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ABSTRACTS

of the

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POSTER PRESENTATIONS

Page

Current Status of Particle therapy Facilities in Japan.

K. Kawachi, Nuclear Safety Technology Center

A similar title was presented at the PTCOG 29th meeting in Chiba, entitled "On going particle therapy projects in Japan". It would be very interest to compare with the previous paper on the progress in these three years.

The PMRC of The University of Tsukuba closed the clinical trial of proton therapy at KEK in 2000 at the time a total number of treated patients reached to 700. And now, the PMRC has been started a new clinical trial using a newly constructed facility attached to the University Hospital since last September. It has two rotating gantries for the treatment and other horizontals for experiments. Although these gantries are using a double scattering method for spreading a field size, they have been installed the respiratory gated irradiation devices.

The NIRS has still continued 70 MeV proton beam therapy for eye treatment using a medical cyclotron. The clinical trials of carbon beam therapy using the HIMAC have progressed quite well, and the total number of treated patients exceeded 1,000 in last July. The 3-D conformal irradiation using broad beam will start next April. A new challenge of radioactive beam therapy using spot beam scanning has been still under preparation.

In the NCC Hospital East, the proton therapy of several sites has been recognized as an advanced medical treatment by the Ministry of Health and Welfare, and the patients have had to bear the cost since last July.

The PATRO of Hyogo Ion Beam Medical Center was completed in 2000 and started the clinical trial of proton therapy in last July. The total number of treated patients is 30. The characteristics of this facility is both protons and heavy ions are available for treatment, and has a 45° oblique beam line for treatment. Although two rotating gantries are designed for proton therapy, the other beam lines for therapy are available for both proton and heavy ion therapy. The clinical trial of carbon beam therapy will start in January of 2002.

An accelerator facility of the Wakasa Wan Energy Research Center was completed in 2000 and has been opened for various researches and experiments. However, the medical facility is now under commissioning. The clinical trial of proton therapy will start next April.

At Shizuoka prefecture, the cancer center building was almost completed and the proton accelerator was once assembled at the factory and has installed into the building. They expect to start the clinical trial in 2003.

Comparing with the previous paper, the most of the Japanese projects are progressed quite well on their schedule. Finally, we expect to come up new projects in near future.

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Clinical result of proton-beam radiotherapy for non-small cell lung cancer

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PURPOSE: To determine clinical result of proton-beam radiotherapy for patients with non-small cell lung cancer (NSCLC).
PATIENTS & METHODS: In Proton Medical Research Center of Tsukuba University, fifty-one patients with non-small cell lung cancer were treated by proton-beam radiotherapy using 250 MeV proton delivered from booster synclotron at National Laboratory for High Energy Physics from 1983 until 2000. The clinical stage by the International Union against Cancer (UICC, 1997) was stage I in 28, stage II 9, stage III 8, and stage IV 1. Five was recurrent cases. Histopathologically, 33 were squamous cell carcinoma, 17 adenocarcinoma and 1 large cell carcinoma. The median total and fraction doses were 76.0 Gy ranging from 49.0 Gy to 93.0 Gy and 3.0 Gy ranging from 2.0 Gy to 6.0 Gy, respectively.
RESULTS: The overall survival at 1 and 5 year for the entire group of 51 patients was 73.9% and 23.7%, respectively. The 5-year cause-specific survival according clinical stage was 41.1% for stage I-II patients. For 28 patients with stage I, the overall and cause-specific survival at 5 year was 23.3% and 33.1%, respectively. In comparison between 9 patients with stage IA (cT1NO) and 19 patients with stage IB (cT2NO), the prognosis was better in stage IA than in stage IB: 5-year overall and disease-free survival was 62.5% and 85.7% for stage IA, and was 14.5% and 16.2% for stage IB, respectively ($p < 0.05$). The 5-year in-field local control rate also tended to be higher in stage IA (87.5%) than in stage IB (34.6%). Loco-regional recurrence including lymph node metastasis outside of radiation field was observed in 8 of 19 patients with stage IB (50%) during follow-up periods (3-40 months). No serious lung toxicities were observed.
CONCLUSION: Proton-beam radiotherapy is considered as a safe and effective treatment for NSCLC. However, optimal method of this treatment remains to be established in future.

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Long-term results of proton beam therapy for carcinoma of the uterine cervix.

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Purpose: To examine the long-term results of patients with carcinoma of the uterine cervix treated with proton beam therapy in order to determine whether proton beam therapy can be an alternative to intracavitary irradiation.
Methods and Materials: From 1983 to 1991, 25 patients with squamous cell carcinoma of the uterine cervix treated with curative intent by proton beam therapy. Nine patients had stage IIB, 15 stage IIIB, and one stage IVA. All patients underwent photon beam irradiation to whole pelvis with or without center shielding combined with proton beam therapy to primary tumors. Doses to the primary tumor ranged from 70.7 to 101Gy (median: 86.2Gy). Proton beam therapy was delivered either by single anterior field in 4 patients or two angled fields with an anterior and a lateral field in 21 patients.
Results: Follow-up times ranged from 11 to 184 months (median: 139 months). Fourteen patients were followed more than 10 years. The 10-year overall survival rates for all patients, stage IIB and stage IIIB/IVA were 59%, 89% and 40%, respectively. The 5-year local control rates for all patients, stage IIB, and stage IIIB/IVA were 75%, 100% and 61%, respectively. Thirteen patients (52%) developed late complication for small/large intestine and/or urinary bladder. Only one patient (4%) experienced severe late complication for small/large intestine and bladder requiring surgical intervention.
Conclusion: Proton beam therapy could produce the equivalent local control and survival to intracavitary irradiation. As compared with intracavitary irradiation, the incidence of severe late complication was similar, although that of mild late complication was higher. Therefore, proton beam therapy could be an alternative to intracavitary irradiation in the treatment of cervical cancers in terms of long-term follow-up results.

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Clinical results of proton radiation therapy for cancer of the esophagus.

