adults such as low and high grade astrocytomas (except pilocytic and glioblastomas), pineal germ cell tumors (except dysgerminomas), medulloblastomas and ependymomas inoperable or with gross residual disease. Total dose will be 60 CGE in low grades and 65 CGE in high grades.

An expected delayed radio necrosis at 2 years should be < 10 % and expected survival at 5 years be > 50 % in high grades and > 60 % in low grades.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## Clinical Results of Proton Beam Irradiation of Uveal Melanomas, at PSI

L. Zografos[1], E. Egger[2], T. Böhringer[2], L. Bercher[1], Chamot[1], G. Munkel[2], C. Gailloud[1], H. Blattmann[2], [1]Höpital Ophtalmique Jules Gonin, Avenue de France 15, CH-1004 Lausanne, [2]Division of Radiation Medicine, Paul Scherrer Institute, CH-5232 Villigen-PSI

Since March 1984 patients with ocular tumors have been treated  with proton beam irradiation in close collaboration between the University Eye Clinic of Lausanne and the Paul Scherrer Institute in Villigen.  Until February 1994, 1609 patients had been treated, that is 1482 uveal melanomas, 46 recurrent uveal melanomas, 34 melanomas of the conjunctiva, 19 intraocular metastases, 20 choroidal hemangiomas and 8 various ocular tumors. Up to now, 1351 unilateral melanomas were treated with a

proton dose of 54.54 in 4 daily fractions, and this is the subject of this statistical analysis. From these cases, 145 patients died, 122 of them had ocular tumor-related death, 42 patients had to receive a second treatment because of local tumor control failure, 87 eyes were enucleated, and 48 patients were lost to follow up.

The tumor volume ranged from 10 to 4040 cm$^3$ with a mean value of 737 cm$^3$. The largest tumor diameter (LTD) ranged from 4 to 26 mm. with a mean value of 16.2 mm., the tumor height ranged from 0.9 to 15.1 mm. with a mean value of 6.l mm. Patients' age ranged from 9 to 87 years. The mean value was 53.4 years. The anterior border of the tumor was located anteriorly to the equator in 57.4% of the cases, an invasion of the ciliary body was present in 28.9% of the cases, an invasion of the iris was found in 3.7% of the cases, and in extraocular extension was present in 4.7%, of the cases. The tumor was located close to the macula in 55.3% of the cases (distance between the posterior tumor border and the macula equal to or less than 3 mm.), and close to the optic disc in 51.7% of the cases (distance equal to or less than 3 mm.).

The tumor-related death rate was calculated with the Kaplan-Meier curves. Tumor-related deaths in 5 years was 16.4 ± 1.6%. The parameters influencing tumor-free survival were calculated using the Cox proportional hazard model. The following parameters were determined to be statistically significant: largest tumor diameter (p = 0.0000), age of the patient (p = 0.0047), presence of an extraocular extension (p = 0.0113), and local tumor control failure (p = 0.0164).

The 5-year tumor-related death rate was calculated in terms of these parameters. It was 5.6% for tumors with LTD less than 15 mm., 17.7% for tumors LTD more than 15 mm., and less than 20 mm., and 38.2% for tumors with LTD of 20 mm. or more. The tumor-related mortality rate was 11.1% for patients aged less than 53 years and 21.1% for patients older than 53 years. Patients with no extrascleral extension had a mortality rate of 14.9% versus 53.9% for patients with extrascleral extension. Patients where local tumor control was achieved after the first treatment had a mortality rate of 15.1% versus 43.3% for patients who had a local tumor control failure.

After proton beam irradiation, 87 of 1351 eyes had to be enucleated. The causes for enucleation were identified to be local tumor control failure in 13 cases, painful eyes with neovascular glaucoma in 44 cases. Impossibility to perform fundus examination and appreciation of the local tumor control in 4 eyes, unconfirmed suspicion of local recurrence in 5 cases, phthisis bulbi with aesthetic damage in 3 cases, uveitis in 3 cases, functional loss in 5 cases, total retinal detachment in 2 cases and psychological causes in 1 case. In 7 other cases, enucleation was performed by the referring ophthalmologist for reasons unknown to us.

The eye retention probability at 5 years was calculated to 88.3 ± 1.3%.

The main complications leading to a severe functional loss are neovascular glaucoma and radiation-induced optic neuropathy.

Radiation-induced optic neuropathy occurred only in patients who received an irradiation to the optic disc. For statistical analysis we took into account only cases followed up exclusively in the Eye Clinic of Lausanne and examined by one of us (LZ, LB, LC, CG). Among these 765 patients, 367 received an irradiation to the optic disc. From these cases, 90 presented with radiation-induced optic neuropathy. The complication-free survival rate at 5 years was 42.9 ± 5.8%. Optic atrophy developed in 95 of these cases and the optic atrophy-free survival rate of cases with irradiation of the optic disc was 29.9 ± 6.1%.

We used the Cox proportional hazard model for the identification of significant parameters for the development of neovascular glaucoma. This was tumor height (p = 0.0000), invasion of the optic disc by the tumor (p = 0.0140), and irradiation of the optic disc (p = 0,00047). The 98.2% of tumors with a height inferior to 5 mm., the 83.5% of tumors with a height ranging from 5 to 10 mm., and the 60% of tumors with a height superior to 10 mm. did not develop neovascular glaucoma.