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Purpose: To describe the outcome of proton radiation therapy for patients with carcinoma of the esophagus.
Methods and Materials: Fifty-two patients with cancer of the esophagus who were treated with 250 MeV protons with or without x-rays were analyzed; they were chosen from among 59 such patients treated at our institution between 1985 and 2000. All were locoregionally confined and had squamous histology but one adenocarcinoma. The median tumor length was 4.7 cm (range, 1.5-15). Six patients received proton radiation therapy alone (75 Gy - 89.5 Gy, median 82 Gy) over 33 - 62 days (median 54 days), and forty patients received combination of x-rays and protons (69.1 Gy - 87.4 Gy, median 76 Gy) over 44 - 99 days (median 61 days) with conventional fractionation. The remaining six patients were treated with concomitant boost technique (73 Gy - 79.8 Gy, median 75.1 Gy) over 38 - 53 days (median 48 days). The median follow-up period was 30 months.
Results: Five-year actuarial survival for the 52 patients, and for patients with TI (n=26) or T2 - 4 (26) were 39.4%, 57.7%, and 22.0%, respectively. The disease-specific survival for the 52 patients, and for patients with T1 or T2 - 4 were 70.2%, 95.8%, and 40.2%, respectively. Two-year local control rates for patients with T1, T2/3 lesions were 90.5%, and 61.4%, respectively. Median follow-up time of the patients with T4 lesion was so short as 8 months that local control for these patients was not assessed. The sites of first treatment failures were local-regional for 16 patients, and distant organs for 2 patients. Acute esophageal reactions were modest. Forty-nine percent (21/ 43) of the patients developed treatment-related esophageal ulcer, and the ulcers subsided with conservative treatment in 67%: of these cases.
Conclusions: The results suggest that proton radiation therapy is a feasible and effective modality for patients with locally confined esophageal cancer. Further studies will be needed to determine the optimal total dose, fractionation schedules, and better combinations of protons and conventional x-rays.

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Short-Course Radiotherapy with Carbon Ions for Hepatocellular Carcinoma.

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Purpose: To evaluate safety and clinical efficacy of short-course radiotherapy with carbon-ion beams in hepatocellular carcinoma (HCC).
Methods and Materials: Between April 1997 and March 2000, 82 patients with HCC (most of them were associated with liver cirrhosis) were treated in a Phase I/II dose escalation study using short-course carbon-ion therapy : 33 patients were treated with 12 fractions / 3 weeks, 22 patients with 8 frs./ 2 wks., 27 patients with 4 frs./ 1 wk.). These patients had a history of previous unsuccessful treatments or had tumors not suited for other modalities including surgery, TAE or ethanol injection. Radiation-related morbidity was evaluated using RTOG/EORTC criteria and Child-Pugh's grading score. The tumor effect was assessed by local control rates and cumulative survival rates.
Results: Median follow-up time was 22 (range 4-54) months. So far, none of the patients developed severe morbidity. There were no treatment-related deaths. Local control rates were 94.1 % at 1 year and 87.2% at 2 and 3 years after the treatment. The overall and cause-specific survival rates at 2 years were 71.0% and 77.4%, respectively.
Conclusion: It is preliminarily concluded that, based on the results of PhaseI/II trials, the short-course carbon-ion therapy is a safe and effective method in the management of HCC not suited for other treatments.

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Preliminary results of a phase II study of proton therapy for hepatocellular carcinoma.

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Backgrounds: Proton therapy is thought to be a promising method for local cure even for patients with HCC that is not amenable to surgical resection or local ablation therapy.
Patients and Methods: Twenty-two patients with localized HCC had been already enrolled in this study between May, 1999 and May, 2001. A total dose of 76 GyE / 20 fractions was administered with 3.8 GyE, once-daily fractionation from Monday through Thursday in a week, using respiration-gated irradiation system. Relative biological effectiveness was estimated as 1.1.
Results: Histological confirmations were obtained in all but 2 patients with fine needle biopsy. All patients were completed their treatments. For 11 patients who were followed-up for more than 1 year, all but 1 were locally controlled. Four out of the 11 patients died of multicentric intrahepatic recurrence (1), lung metastasis (1), and liver failure (2).
Conclusion: High efficacy of proton therapy for local cure in patients with HCC was suggested. Predicting a risk of treatment-related liver failure is the problem of subsequent study. Expected total number of patients enrolled is 30.

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Results of proton therapy for hepatocellular carcinoma at University of Tsukuba.

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Purpose: To retrospectively evaluate the effectiveness of proton therapy for hepatocellular carcinoma.
Materials and methods: From August 1983 to March 2000, 236 patients were treated with proton therapy with or without transarterial embolization and /or percutaneous ethanol injection. The majority of patients were unresectable because of liver dysfunction or other medical reasons and received 72 Gy in 16 fractions during 3.2 weeks.
Results: Overall median and actuarial 3-year survival rates were 29 months and 43 %, respectively. For 137 patients who underwent proton therapy as the initial therapy, overall median and actuarial 3-year survival rates were 40 months and 56 %, respectively. Actuarial 3-year local control rates for all patients and patients who underwent proton therapy as the initial therapy were 93 % and 97 %, respectively. Prognostic factors for the latter associated with survival rates were clinical stage, tumor size and performance status. Twenty one patients were treated with proton therapy repeatedly without deteriorating liver functions.
Conclusions: High local control and low morbidity rates suggested that proton therapy is effective and safe modality, even for patients with liver dysfunction.

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Proton radiation therapy of lesions of the trunk: experience at PSI.

G. Goitein, A. Lomax, Team Radiation Medicine, PSI

Between 1996 and December 2000, 72 patients underwent proton radiation therapy for deep-seated tumors at PSI. Of these, sixteen patients suffered from various lesions in the trunk, one patients mentioned here presented with multiple lesions based on neurofibromatosis, one of whom was irradiated after complete resection in the upper leg. Histologies : 2 chondrosarcomas (pelvis, neck), 6 sacral chordomas, 1 huge sacral metastasis of a rectal cancer, 2 osteosarcomas, 5 soft tissue sarcomas (2 retroperitoneal, 1 shoulder, 1 thorax/neck, 1 leg). Age varied from 16 to 80 years, mean 51.8, 6 females, 10 males. Most lesions were substantially large, PTVs ranged from 12 to 3903 cc, mean 1235 cc. Most patients received combined photon - proton treatment, mainly due to limitations of the beam time at PSI. Therefore, the proton doses varied between 16.2 and 74 CGE, mean 43.2 CGE.

Four patients (treatments 1997) died from generalization. Of the 12 patients alive (10 - 46 months, mean 17m.), 1 patient presented with tumor regrowth at 8m after a phase of partial regression and clinical improvement. The patient with neurofibromatosis was controlled for 20 m., now we see a marginal relapse beside multiple new lesions of unclear dignity in the abdomen. So far we have not seen any toxicity greater grade 2 in the patients alive. One patient with a huge pelvic chordoma with skin invasion developed a fistula within this region. The histological examination showed tumor necrosis.

The irradiation of tumors of the trunk is often characterized by a) large volumes, b) moving targets, c) complicated postoperative situations including metal implants, unclear surgical margins. Protons offer an excellent tool for highly conformal, high dose irradiation of these challenging lesions.

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PROSCAN: A Long-Term Commitment for the Advancement of Technology in the Field of Proton Therapy at PSI.

M. Jermann, PSI

Based on the past developments and successes of the proton therapy at the Paul Scherrer Institute (PSI) we decided in 2000 to expand the activities in this field and we founded and started the project PROSCAN. The overall objective of PROSCAN is to implement and operate at PSI a base technology laboratory for the advancement of proton therapy system techniques and applications. This long-term program, which is based on the experience with the PSI compact spot-scanning Gantry, aims to optimise the irradiation and treatment technique and to prepare the compact Gantry system for a transfer into a `marketable product' for hospital applications. Within the project an expansion of the technical infrastructure will be realized: The existing spot-scanning Gantry will be connected through a new beam transport system to a dedicated 250 MeV compact proton cyclotron, which was decided and ordered in May 2001. An advanced compact Gantry will be developed, with the objectives, (a) to optimise the irradiation technique and the precision of tumour treatments, and (b) to upgrade the patient positioning and handling procedures. A horizontal beam area, used for the treatment of ocular lesions and for R&D of other specific tumour indications, will also be connected to the new cyclotron. With an extended, but limited clinical R&D program, which runs in parallel to the technological developments, we intend to contribute in the international framework with other centres to the demonstration of the strengths and the potential of this treatment method in a lager number of cancer patients. In parallel, with our ten years program we aim to support the education of technical and medical specialists for the introduction of this new and advanced therapy method in the hospitals. In the presentation we will explain, how we implemented the above strategy for the advancement of proton therapy technologies as part of the activities of a national research centre.

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Respiration Synchronized Operation of the Accelerator System in PMRC, Univ. of Tsukuba.

M. Umezawa, Collaboration of Hitachi, Ltd. and PMRC, Univ. of Tsukuba

We realized the respiration synchronized operation by controlling the synchrotron with variable repetition rate and flattop period and applying transverse RF driven slow extraction. The synchrotron is operated by two trigger signals generated from the patient's respiration. Beam injection and acceleration sequence starts by receiving the "pre-trigger". This means the variable repetition rate. After the end of acceleration, synchrotron waits the "trigger for beam extraction". This means the variable flat-top period. When this trigger ends, the extracted beam can be stopped very quickly within 0.2msec by the termination of transverse RE In this operation, the repetition rate can be changed from 0.15Hz to 0.5Hz and the flat-top period can be extended to 5sec. The present scheme is being applied to clinical trials with satisfactory function and stability.

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FFAG Accelerator for Proton Therapy.

S.Machida and Y.Mori, KEK, Japan

FFAG (Fixed Field Alternating Gradient) synchrotron has a enormous potential for medical applications. It is easy to operate, easy to change beam energy with high repetition rates, and can deliver high average beam current. We will present the recent development of a FFAG synchrotron and show an example of medical applications.

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Implementing a smooth-beam extraction control method in a synchrotron-based PBTS for active and gated beam treatments.

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Active beam delivery and intensity-modulated proton therapy requires improved techniques for spatial and intensity control, as compared to passively scattered treatments. Ability to gate beam intensity is also desired for improved dose conformity when treating targets with motion. For synchrotron-based accelerator sources, feedback control is needed to compensate for natural variations in the slow resonant extraction process. Trade-offs can be made to determine the optimal allocation of intensity control performance requirements for accelerator and beam delivery systems. For the LLUMC Proton Beam Treatment System, a smooth extracted beam intensity goal of 5% uniformity up to 1 kHz frequency was established. Preliminary test results of a non-destructive intensity monitor and extraction control magnet already demonstrate the ability to monitor and regulate the extraction process to better than 15%. Additionally, beam gating capability has been demonstrated, and achieved turn-on times of less than 2 milliseconds, and turn-off times of less than 1 millisecond. Suggestions for follow-on work to further improve performance of the system are also presented. The achieved results thus far demonstrate the ability to achieve good beam intensity and gating control while also providing the safety and electronic beam energy selection capabilities using a synchrotron-based proton accelerator.

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Beam Optics for a Scanned Proton Beam at Loma Linda.

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The next nozzle at Loma Linda will use two scanning magnets, which will be installed on one of the three Loma Linda gantries. This will require a small beam at isocenter, which can be swept across the tumor with the scanning magnets. The accelerator group has developed magnetic quadrupole solutions in the gantry beam lines, which can deliver a small beam (less than 6 mm diameter) to isocenter. The strategy has been to find a solution for one energy, at one gantry angle, in one room and then find a general solution, which can be used for all energies, all gantry angles and any gantry room. The simulation program TRANSPORT, first developed at Stanford Linear Accelerator Center, was used to find magnetic quadrupole strengths along the beam lines, which must satisfy multiple constraints including a small beam at isocenter. Starting with the first gantry, we present a small beam solution for 155 MeV and compare TRANSPORT predictions with beam size measurements at nine positions along the beam line. Due to passive scattering systems in the nozzles, a small beam measurement at isocenter in the gantry rooms is not possible at this time. However, the research room has been instrumented with scanning magnets and allows for small beam measurements at the appropriate distance to the patient. Small beam measurements and two dimensional patterns using the scanning magnets will be presented in this report.

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CT and MR imaging in the detection of early radiation-induced hepatic injury.

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Purpose: CT and MRI have been widely used to evaluate patients with radiation-induced hepatic injury. However, CT and MR imaging in the detection of early radiation-effects on the liver in the acute period within 6 months after completion of radiotherapy is little known. Therefore, we investigate the CT and MR findings in the detection of radiation-induced hepatic injury in the acute period.

Materials and Methods: Nine patients with proved hepatocellular carcinoma underwent proton irradiation using a 150-190 MeV beam at a mean actual dose of 76.0Gy/20 fractions between May, 1999 and June, 2000. CT and MRI study was performed immediately, 3 months, and 6 months after completion of radiotherapy. For CT scans, a multidetector CT was used to perform five phases study (precontrast and postcontrast, including arterial, portal venous, equilibrium, and late phases). MR images included precontrast TI-, T2-, and T2*-weighted images, Gd-DTPA-enhanced multislice dynamic study covering all the liver, and ferumoxides-enhanced MR images. Changes in the irradiated area were visually compared with those in the surrounding non-irradiated areas.