In conclusion, an accelerated proton beam irradiation appears to be a valuable alternative therapeutic method for the treatment of uveal melanomas. The survival rate appears comparable with the survival rate obtained with other therapeutic modalities, the recurrence rate is lower than that expected following

brachytherapy, and the severe complications rate appears to be mainly dependent on parameters related to the tumor volume and location. Major further developments have to be made in earlier detection and treatment of micro-metastases, as well as in reduction of the complications rate of large uveal melanomas and tumors located close to the optic disc.

**\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\***

### Proton Beam Irradiation of Uveal Melanomas at PSI: Analysis of Successes and Failures

E. Egger[1], L. Zografos[2], T. Böhringer[1], L. Bercher[2], L. Chamot[2], G. Munkel[1], C. Gailloud[2], H. Blattmann[1], [1]Division of Radiation Medicine, Paul Scherrer Institute, CH-5232 Villigen-PSI, [2]Höpital Ophtalmique Jules Gonin, Av. de France 15, CH-1004 Lausanne

Among 1448 cases of uveal melanomas treated with proton beam irradiation between March l994 and February 1994, 52 cases (3.6%) presented with a local tumor control failure. Since recurrences seem to be a significant parameter for tumor-free survival, the achievement of local tumor control appears to be one of the main goals of the conservative treatment.

In this study we analyze the causes for local tumor control failure which were recognized during the last 10 years.

The following causes for recurrence were identified:

l) Reduced safety margins: 5 cases
2) Micro-invasions of the ciliary body: 16 cases
3) Diffuse pattern of uveal melanoma: 1 cases
4) Tumor localisation not accurate: 7 cases
5) Eye model not reliable: 3 cases
6) Recurrence independent from treated tumor: 2 cases
7) No information available: l case
8) Eyelid model not accurate; 14 cases.

l) In the first years of proton beam irradiation at PSI we tried to avoid the irradiation of the optic disc and of the fovea for posteriorly located tumors by reducing the safety margins. A detailed analysis of tumor localisation through the clips, by measuring the distance between the clips and the optic nerve, as well as the distance between the tumor border and the optic disc with different methods led us to the conclusion that the distance between the clips and the optic nerve cannot be determined with a precision higher than 0.5 mm in the best case. The mean precision that can be achieved is in the order of l mm. For this reason, we renounced reducing the safety margins already in the year 1987.

2) We observed a local tumor control failure in 3l of 439 tumors involving the ciliary body. Sixteen of them recurred in the ciliary part. Micro-invasions of the ciliary body may be more frequent because of the peculiar vascular architecture of the anterior uvea, or it may not be detected in transillumination due to the dark appearance of the ciliary body. For these reasons, we now enlarge the safety margins in order to irradiate a larger field in the ciliary body by keeping the same safety margins in the choroidal part of the tumor.

3) Flat tumors with no or little pigmentation are difficult to delimit since the tumor borders cannot be determined very accurately even with indirect binocular ophthalmoscopy. We now treat diffuse uveal melanomas with an increased safety margin of 3, even 4 mm.

4) Inaccurate tumor localisation was at the origin of a tumor recurrence in 7 cases treated before 1987. At present, we take into consideration the parallax that displaces the tumor basis towards the observer.

5) Some tumors have a very irregular profile, which can be modeled only by introducing each slice individually. However, the exact position of every slice is not accurate since the position obtained from B-ultra-sonography is not known with enough precision. In 3 cases, the recurrence was due to this technical insufficiency. The only way to plan such tumors accurately would be to have a treatment planning system based on CT or MR imaging scans. Since this technique is not available at present, we now enlarge the safety margins around the tumor. This leads to a good local tumor control, however with a more peritumoral tissue irradiation.

6) In 2 cases, the tumor was locally controlled but a second tumor appeared in another part of the eye. This included eyes with ocular melanocytosis which is a predisposing factor for the development of uveal melanoma. In these 2 cases, we suspect that newly formated tumors were not related to the originally treated tumor.

7) One case was enucleated by the referring ophthalmologist for a local recurrence. We did not have the opportunity to examine fundus pictures, B-ultrasounds or histological slides of this case.

8) The original treatment planning program "EYE" considered the eyelid as a plane that could be placed at a desired position and distance from the limbus. This is a simple and useful model for most of the cases. Nevertheless, the geometry of the eyelids has to be taken into account in some special situations. In 14 cases, the recurrence was due to an insufficient appreciation of the eyelid thickness inside the irradiation field. The Clatterbridge group has developed a new model which allows a much more accurate reproduction of the eyelids. This model was made available to us and we implemented it in summer 1993. At present, simulations are carried out with lid retractors, so as to determine the position of the eyelids and their thickness in the irradiation field on the positioning X-ray pictures. If necessary the treatment plan is modified taking these parameters into account.

Before January 1988, 28 of 320 patients were subject to local tumor control failure. The suppression of reduced safety margins, the better tumor localisation and the increase of the safety margins for flat uveal melanomas, as well as for melanomas invading the ciliary body, reduced the number of recurrences to 24 of 1128 patients treated since January 1988.

This data suggests that first, proton beam irradiation of uveal melanomas is a more accurate technique than brachytherapy for local tumor control and second, that an increase of the local tumor control rate may only be obtained in some particular cases by increasing the safety margins of the irradiation around the tumoral mass.