Results: Immediately (within one week) after radiotherapy completion, contrast- enhanced MR images revealed an early radiation-induced hepatic area missed by all CT scans (n=8). The radiation effects on the liver appeared as high intensity on Gd-DTPA-enhanced images and as less decreased signal intensity area on ferumoxides-enhanced images. Among MR imaging, ferumoxides-enhanced T2*-weighted images showed the highest contrast and contrast-to-noise ratio. In two of three patients examined by CT and MR during radiotherapy (at the time of 38 Gy irradiated), ferumoxides-enhanced T2*weighted images detected the irradiated area that Gadolinium-enhanced T1-weighted images missed.

Conclusion: Ferumoxides-enhanced T2*-weighted images was the most sensitive among all the images done in this study and can demonstrate hepatic parenchymal changes immediately after proton beam radiotherapy completion, even during radiotherapy.

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Evaluation of Hepatocellular Carcinoma Following Proton Radiotherapy using Contrast Enhanced Power Doppler Ultrasonography Observation.

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[Background & Aims] We have reported that the proton radiotherapy for hepatocellular carcinoma (HCC) is safety and effective therapeutic option. However, it is difficult to evaluate its effect in some cases. Although there is no obvious change in the image of the irradiated lesion one or two months after proton radiotherapy, we have good therapeutic effects one year later. Recently, it is reported that the usage of contrast enhanced color Power Doppler ultrasonography(CE-power Doppler US) , which is reinforcing the signal by the contrast agent, can improve the diagnosis accuracy for the hepatic tumor and the effect evaluation for the transcatheter arterial embolization and the percutaneus ethanol injection therapy. The aim of the present study is to establish the method of the assessment of the therapeutic effect of proton radiotherapy for HCC by CE-power Doppler US.
[Method] The examined cases were 11 patients with HCC (5 males and 6 females) who have been treated the proton radiotherapy (total dose 50-75 Gy) and 11 lesions, with a diameter of 15-80 mm (an average of 34 mm). We inspected both the unenhanced and the enhanced color Doppler ultrasonography by using the color Doppler ultrasonography apparatus (HDI, ATL-Hitachi Co.) and the electronic convex probe, just before the proton radiotherapy, just after that and after the completion of that. We infused 8 ml of the galactose-air-microbubble US contrast agent (Levovist®; Schering, Berlin, Germany) at 300mg/ml concentration intra-venously in all patients by bolus injection (0.5 ml/second). Quantitative analysis was used by computerized imaging analyzer. Furthermore, we compared 3 phase CT at the same time.
[Result] 1) We have recognized the increase of blood flow in tumor and around it just after proton radiotherapy by CEpower Doppler US in 7 cases (63.6%) except 4 cases. The one case had no tumor blood flow, other 3 cases of tumor blood flow have decreased.
By Unenhanced Color Doppler, there has been no obvious change in all cases. According to 3 phase CT images at the same time, we have recognized a clear tumor stain in arterial phase after proton radiotherapy. 2) The cases 3 month after proton radiotherapy had the significant decrease of blood flow and reducing its size compared to these before treatment by CEpower Doppler US. We have also confirmed an attenuation of tumor stain by 3 phase CT.
[Conclusion] There is a possibility of the evaluation of blood flow in HCC by CE-power Doppler US. It is suggested that the enhanced color Doppler sonography might be a simple and non-invasive newly assessment method as same as 3 phase CT for the proton radiotherapy for HCC.

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Analysis of Pulmonary Morbidity in Carbon Ion Therapy for Non-small Cell Lung Cancer.

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Purpose: To evaluate clinically relevant parameters and to identify stagel non-small cell lung cancer patients at risk for acute pulmonary morbidity (RTOG • Grade2) when treated with carbon ion therapy.
Methods and Materials: Eighty stagel NSCLC patients were treated between November 1994 and January 1999 in phase UII dose escalation study. Forty-six patients were treated with a total dose of 59.4 GyE - 95.4 GyE in 18 fractions over six weeks, and 34 patients with a total dose of 68.4 GyE - 79.0 GyE in 9 fractions over three weeks. The normal tissue responses were scored using acute RTOG scoring system. The comparative treatment plannings were also done for multiple plans using carbon ions and X-rays.
Results: Eight patients developed acute pulmonary morbidity of Grade 2 or 3 in 3 months after treatment. It revealed that risk factors for the development of • Grade2 acute pulmonary morbidity included the use of two opposing fields, the highest dose(95.4 Gy/18 fractions and 79.2 GyE/9 fractions), and associated idiopathic interstitial pneumonia. Lung function tests including %vital capacity, %forced expiratory volume, and oxygen pressure, the use of respiratory gated irradiation, past history of pulmonary operation, and DVH curves of the lungs were not able to predict who was at risk for acute pulmonary morbidity development. Comparative study has revealed that carbon ions were substantially superior to X-rays in dose distribution of the CTV and lungs. In carbon ion therapy, field number of 3 or 4 appeared to be satisfactory in terms of the dose distribution.
Conclusion: Carbon ion therapy was safely carried out for the patients who had poor lung function. Based on this study, four fields irradiation without opposing fields and the total dose of 72 GyE/9 fr were adopted in the following protocols, and we are using respiratory gated irradiation in an effort to further reduce the irradiated volume. The patients with IIP should be carefully treated or excluded from protocol study.

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Targeting accuracy of respiration-gated proton beam irradiation for hepatocellular carcinoma.

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Purpose: To clarify targeting accuracy of respiration-gated (RG) proton beam irradiation by using a strain gauge.
Materials and Methods: Data set of 275 sessions of irradiation in 15 patients who received proton beam radiotherapy for hepatocellular carcinoma was analyzed. Metallic markers were inserted near the target in all the patients. Following data were used for the analysis; 1) A series of digital radiographies (7.5 frames/sec) for positioning verification before each irradiation, 2) timing of gating signal (gated at the end-exhalation phase) and markers' displacement on digital radiographies, and 3) actual respiration-gating status during treatment.
Results: Maximum target displacement including non-RG phase was 15.4 (range: 10-22) mm in average. Maximum target displacement during RG phase was 3.6 (range: 1.4-5.4) mm in average. Gating duration of a respiratory cycle was 2.1 (range: 1.1-3.8) sec. Beam utility rates was 33.4 (range: 25.3-50.3)%.
Conclusions: Targeting accuracy during respiration-gated proton beam irradiation by strain gauge for hepatocellular carcinoma was 5 mm in cranio-caudal direction. Therefore, internal margin to the cranio-caudal direction of 5 mm was estimated to be appropriate.

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The dose-volume histogram analysis for the bone and soft tissue sarcoma.