*************************************

24

**Preliminary results with one year minimum follow-up of the first 146 uveal melanomas treated with protons at C.P.O. (ORSAY)**

P. Schlienger[1,2], L. Desjardins[1,2], F. d'Hermies[1,3], L. Schwartz[1,4], A. Mazal[1],
S. Delacroix[1], C. Nauraye[1], R. Ferrand[1], M. Louis[1], E. Frau[1,5], J.L. Habrand[1,5], [1]Centre de Protonthérapie d'Orsay, Bat. 101 - Synchrocyclotron - 15 rue Georges Clemenceau, 91400 ORSAY, [2]Institut Curie, 26 rue d'Ulm, 75231 PARIS Cédex 05, [3]Hôtel Dieu de Paris (Assistance Publique), 1 place du Parvis Notre Dame, 75181 PARIS Cédex 04, [4]Hôpital Tenon (Assistance Publique), 4 rue de la Chine, 75970 PARIS Cédex 20, [5]Institut Gustave Roussy, Hautes Bruyères, Rue Camille Desmoulins, 94805 VILLEJUIF Cédex,

405 patients has been treated with protons at C.P.O. (ORSAY) from september 1991 to april 1994 included; 392 were uveal melanomas.

Initial work-out included visual acuity, findus photography, fluoroicinic angiograms and ultrasound of tumoral eye. General work-out was chest X Ray and liver ultrasound examination our therapeutical indication were as follow: enucleation for papillary tumors in young people, iodine plaques for small tumors anterior to the equator and protontherapy for all others choroidal tumors. Our protocol of treatment was 60 Gy Co equivalent in 4 fractions in 4 days with 2,5 mm of margin. The energy of the proton-beam was 73 Mev with a RBE of 1.10.

Mean age of the patients was 56 years. The mean tumor diameter was 13,1 mm and the mean tumor thickness 6,3 mm. Mean initial visual acuity cas 20/50, going from 0 to 20/20. Findings of the initial work-out were: retinal detachment in 20% and invasion of optic nerve head 8%.

**Results**: our results are only preliminary results of the first 146 patients with a follow-up of one or 2 years. 8 patients (5%) developed liver metastases. At one month tumor response at protontherapy is complete: 1,5%, partial: 10,4% and stable: 18,6%.

There is 3 recurrences (2%): one at the border of the field and 2 at 6 o'clock (there was a good control of the primary tumor but there was also an initial retural detachment).

6 eyes were enucleated (4%): 1 for tumor progression at one month, 1 for local recurrence, 2 for complications: 1 glaucoma and one perforating corneal ulceration, 2 for non seeing eye.
Visual results are: non vision 7,5%, vision between 20/40 and 20/200: 43,5%, vision bigger than 20/200 and lower than 20/40: 34%, vision superior than 20/40: 15%. If we compare initial visual acuity and visual results visual acuity is stable in 50,7%, improved in 9,7% and diminished in 39,5%.

Complications are listed and we discuss 4 points: metastases, the 12 progressions of the tumor at one month, the factors for retinal detachment at one or 2 years, and the factors influencing visual results.

**Conclusions**:
1. our preliminary results with one year minimal follow-up are equivalent with others published results,
2. Improvement in eye preservation don't change vital prognosis so we have a protocol of adjuvant chemotherapy for big tumors,
3. We persevere in protontherapy of uveal melanomas,
4. We treat also with protons choroidal angiomas and,
5. We begin to treat intracranial tumors with protons.

*************************************

**Protontherapy of Vascular Malformations in Ophthalmology.**

P. Chauvel[1,2], W. Sauerwein[1], N. Bornfeld[1], W. Friedrichs[1], W. Strunk[1], C. Mosci[1], A. Polizzi[1], A. Porta[1], E. Menci[1], T. Scolaro[1], N. Brassart[1,2], J. Hérault[1,2], A. Courdi[1,2], [1]SERAG (South Europe RAdiotherapy Group), [2]Centre Antoine-Lacassagne - Cyclotron Biomédical 227 avenue de la Lanterne NICE - France

The techniques used for the treatment of uveal melanomas have been adapted to the treatment of ophthalmic vascular malformations. As for uveal melanomas tantalum rings are inserted to delineate the treatment area and allow a good modelization of the eye. This relatively heavy technique has been preferred to the often used "light field set-up" in order to spare as much healthy tissue as possible, the first patients having previously been multi-treated by radiotherapy laser, cryosurgery, photontherapy, brachytherapy etc... The treatment planning was generally made with a very small lateral safety margin and a range reduced to avoid the irradiation of the optic disc and/or macula, the treatment only aiming to induce fibrosis in a part of the lesion and not to irradiate homogeneously a tumour volume.

9 patients were treated since September 1992, 7 for a von Hippel-Lindau (vHL) syndrom, 2 for a choroidal hemangioma. The doses used for the vHL were either 42 CGE/14 fractions/23 days or 20 CGE/4 fractions/4 days, while a dose of 50 CGE/4 fractions/4 days was delivered to the choroidal hemangiomas. The tolerance of the treatments was excellent and the first results encouraging, with a disappearance of the malformation and a fast regression of retinal detachment for the 6 first patients with a sufficient follow-up.

******************************************

**Protontherapy of Conjunctival Melanomas**

P. Chauvel[1,2], J.P. Caujolle[1,2], W. Sauerwein[1], W. Friedrichs[1], N. Brassart[1,2], J. Hérault[1,2], A. Courdi[1,2], [1]SERAG (South Europe RAdiotherapy Group), [2]Centre Antoine-Lacassagne - Cyclotron Biomédical, 227 avenue de la Lanterne NICE - France

The techniques developed for the treatment of uveal melanomas using the medical proton beam in Nice have been extrapolated to the treatment of multi-relapsing conjunctival melanomas. This preliminary study mainly aims at avoiding enucleation. Due to the natural history of the disease the target volume to be considered is very large. It includes ocular and lid conjunctiva and at least half of the total surface of the conjunctiva, in order to try to avoid further relapses at the margin of the treated volume. To preserve the visual outcome and prevent neovascular glaucoma, the beam has to pass through the lid but must avoid the internal structures of the eye. A "semi-spherical" plexiglas compensator is designed to treat the sclera on 1 mm thick from the cornea to the equator. This compensator is centered on the eye, fixed by iron rods to the collimator of the patient. To obtain the prescribed dose distribution, it is necessary to have a plane entrance orthogonal to the proton beam. This is given by a bolus mainly made of wax. Ultrasonographic gel avoids air gaps between the skin and the wax. The range and modulation of the proton beam are calculated to take in account these thicknesses. A special tool has been designed to check the thickness and the orthogonality of the bolus. Tantalium rings are inserted to delineate the target volume and allow a perfect repositioning from day to day. The possibility to treat the whole conjunctiva is under test. From June 17th, 1991 to December 17th, 1993, 338 patients have been treated by protons in Nice for an ocular disease. From these 338 patients 10 treatments have been achieved on 9 patients presenting with a conjunctival melanoma (4 men and 5 women) from March 92 to December 93. The patients were referred in various situations, from post-operative positive margins to palpable multilocated tumor. This led us to use some different                    fractionation schedules generally giving 30 CGE on

the non invaded conjunctiva and thereafter a boost of 15 to 30 CGE on the positive margin or visible tumor. The most used schedule gave 7.50 CGE/fraction. The short term follow-up does not demonstrate a particular toxicity. The first preliminary results on local control are satisfying.

*************************************

### Development of the EYE Proton Therapy Planning Program
<u>M.A. Sheen</u>, Douglas Cyclotron Unit, Clatterbridge

The program has undergone a few modifications since PTCOG XVIII:

- The drawing of the intersection of eyelid surfaces with dose planes has been improved, and is now more comprehensive.
- There is now a choice of <u>where</u> structures such as the optic disc, the macula, the limbus and the tumor itself are modeled. Instead of being restricted to the outer surface of the eye as at present, they may now be placed anywhere between the outer and inner surfaces of the eye. The fundus isodoses can also be calculated on e.g. the inner retinal surface.
- We are at last catching up with the PSI program in including all simulation data within the plan file, instead of in separate disposable clip files. This will make it possible to compare simulations automatically.

What of future developments?
The eye could certainly be modeled more accurately. For example:

- Structures are modeled in "standard" proportions and positions: these may not always be appropriate. However, maybe there are more significant sources of error:
- The limbus position in particular is important for healthy-eye fixation, yet clip-to-limbus measurements do not correspond well even for (reliable?) tumour eye fixation; a quick survey of the last 21 tumour-eye fixations gave an average clip-to-limbus measurement error of $0.2 \pm 1.3$ mm.
- We rely on ultrasound sans for the tumour height and cross-section. but experience suggests that MRI may be necessary for large and anterior tumours; a recent case with both scan modalities gave an ultrasound height of 10 mm. but MRI heights of 6 1/2 - 7 1/2 mm, the latter corresponding best to clinical observations.
- Accurate range calculation for posterior tumours requires an accurate measure of eye length & scleral thickness, but the measurement on B-scan does seem to be somewhat subjective; there is for example a difference of average scleral thickness of 0.3 mm between referral centres. Would A-scan be more reliable?
- The range is also dependent on the assumed density of tissue: we use a constant 1.05 but published values for various structures vary between 1.002 and 1.12. Maybe we should be taking account of density variations; the difference between a constant 1.050 and eg. 1.010 means a difference in range of 1 mm over 25 mm.
- Eyelids; they can be modeled quite accurately, but how to measure them satisfactorily? Photographs with superimposed fiduciary grids would be a start.
- Non-spherical eyes eg. myopic ones. Even if possible, is data up to it?
- Possible future extensions to the model may be:
  - Eyelids parabolic in plan / curved from the side.
  - A model of the tear duct.

- A model of the supra-orbital margin (currently we use a dummy "wedge" for this).
- Skin plane: more than one value for different areas ?
- Non-spherical eyes
- Multiple fields
- Any other suggestions?