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<Purpose> Dose-volume histogram (DVH) analysis of skin reactions for patients with bone and soft tissue sarcoma treated by carbon ion radiotherapy was carried out in order to predict the skin damage and optimize treatment planning. <Materials and Methods> Sixty four lesions in fifty seven patients with bone and soft tissue sarcoma were treated with carbon ions between 1996 and 2000. DVHs of the skin in forty five lesions were calculated and analyzed in relation to the skin reactions.
<Results> Acute skin reaction of grade three was observed in eight lesions (13%, 8/64), and late skin reaction of grade three was observed in six lesions (10%, 6/60). In DVH analysis, the grade three skin reactions were correlated with the irradiated dose and volume, though the difference was not statistically significant. It was also considered that site of the body irradiated such as gluteal fold was one of the risk factors for sever late skin reactions.
<Conclusions> DVH analysis was useful to predict the skin reactions in carbon ion therapy for bone and soft tissue sarcoma, and was one of the useful methods for evaluation of treatment planning.

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RBE values for proton beam therapy.: A survey on RBE dependencies on physical and biological parameters *in vitro* and *in vivo*

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Clinical proton beam therapy has been based on the use of a generic RBE and that has been 1.0 -1.1. A generic RBE has been used because the available evidence has been interpreted as indicating that the magnitude of RBE variation with treatment parameters is small relative to our abilities to determine RBEs. As substantial clinical experience and additional experimental determinations of RBE have accumulated and the number of proton radiation therapy centers is projected to increase, it is appropriate to re-assess the rationale for the continued use of a generic RBE and for that RBE to be 1.0-1.1. That a generic RBE cannot be the true RBE for each tissue, dose/fraction etc has long been recognized due to the fact of variation in experimentally determined RBEs for both *in vitro* and *in vivo* systems. The question is: are proton RBE variations of sufficient degree to be important clinically?

Results of experimental and theoretical determinations of RBE of *in vitro* and *in vivo* systems are examined and then several of the considerations critical to a decision to move from a generic to tissue-, dose/fraction- and LET-specific RBE values are assessed.

The published RBE values, using colony formation as the measure of cell survival, from *in vitro* studies indicate a substantial spread between the diverse cell lines. The mean value over all dose levels is -1.2. Most of the *in vitro* data indicate an increase in RBE as dose/fraction is reduced below 4 Gy. By contrast, for *in vivo* systems, there was no increase in RBE as dose was reduced below 4 Gy. The mean RBE value *in vivo* is g:4.1. There is agreement that there is a measurable increase in RBE over the terminal few mm of the Spread Out Bragg Peak (SOBP). This rise in RBE is quite steep in the trailing edge of the final Bragg peak, which results in an extension of the bio-effective range of the beam in the range of 1-2 mm.

In conclusion, at present, there is too much uncertainty in the RBE value for any human tissue to propose RBE values specific for tissue, dose/fraction, proton energy etc. The experimental *in vivo* and clinical data have been interpreted as indicating that continued employment of a generic RBE value and for that value to be 1.1 is reasonable. However, there is a local "hot region" over the terminal few mm of the SOBP and an extension of the biologically effective range. This needs to be considered in treatment planning, particularly for single field plans or when an end of range of one or more beams is in or close to a critical structure. There is a clear need for prospective assessments of normal tissue reactions in proton irradiated patients and determinations of RBE values for several late responding tissues in laboratory animal systems, especially as a function of dose/fraction in the range of 1-4 Gy. Elucidation of the evident divergence between *in vivo* and *in vitro* RBEs may also be of mechanistic interest.

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The riddle of proton RBE: new approaches to an old problem.

R. W. Schulte, Dept. of Radiation Medicine, Loma Linda University Medical Center, Loma Linda, CA 92354, USA

The relative biological effectiveness (RBE) of protons remains an issue of continued discussion. It is generally accepted that the proton RBE in the spread-out Bragg peak (SOBP) region is in the order of 1.1 with respect to high-energy photon or ^{60}Co beams, but an enhanced biological effectiveness is expected in the distal SOBP region. Since proton treatment planning systems display physical dose but not biologically effective dose, the treatment planner is not alerted to situations where critical tissues may be exposed to doses of relatively higher biological effectiveness. One of the major problems of the RBE concept is that it represents a ratio of doses for a given isoeffect level rather than a ratio of biological effectiveness for different types of radiation. Determinations of RBE also depend on the choice of the biological endpoint and the selection of physical beam parameters. Non-linear dose response relationships further complicate the RBE issue by making RBE dependent on dose and effect level. In this presentation, some of the inherent weaknesses of the RBE concept will be demonstrated and illustrative clinical examples will be presented. Recent insights into the repair mechanism of radiationinduced DNA damage will be reviewed and new approaches to describing the radiobiological quality of therapeutic proton beams will be discussed.

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Biological effectiveness of high energy protons at three facilities in Japan.

K. Ando[1], Y. Furusawa[1], T. Ogino[2], K. Kagawa[3] and G. Kagiya[4], [1]Natl Inst Radiol Sci, Chiba, [2]Natl Cancer Center HospitaEast, Kashiwa, [3]Hyogo Ion Beam Medical Center, Hyogo, [4]Wakasa Energy Research center, Tsuruga, Japan

Proton therapy in Japan is booming. National cancer center Hospital East at kashiwa installed a therapy-dedicated cyclotron in 1997. Hyogo Ion Beam Medical Center installed a therapy-dedicated synchrotron in 2000. Wakasa Energy Research center is now completing installation of a multipurpose synchrotron that would be used for therapy. A facility with proton accelerator needs its own biological data prior to start therapy. Relative biological effectiveness (RBE)of therapeutic proton beams is not a single value, but depends on both physical factors such as proton energy and biological factors including endpoints and fractionation method. A requirement to pre-clinical studies is to provide, within limited time, a single RBE value representative to all beam path including entrance plateau and Spread-Out-Bragg-Peak. We planed to obtain data in short time using highly reproducible endpoints including normal tissue damages. Reference beams to compare with protons would be linac X rays rather than low energy X rays or cobalt-60 gamma rays. For 235 MeV protons at National cancer center Hospital East, we used mouse intestinal crypt cells and three in vitro cell lines, including SCC61 human squamous cell carcinoma, NBIRGB human fibroblasts and V79 Chinese hamster cells. The dose responses after irradiation at either the entrance plateau or the middle portion of SOBP were compared with those after linac 6 MV Xray irradiation. At Hyogo Ion Beam Medical Center, HSG human salivary gland tumor cells and mouse intestinal crypt cells were irradiated at several points along a 190 MeV proton. HSG cells and mouse intestinal crypt cells were also used at Wakasa Energy Research center for 180 MeV proton beams. RBE values obtained for the three proton beams would be presented and discussed.