*************************************

### RBE Determinations for the 70 MeV Proton Beam at TRIUMF using Cultured V79-WNRE Cells

L.D. Skarsgard, B.G. Wouters, G.K.Y. Lam, R.E. Durand and A. Sy, B.C. Cancer Research Centre and TRIUMF, University of British Columbia, Vancouver, B.C., Canada

We have carried out preliminary RBE measurements on the 70 MeV proton beam at TRIUMF using cultured V79-WNRE Chinese hamster cells.  The beam which we used had a modulated stopping peak width of 1.8 cm and a field diameter of 2.5 cm.  Cell survival was measured on the axis of the beam, using the sliced gel technique of Skarsgard *et al.*, developed for similar studies of the pion beam at TRIUMF some years ago.  One upgrade which went into these experiments was the use of the cell-sorting technique to improve the precision of the survival measurements, particularly at low dose.  Briefly, cells were suspended in 37° C medium containing 12% gelatin; this was poured into 12.5 mm diameter ABS plastic tubes which were then sealed, cooled and irradiated end-on, at ~ 0° C.  After irradiation the gel was extruded and sliced in 2 mm steps, the slice was melted in warm medium and the sample passed through a cell sorter which dispensed a known number of cells into a test tube, for plating and scoring in the conventional manner. Cobalt-60 was used as the comparison radiation.  The results of these preliminary measurements gave a median RBE relative to $^{60}$Co of $1.22 \pm 0.12$ at the centre of the dose distribution, measured in these V79-WNRE cells at S.F. = 0.01.  The RBE was found to increase with depth in the modulated stopping peak, and at the distal edge appears to rise more sharply, to an extent that may be of concern when this part of the treatment volume is close to sensitive normal tissues.  The RBE for protons was also found to be dose-dependent and increases significantly for doses less than 4 Gy.

*************************************

### The RBE of Low-Energy Protons

Melvyn Folkard, Kevin M. Prise, Heidi C. Newman, Michael J. Roper and Barry D. Michael, Cancer Research Campaign, Gray Laboratory, P.O. Box 100, Mount Vernon Hospital, Northwood, Middx, HA6 2JR, U.K.

In recent years we have undertaken a considerable study of the effectiveness of protons and deuterons with energies below 2 MeV (i.e. in the LET range 15-60 keV  m$^{-1}$).  In this region the biological effectiveness for a number of functional endpoints exhibits a strong dependence on LET (although significantly, not for DNA double-strand break induction).  The experiments were performed by spreading V79 mammalian cells as a monolayer on membrane filters.  These are supported on a rotating platter that sweeps the cells past a silt-collimated exit window on our 4 MV Van de Graaff accelerator.  The dose is determined by the speed of rotation.  We have shown that in the range 20-50 keV  m$^{-1}$ protons and deuterons are more effective at inactivating cells than that reported for  -particles of equivalent LET, and that the peak effectiveness of singly-charged particles is in the 40-50 keV  m$^{-1}$ region.  These differences may reflect dissimilarities in the track-structures of LET-matched singly- and doubly-charged particles.  Using the technique of neutral filter elution, we have also shown that the induction of DNA double-strand breaks by            protons of all energies studied is similar to that seen

using energetic X-rays.  This suggests that the LET dependence of lethality is due primarily to the greater complexity of DNA double-strand breaks, rather than their yield.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

### A New Proton Dose Algorithm for Radiotherapy

C. Lee, G.A. Sandison, L.S. Papiez and X. Lu, Department of Radiation Oncology, Indiana University Medical Center, Indianapolis, Indiana  46202, U.S.A.

This algorithm recursively propagates the proton distribution in energy, angle and space at one level in an absorbing medium to another at slightly greater depth, until all the protons are stopped.

The angular transition density describing the proton trajectory is based on Moliere's multiple scattering theory and Vavilov's theory of energy loss along the protons' path increment. These multiple scattering and energy loss distributions are sampled using equal probability spacing to optimize computational speed while maintaining calculational accuracy. Nuclear interactions are accounted for by using a simple exponential expression to describe the loss of protons along a given path increment and the fraction of the original energy retained by the proton is deposited locally.

Three levels of testing for the algorithm are provided: 1) Absolute dose comparisons with PTRAN Monte Carlo simulations in homogeneous water media, 2) Modeling of a fixed beam line including the scattering system and range modulator and comparisons with measured data in a homogeneous water phantom, and 3) Relative dose comparisons with the predictions of an equivalent pathlength method for a patient's anatomy described X-ray CT.

The dose accuracy of this algorithm is shown to be within 5% throughout the range of a 200 MeV proton and it has an adequate spatial accuracy of 1 mm.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

### Proteus 3D: A Complete Proton Radiotherapy Planning System 50-250 MeV

H. Breuer, Stellenbosch Scientific Instruments CC, 20 Constantia Avenue, Stellenbosch 7600, South Africa

Criteria for a useful planning system were developed: maximizing target dose, high accuracy, minimal planning time, steep learning curve, etc. Semi-automatic planning according to optimization criteria is a desirable feature in a 3D planning program.  In addition, the planning system should be complete, i e. consist of matching hard- and software to eliminate compatibility problems. The Proteus 3D system has been developed with the above features in mind.  Its input consists of an arbitrary number of CT/MRI slices, a 3D beam intensity matrix and outlined target and radiosensitive volumes.  Contour-, density- and scattering corrections are performed. The system can handle up to six beams simultaneously, at any entrance angle.  The energy range supported is 50-250 MeV. Output includes: isodose distribution in 3+1 planes and 3D, dose distribution along any user- defined line, beams-eye view and many other relevant information.  Typical computation time for one fully adjusted beam is less than a minute; this allows a complete treatment plan to be generated within an hour. Uncertainties inherent to a planning system were presented in detail. The Proteus system has been verified at NAC, using a 193 MeV proton beam. The average deviation from the measured 50% isodose line was about 3 mm.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