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Experimental in vitro proton RBE values (relative to 137 Cs gamma-ray) at PMRC (Preliminary report).

A. Maruhashi' K. Tsuboi[1], N. Kubota[2], A. Nohtomi[1], M. Satoh[1], T. Terunuma[1], M. Miyakawa[1], and Y. Akine[1], [1]University of Tsukuba, [2]Ibaraki Pref. Univ. of Health Science, Japan

We report experimental proton RBE values measured at the new Proton Medical Research Center (PMRC), University of Tsukuba. These RBE values were obtained as results of colony formation probability of single cells irradiated with the modified proton beam of the initial energy of 200-MeV and with 137Cs gamma-ray (662 keV) used as a reference radiation. Four cell lines, 3 cultured cells of human origin (SQ-5, TK-1 and Becker) and one of mouse origin (V-79) were used in this experiment. Monoenergetic pencil proton beam was modified as a beam of 6 cm SOBP and the maximum range of 16 cm in water. Cells inoculated in culture bottles were irradiated in the center of the SOBP of this modified proton beam. Both dose rates of proton and gammma-ray used in this experiment were about 1 Gy/min. As results, it was shown that all RBE values obtained in this experiment are between 0.97 and 1.05 for end points of SF2 and 10% survival level.

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Preclinical biological assessment of proton and carbon ion beams at Hyogo Ion Beam Medical Center

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Purpose: To assess the biological effects of proton and carbon ion beams before clinical use.
Methods and Materials: Cultured cells from human salivary gland cancer (HSG) were irradiated at 5 points along a 190 MeV proton and a 320 MeV carbon ion beam with Bragg peaks modulated to 6 cm widths. A linac 4 MV X-ray was used as a reference. RBE values at each point were calculated from survival curves. Cells were also irradiated in a cell-stack phantom to identify that localized cell deaths were observed at predefined depth. Total body irradiation of C3H/He mice was performed and the number of regenerating crypts per jejunal section was compared to calculate intestinal RBE values. Mouse right legs were irradiated by 4-fractional treatment and followed-up for skin reaction scoring.

Results: RBE values calculated from cell survival curves at D10 ranged from 1.01 to 1.05 for protons and from 1.23 to 2.56 for carbon ions. The cell-stack phantom irradiation revealed localized cell deaths at predefined depth. The intestinal RBE values ranged from 1.01 to 1.08 for protons and from 1.15 to 1.88 for carbon ions. The skin RBE value was 2.16 at C320/6cm SOBP center.
Conclusions: Expected biological depth-dose distributions were observed on both proton and carbon ion SOBP beams.

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What I expect for proton therapy: from a surgical oncologist's point of view. As a neurosurgeon.

K. Tsuboi, Department of Neurosurgery, Institute of Clinical Medicine, University of Tsukuba.

Tumors of the central nervous system comprise a complex classification of neoplasms, and various multidisciplinary therapeutic approaches have been conducted to achieve favorable outcomes. Among these treatments, stereotactic radiotherapy is an essential tool not only for malignant but also for benign intracranial tumors, because it is possible to obtain the best relative therapeutic effect by maximally sparing normal brain or cranial nerves. Proton radiotherapy is one of the modalities that can achieve this aim. A very sharp Bragg peak ionization curve enables proton beams to yield very attractive dose distributions, especially for intracranial tumors with irregular shapes regardless of volume. At the University of Tsukuba, we have been applying 250 MeV/u proton beans to intracranial tumors since 1983 with certain favorable results. Included in these cases are 24 malignant gliomas, 12 chordomas and 8 pituitary adenomas. A thorough review of these cases with reference to the results from other facilities is essential for developing improved treatment protocols for intracranial tumors. We at the new Proton Medical Research Center, University of Tsukuba are especially working on new strategies against intracranial tumors which are incurable by other modalities, and new detailed protocols could be applied with ethical approval. At the same time, further investigation regarding proton radiobiology, i.e. the mechanisms of radionecrosis and sensitivity of brain tumor cells, is necessary to achieve better prognosis of the patients with intracranial tumors.

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Proton therapy for pediatric surgical cases.

H. Ohkawa, Ibaraki Children's Hospital and university of Tsukuba, Japan

With great advancement of chemotherapy for the pediatric solid tumors, the role of radiotherapy has been reduced in the multi-modal treatment schedule. Recently we have used more of an intra-operative irradiation and a proton beam irradiation for the support of pediatric surgical cases. I am discussing here on the experience of proton beam irradiation, using old Proton Medical Research Center of University of Tsukuba.

Proton beam of 250 MeV was equipped both from vertical and horizontal direction. We treated 14 cases in pediatric age, out of whole number of 593 cases including various adult malignant tumors. Among pediatric tumors, there were 6 rahabdomyosarcomas and one spindle cell carcinoma in the naso-pharyngeal portion, one Ewing's sarcoma and 2 neuroblastomas, one hepatoblastoma with huge tumor of the central lobe of the liver and one hepatocarcinoma after the biliary atresia treatment, and one fibromatosis.

Mostly the tumors were treated successfully except two cases of Ewing's sarcoma and rhabdomyosarcoma. Large and inoperable tumors around the nasopharynx area were most effectively treated without any damage on both eyes' visual ability.

Precise irradiation on the confirmed target with large volume was achieved by proton irradiation. Further possibility on the pediatric tumors must be investigated.

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Treatment planning system using a multilayer energy filter for proton therapy.

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A treatment planning system to realize a three-dimensional conformal irradiation by a new method is developed for charged particle radiotherapy. The new filter can yield a static irradiation field where the width of the spread-out Bragg peak is adjusted to the target as a two-dimensional continuous function in the transverse plane. The system calculates the outward forms of the bolus and the new filter by using three-dimensional data of computer tomography. The parallel broad beam method is utilized to decide the design parameters for real human cancers. Comparisons between the traditional ridge filter and the new filter is shown in the calculated results of dose distribution on the CT images.

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Use of a miniature ripple filter for filtering ripple found in the distal part of SOBP.