**Proton treatment planning software at Orsay: a preliminary version.**

A. Mazal, J.C. Rosenwald, R. Belshi, R. Oozeer, J.P. Houlard, F. Berre, G. Gaboriaud,
H. Bouhnik, J.L. Habrand, D. Ponvert, Centre de Protonthérapie d'Orsay

The ophtalmological beam line at Orsay has been modified to allow the treatment of brain lesions at higher energies. Such treatments are planned using a preliminary version of a ray-tracing algorithm incorporated into a general treatment planning system for conventional therapy (photons, electrons). CT slices are used interactively to generate beam's eye views, x-ray views for patient positionning with fiducial points, and to calculate range, modulation, collimators and compensators.

Only the "primary" component is used for the proton beams calculations. Modulated depth dose data are stored in files. The lateral penumbra is calculated using scaled variables (depth/range), taking into account the depth, the range, the collimator-skin distance, the compensator width and the compensator to skin air-gap. Heterogeneities are taken into account using the equivalent path length method based on mean electronic density of structures. At a research stage, a pencil beam algorithm, dose-volume histograms, digital reconstructed radiographs and other routines give us additional information.

Clinical applications started in december 1993 (intracranial targets), and the preliminary version is continuously being improved, particularly to take into account complex bone heterogeneities of the base of the skull and air cavities.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

**Status Report of the Proton and Neutron Facility in Nice.**

P. Chauvel[1,2], N. Brassart[1,2], J. Hérault[1,2], A. Courdi[1,2], J.P. Caujolle[1,2], J.D. Grange[1], O. Mouries[1], L. Diallo-Rosier[1], C. Mosci[1], A. Polizzi[1], A. Porta[1], E. Menci[1], N. Bornfeld[1], W. Friedrichs[1], J. Sahel[1], F. Bacin[1], J.P. Gérard[1], W. Sauerwein[1], T. Scolaro[1], C. Carrie[1], G. Kantor[1], R. Rozan[1], E. Teissier[1,2], R.J. Bensadoun[1,2], J.L. Lagrange[1,2], F. Demard[1,2] [1]SERAG (South Europe RAdiotherapy Group), [2]Centre Antoine-Lacassagne - Cyclotron Biomédical, 227 avenue de la Lanterne NICE - France

Since June 1991, the proton facility installed in the Centre Antoine-Lacassagne has treated a total number of 401 patients presenting an ophthalmic pathology. The tantalum rings are inserted by the ophthalmologists participating in the SERAG and following their own treatment policy between surgery, plaques and protons. From june 17th, 1991 to december 17th, 1993, a total number of 338 patients have been treated (Nice: 108, Lyon: 101, Berlin: 40, Essen: 33, Bordeaux: 21, Genova: 17, Strasbourg: 10, Clermont-Ferrand: 6, others: 2). This number encompasses 320 uveal melanomas (157 men, 163 women), 10 conjunctival melanomas, 6 hemangiomas, 1 retinoblastoma and 1 ocular metastasis. For the series of uveal melanomas, the distribution by site and T was: posterior pole 64%, equator 26%, ciliary body 10%, T1 7%, T2 27%, T3 66%. The tumor thickness (in mm) was: $\leq$ 3: 22.1%, $\leq$ 5: 26%, $\leq$ 7: 21.4%, $\leq$ 10: 23.1%, > 10: 7.4%, while the tumor volume was: $\leq$ 1cc: 49.7%, $\leq$ 2cc: 40.5%, < 3cc: 8.3%, > 3cc: 1.5%. The maximum range distribution (in mm of eye tissue) was: < 15: 2.4%, < 20: 7.7%, < 25 35.6%, < 30: 50.7%, $\geq$ 30 3.6% and the % of the total range spread-out was: < 50%: 17.1%, < 70%: 25.2%, < 90%: 37.4%, $\geq$ 90%: 20.3%. The treatment was given through a bolus in 72% of the total number of patients. For 1993, 96% of the patients had a bolus. A wedge filter (or 2) was introduced in the beam in view of disc and/or macula protection in 53.4% of the total number of patients versus 74% in 1993. The distal safety margin was as follows for the total series: $\leq$ 0.5mm: 33.1%, $\leq$ 1.5mm: 36.6%, $\geq$ 1.5mm: 30.3%. For the patients treated in 1993 the use of reduced margins was more important: $\leq$ 0.5mm: 52.7%, $\leq$

1.5mm: 32%, $\geq$ 1.5mm: 15.3%. The first data obtained from the actuarial follow up of posterior pole tumors are:

| % of | 12 months | 24 months | 30 months |
|---|---|---|---|
| eyes retained | 97.5 | 89.4 | 89.4 |
| metastasis free | 98 | 91 | 83 |
| survival | 99 | 95 | 95 |

It is too early to give any formal conclusion but these figures seem to be in agreement with other published data.