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When a ridge filter optimized for a certain proton energy is used for beam with lower energy, we observe a ripple in the depth-dose curve especially at the distal part of the curve. This is due to the mismatch between the individual Bragg curves comprising the SOBP and the Bragg curves assumed at the design. Ridge filters are designed based on the raw Bragg curve, which is dependent of the incident beam energy. Therefore a large number of ridge filters are required in principle to obtain optimized SOBPs for different incident beam energies. Since reduction of numbers of ridge filters is usually imposed from practical reasons, some compromise is made. We propose use of an additional miniature ripple filter for filtering ripple found in the distal part of SOBP. The filter broadens the energy spread so as to match the energy of the incident beam with the used ridge filter. For that purpose, we manufactured a miniature ripple filter optimized for 125 MeV beam when ridge filters optimized for 155 MeV beam. The ripple filter is made from a aluminum alloy, the pitch and height are 2.4 mm and 2.85 mm, respectively. A cross section of one unit is 7-step up and down stairs. Since it requires precise machining, it took about one month to complete the machining. It is placed at 40-50 cm upstream the patient surface. Measurement results are shown.

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Membrane Type Liquid Variable Compensator.

Y. Hayakawa, Dept. Biomed. Eng., Toin University of Yokohama, JAPAN.

Conventional compensators are time consuming due to mechanical machining for production, replacement for each irradiation and storage. To simplify the process, a membrane type liquid variable compensator is proposed. Elastic membrane in which liquid is enclosed is controlled of its shape by strong threads. Deformed liquid serves as a variable compensator. Strong threads to deform the elastic membrane are to be controlled by a controlling system depending on the treatment planing of irradiation. The form of membrane is to be monitored by ultrasound reflection technique to ensure the quality assurance.

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Performances of a Test Model of a Compact Parallel Proton Beam Scanner for Proton Therapy.

Y. H. Pu, T. Nakanishi, T. Kim, and S. Nakamura, R&D Center, Mitsubishi Electric Corp., Amagasaki, Japan

As part of the effort to realize an inexpensive and compact rotational irradiation system for proton therapy, we have been developing a compact beam scanning system. This scanning system is composed of a pair of scanning magnets, which can scan the incident beams over a 16 cm • field while keeping the beam parallel to the axis all the time. The immediate advantage of this modality, which is characterized by an infinite SAD length, is about 20% reduction of skin dose compared with the conventional divergent scanning method. The total length of this parallel beam scanner is designed to be 1.2 m and the gantry size equipped with this scanner is shown to be 3 m in radius. We will report the design details in both mechanical and electrical aspects. Test results of a fabricated model scanner will be presented with the help of a digital movie.

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Proposal of a Cylinder Type Liquid Variable Compensator.

M. Ochiai and Y. Hayakawa, Dept. Biomed. Eng., Toin University of Yokohama, JAPAN.

Conventional compensators are time consuming due to mechanical machining for production, exchange for each irradiation and storage. To simplify the process, a cylinder type liquid variable compensator is proposed. Hexagonal cylinders are arranged in honey-comb structure. Each hexagonal cylinder is divided with a piston separating fluids of different electron densities. The energy of protons penetrating the cylinder depends on the length of two fluids in this cylinder. By changing the position of the piston in the cylinder the energy of the transmitted protons is changed. A controlling cylinder is connected with the upper part and the lower part of each hexagonal cylinder with pipes filled with liquids. A control rod moves an inner piston in the controlling cylinder. If the piston in the controlling cylinder moves, the position of the piston in a hexagonal cylinder moves. The control rods are moved by computer control depending on the treatment planning of the patients.

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New Patient Positioner for Proton Beam Therapy.

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All existing isocentric proton therapy gantries have large pits directly beneath the isocenter preventing the use of most standard radiotherapy patient positioners. A computer-controlled radiotherapy positioner has been modified and extended for use with precision proton therapy. The positioner has a 0.05 mm relative accuracy for translational moves and pitch and roll capabilities up to ±5". A description of positioner features and changes in the facility necessary for installation will be given.

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Range Measurement System of Patient Body using Positron Camera in Heavy Ion Therapy.

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The positron camera system has been developed for use in the secondary beam course of HIMAC to measure heavyion ranges in patient bodies. There are a few percent errors in the estimation of the range in patient body now. Using the range measurement system, we can measure the beam stopping point with error less than lmm. "C generated by projectile fragment reaction from ^{12}C beam, is selected by bending two pairs of a magnet and a slit and is further collimated and irradiated to the patient. "C emits the positron at the end of its range and the pair gamma-rays produced by positron annihilation are detected by the positron camera. It consists of two Anger cameras in coincidence and is set both side of the beam line. Positron camera is deficient of the position information along the direction perpendicular to the camera surface, yet we can measure the beam

stopping point in three-dimensions by setting the beam direction at will. In practice, we irradiate a few percent of the fractionation dose (one fraction of about 20 separated irradiation) to a patient before the treatment and confirm the stopping point with the one calculated by CT. After confirmation, treatment starts. Thus, we expect therapy of better precision.

Each Anger camera consists of 60 cm diameter and 3 cm thick NaI(TI) crystal. 109 Puts are attached to the crystal with 1.3 cm light guide. The outputs of the PMTs are converted to digital data from which the position of gamma-ray incidence is calculated by the center of gravity. The size and the thickness of the camera were decided to maximize the spatial resolution by numerical simulation. The camera was set last year and is now under test. The spatial resolution of the camera measured by a pin-type ^{22}Na source is about 6 mm in standard deviation. At beam test, we irradiated 50 % of daily therapeutic dose to the polyethylene block and after irradiation we measured the range for 7 minutes. The beam was 350 MeV/n "C of about 3500k particles and the range straggling is about 4 mm and the diameter of the collimator was 5 mm. Result was that we could measure the range precisely within the experimental error though it is still a preliminary data. The problem is high background and now we try to decrease it and increase S/N ratio to use the system under practical dose level (a few percent of therapeutic dose).

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A simple pencil beam dose calculation module for daily treatment planning.

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For daily treatment planning, an adequately accurate and a reasonably fast dose calculation is strongly needed. We have developed a dose calculation module based on a simple pencil beam technique which includes multiple-scattering effect in the complex heterogeneities in the human body. This dose calculation module calculates a longitudinal depth-dose and a lateral beam spread independently along the ray-path from a point source. A depth-dose distribution measured in a water-phantom is applied to voxel by voxel reflecting its CT-value and a lateral spread is calculated assuming a finite source size. Then the total dose is computed by convoluting the depth-dose and the lateral distribution. Also, this module is implemented on a fully 3D basis, that is, beams of any direction to a plane of CT slice can be handled corresponding to non-coplanar irradiation. Computation time is typically several minutes with 1-mm voxel size on a COMPAQ Alpha 21264 (667MHz) workstation. Comparison between calculation results and water-phantom measurements has shown that the present module has sufficient accuracy for daily treatment planning.

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The pixel ionisation chamber: a detector for beam monitor and dosimetry.