The clinical neutrontherapy program started by november 8th, 1993 and up-to-now 7 patients were treated. The 3 treated in 1993 presented: 1 advanced maxillary antrum, 1 angiosarcoma (ilio-pubic relapse), 1 cutaneous melanoma (hand metastasis). The 4 patients of 1994 are: 1 cutaneous melanoma (leg metastasis), 3 adenoid cystic carcinomas (1 relapse of a parotid, 1 hard palate involving the pterygo-maxillary fossa, 1 superior gingival sulcus involving the pterygo-maxillary fossa). The program will be extended during 1994 and 1995 to inoperable bone and soft tissue sarcomas and advanced prostatic adenocarcinomas .

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

## The Neutron and Proton Therapy Programmes at the NAC.

C. Stannard, F. Vernimmen, J. Wilson, J. Hough, D. Jones, N. Schreuder, J. Symons, D. Werner, B. Smit, G. Schmitt

Neutron therapy, p (66 MeV)/Be, have been available on a regular basis since February 1989 and 608 patients have been treated in the last 5 years.

Proton therapy for intracranial lesions was started on 10 September 1993 using a 200 MeV fixed horizontal beam and the stereophotogrammatic patient positioning system, SPG.

The beam is available once a week but as the system is non-invasive and easily reproducible with an accuracy of less than 1 mm, fractionated treatment is possible. Treatment was started with the cross fire plateau technique and since 18 February 1994 treatment on the SOBP is also possible.

Twenty one lesions with a median volume of 9.2 cc (1-43 cc) have been treated. AVM's received 24-34 Gy in 2 or 3 fractions, metastases 16-25 Gy in 1-3 fractions and meningiomas 30-34 Gy in 3 fractions. The dose and number of fractions depended on the size of the lesion and previous radiotherapy.

The initial results are very promising in terms of tumour response and improvement of symptoms.

The future:- because of the limitations of available commercial planning systems we have recently acquired VOXELPLAN from DKFZ, Heidelberg, into which the Royal Marsden proton module has been integrated. This will shortly be used for full 3D noncoplanar planning with inhomogeneity corrections. The availability of the proton beam for 2 and eventually 3 days per week together with another proton beam line and possibly an isocentric gantry would allow fractionated treatments and boosts to a variety of intracranial, head and neck and pelvic tumours.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

# Recent Developments at the TRIUMF Eye Facility

U. Oelfke, S. Atkins, E. Blackmore, S. Chavez, K. Gardey, E. El-Khatib, G. Lam, M. Nicolic, K. Paton,
T. Pickles, J. Rootman, L. Skarsgard and J. Vincent,
TRIUMF, University of British Columbia, Vancouver, Canada

The development of the proton facility for the treatment of ocular tumors at TRIUMF approaches its final stage. Within the last three months the installation of beam delivery and monitoring devices at the proton channel 2C were completed and the first patient treatment is anticipated for August or September 1994.

The layout of our beamline follows closely the standard setups of existing facilities. The beam of 70 MeV protons, with an extracted current of 1 - 5 nA in order to achieve the required dose rate of 15 - 30 Gy/min, is monitored by a system of standard devices, consisting of i) an SEM watching for beam bursts, ii) a profile wire chamber for first beam alignment and iii) a multipurpose ionization chamber complex with an independent transmission foil as a backup and a quadrant foil for the detection of lateral beam displacements. The delivery of the clinically required dose profiles is achieved by a conventional system of a single scattering foil (1/32 in. of Pb), various collimators and the standard range shifter and range modulator devices. The various components were successfully tested in recent dosimetry studies in March 1994. The installation of the two crucial remaining hardware components, the control console and the treatment chair, as well as the final testing of the controls software are expected to be completed in early July.

The acquisition of dosimetry data as required for treatment planning with the code EYEPLAN is also almost completed. Relative proton dosimetry data were obtained by using diode detectors in a water phantom. For a stable cyclotron tune dose calibrations and dose profiles were observed to be reproducible within 1% and 2 -3% respectively. A dose uniformity of ± 2% was achieved for SOBPs of plateau widths ranging from 5 - 20 mm. Furthermore, first RBE measurements were recently completed and analyzed, indicating an average RBE of 1.2 ± 0.1 for a SOBP of 20 mm.

Further ongoing developments in treatment planning and dosimetry at TRIUMF are related to the eye facility as well as to the proposed treatment site for larger fields. For the eye project, various options to improve the standard treatment planning procedure are investigated, e.g. computer automated search for eye fixation angles or the benefits of a treatment with two different ports. For larger fields, the feasibility of quantitative 'in vivo' proton dosimetry with PET techniques is under study. Furthermore, a collaboration with the German cancer research centre (DKFZ) in Heidelberg was started to develop a 3D dose algorithm for proton therapy of larger fields. The long term aim of this work is to create a unified 3D treatment planning system for photon and proton therapy by integrating the developed proton dose algorithms into the 3D photon treatment planning system VOXELPLAN of the DKFZ.

**************************************

# Status of the Berlin Eye Treatment Facility

J. Heese, H. Homeyer, H. Kluge, H. Morgenstern, J.-U. Schmollack [HMI Berlin];
N. Bornfeld and M. Foerster [Klinikum Steglitz der FU Berlin];
V. Budach [Universitatsklinikum Charite der HU Berlin]

A collaboration between the ophtalmic hospital of the Klinikum Steglitz (Free University Berlin), the radiotherapy department of the Charite (Humboldt University) and the Hahn-Meitner-Institute was initiated to establish a facility for the treatment of ocular melanoma using proton beams of the VICKSI cyclotron at HMI. The funding of this facility will be provided by the Klinikum Steglitz. The VICKSI cyclotron can accelerate protons up to an energy of 72 MeV which is suitable for the treatment of ocular

melanoma. Measurements using a beam of 72 MeV protons and tests of the beam delivery reliability have been carried out since summer 1993.

An existing beamline has been modified (installation of a scattering foil and collimators) for experiments with the 72 MeV proton beam and is presently used 1-2 days/month for experiments with the beam. Depth-dose curves of a collimated beam in water show Bragg peak to entrance dose ratios of 5:1. The measured relative dose fluctuations across the lateral beam profiles in water are smaller than 5%. Measured energy spectra of the proton beam show besides the full energy peak at 72 MeV a continuous background with approx. 5% of the total intensity.

A therapy control room and a patient waiting room with a separate entrance to the treatment area are planned and have to be added to the cyclotron building. It is planned to start treatments in late 1995. The cyclotron will then be used for the proton therapy of ocular melanoma one week per month. The treatment capacity will be approx. 150 patients/year.

*************************************

## Physical specifications of therapeutical proton beams from a synchrotron

G. Arduini[1], C. Canz.i[2], R. Cabria[2], F. Gerardi[3], R. Leone[3], L. Sangaletti[3], M. Silari[4.]
[1]Associazione per lo Sviluppo Scientifico c Tecnologico del Piemonte, Villa Gualino, Via Scitimio, Severo 65, 10133 Torino, Italy, [2]Fondazione per Adroterapia Oncologica, Via Puccini 11, 28100 Novara, Italy [3]Fondazione Italiana per la Ricerca sul Cancro, Via F. Corridoni 7, 20122 Milano, Italy, [4]Consiglio Nazionale delle Ricerche, Istituto Tecnologie Biomediche Avanzate, Via Ampere 56, 20131 Milano, Italy

The higher  ballistic selectivity of protons as compared to photons and electrons used in conventional radiation therapy requires that stringent specifications on the dose delivery be met, in order to achieve a full 3-D conformal therapy.  These clinical requirements translate into a set of performance specifications on the accelerator and the beam transport and delivery systems.  Ref. 1 has been used as a guideline in elaborating the clinical, physical and engineering aspects related to the use of protons in radiation therapy.

A discussion is given on energy range, energy variability, beam intensity, dose uniformity, lateral penumbra, distal dose fall-off, source-to-surface distance (SSD), time structure of the extracted beam, raster scanning system specifications and beam abort time.  These aspects are treated with reference to a synchrotron.  The accelerator complex under design is described in Ref. 2. Conservative assumptions have been made for those components which are not completely defined at the present stage of the project.  The physical specifications for the Hadron therapy Centre are shown in Table 1 in comparison with the equivalent requirements developed by the LBL group.

The beam delivery systems resulted to be crucial in defining the physical performances.  On the one hand the passive beam spreading system mainly affects the accelerator design in terms of the maximum energy and intensity of the proton beams.  On the other hand, the time structure of the extracted beam (i.e. the spill length and the intensity fluctuations) must be compatible with the active intensity-controlled raster scanning system, in particular with the switch-mode power supplies features and with the dose and position monitoring system.

The gantry design must fulfill the clinical requirements on the minimum (greater than 2 m) source-to-surface distance.  At the same time, the gantry features affect the design of the scanning system because of the constraints on the magnet length and gap (and therefore weight) as well as on the maximum current in the scanning magnets, fixed by the maximum field size and by the distance between the centre of the downstream magnet and the target.

1. W.T. Chu *et al., Performance specifications for proton medical facility*, LBL 33749 (March 1993)
2. G. Arduini, R. Leone, R.L. Martin, S. Rossi and M. Silari, *The ltalian hadrontherapy accelerator complex,* Proc. of the Int. Symposium on Hadron, Therapy, Como (Italy), October 18-21, 1993, in press

**Table 1. Physical specifications for the Hadrontherapy Centre and equivalent requirements developed by the LBL group.**

| | **Hadrontherapy centre** | **LBL** |
|---|---|---|
| Energy range | 60 - 250 MeV | 70 - 250 MeV |
| Energy variability | $\leq 0.8$ MeV | $\leq 0.4$ MeV |
| Energy variability accuracy | $\pm 80$ keV | $\leq \pm 0.4$ MeV |
| Beam intensity measured at the vacuum exit window of the beam lines | $\geq 9$ nA[a] over the full energy range | 16 nA at 200 MeV |
| Momentum spread | $\leq \pm 3.3$ x $10^{-3}$ | $\leq \pm 1$ x $10^{-3}$ at 100 MeV ($\leq \pm 0.1\%$ FWHM at 100 MeV) |
| Spill length | 250 ms (normal operation) | $> 1$ s (down to 0.1 s if the synchrotron cycle rate can be increased) |
| Repetition rate | 2 Hz | 0.5 Hz |
| Duty cycle | 50% | $> 50\%$ |
| Beam abort time (after reception of a trigger signal) | $< 60$ µs | |

[a] 90% transport efficiency has been assumed for the beam transport system.

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*