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The control and dosimetry of intensity modulated beams need detectors with good spatial resolution, high granularity and fast readout. As an improvement of the Magic Cube, we have developed a parallel plate ionisation chamber with one of the two electrodes segmented in pixels and a fast readout. The chamber features 24x24cm^2 sensitive area, divided in 1024 square pixels with 7.5mm side. The water equivalent thickness of the chamber is 1mm. The whole chamber is readout with custom designed VLSI electronics, 16 chips each with 64 recycling integrator channels, dead-time free read-out, 16-bit dynamic range and charge resolution variable between 100fC and 800fC. The front-end electronics is read-out using fast memories and real time CPU; the total time needed to read-out the 1024 channels can be as fast as 100•s and the read-out operations are performed without introducing any dead-time in the measurement.

A description of the detector will be presented, along with the results of a beam test performed on the Carbon beam at GSI Darmstadt.

*Partially supported by: Ion Beam Application (IBA), Av. A.Einstein 4, B-1348 Louvain-la-Neuve, Belgium

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Proton dose calculations in heterogeneous media: Pencil beam scaling versus Monte Carlo.

H. Szymanowski and U. Oelfke, German Cancer Research Center (DKFZ), Dept. of Medical Physics, Heidelberg, Germany

Two methods to account for tissue inhomogeneities with proton pencil beam algorithms have been assessed by using Monte Carlo simulations.

Starting point is the dose distribution for a proton pencil beam computed in water. The corresponding dose distribution for a heterogeneous medium is derived from the dose for a homogeneous water phantom via two different scaling methods.

The first approach is the well known one-dimensional pathlength scaling applied along the central axis of the pencil beam. Only the energy loss due to the material traversed is considered, but neither the depth nor the scattering properties of the inhomogeneities are taken into account. The lateral spread of the pencil beam at a given depth in a heterogeneous medium is simply equal to the spread in water at the depth where protons have the same residual energy.

Second, we present a two-dimensional scaling method, which combines a pathlength scaling with an additional lateral scaling. The factors influencing the lateral scaling are derived from Highland's and Gottschalk's formulas for the description of multiple Coulomb scattering for protons. This scaling approach depends on the radiation lengths and the stopping powers of the traversed materials, and also on the depth location of the inhomogeneities.

Dose distributions are computed for both scaling methods in homogeneous non-water media and for various slab geometries. Next, the results are compared to Monte Carlo simulations performed with the GEANT3 code. A good agreement between the results of the new two-dimensional scaling method and the simulations was observed (less than 2.0 %). These results were found to improve the conventional pathlength scaling of proton pencil beams, which showed in some cases non negligible dose deviations of maximal 10.0%, e.g., observed for a 2 cm large air cavity.

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Implementation of a Pencil Beam Algorithm for Proton Treatment Using Different Kernels.

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Aim of this is to use an unique platform for treatment planning including photon, electron and proton beams. Using Pinnacle3 we have implemented 2 analytic pencil beam kernels. The simpler and faster one ("ray casting") is appropriate for defining a geometric grid corresponding to a given energy selection on the basis of a real CT volume. With the second one ("fluence-dose") we are able to simulate realistic dose distributions on real CT-based density matrices without any geometric constrains. We are ready for calculating spread-out-bragg-peaks (SOBP). The ongoing work is the implementation of a Monte-Carlo based kernel including inelastic scattering (s. our poster). We are also developing an optimisation algorithm for the SOBP and for fluence modulated proton therapy (IMPT).

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Quality Assurance Applied to Proton Beam Therapy.

M. F. Moyers, Loma Linda University Medical Center

The introduction of any new technology will be accompanied by a barrage of measurements. After some time using the technology, the measurement effort required to have confidence in its use will decrease. Published references and the experience of others may be useful in decreasing the time and effort to obtain this level of confidence. This presentation will describe categories of measurements performed, the frequency and level of testing, and types of periodic tests. In addition, examples of tests that are critical when using proton beams will be described.

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QA Protocol in Japanese Particle Therapy Facilities.

T. Kanai, National Institute of Radiological Sciences JASTRO QA working group of particle therapy

In Japan, particle therapy using proton beams or carbon ions are carried out at four facilities, and other two facilities will join this group in one or two years. Then, it is very important for this Japanese particle therapy society to establish a quality assurance system of the treatment. In Japanese Society for Therapeutic Radiology and Oncology (JASTRO), a working group for this QA program of particle radiotherapy has started its activity and to show a standard guideline for the particle therapy.

In this report, outline of the protocol for Japanese QA program will be presented.

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QA practice at PSI.

E. Pedroni for the team of radiation medicine Paul Scherrer Institute Switzerland

The approach to QA of PSI is in many aspects rather unusual, since it is based on the spot scanning technology. It is quite difficult to summarize in a short abstract all aspects relevant to QA. We will therefore just mention here the points, which we suppose to be quite different than at other institutions.

Most of the requirements on safety and accuracy are automatically satisfied by the architecture of our beam delivery system. We use redundant independent computers system to control the beam delivery. The most relevant tests for the beam delivery are performed at the end of each spot, on line during the application of the treatment. In addition to these tests, we perform also off line retrospective checks using the logging file of each treatment, a file which contains measured data for each spot, including also interrupted spots (spot by spot bookkeeping of the dose delivery). If necessary the dose can be recalculated from the logging file.

Each new steering file (our treatment planning predicts dose as absolute dose) is checked with an array of ionization chambers (dose profiles measured underneath a water column) before the file is used for the actual patient treatments.

Each day the machine is checked with daily-check procedures (to guarantee a proper startup of the machine using checklists, safety interlocks tests and dosimetric tests).

In addition we perform yearly, monthly, weekly, and daily QA tests.

Typical QA procedures include the maintaining of the data of the mechanical system of the gantry (definition of coordinates and linearity of the axis including the transfer of coordinates from the CT to the gantry - which is done on the basis of fixed absolute coordinates).

Fortunately for the beam delivery we can rely on the exact reproducibility of the beam settings without any need to retune manually the beam. The precise position of the actual beam is checked with submillimetric precision with an ionization chamber with strips (strip monitor). Task of the QA is to guarantee that checking the centering of the beam on the strip monitor is equivalent to centering the beam at the tumor location. QA is also used to provide reproducible small corrections needed to guarantee the exact centering of the beam at different gantry angles (typical corrections < 1 mm).

The control of the dose is based on the calibration of the flux monitors in front of the patient with a Faraday cup and on the physical modeling of the dose distribution of the pencil beam. The official definition of the dose is however taken over from measurements using ionization chambers calibrated in a Cobalt beam according to the accepted international code of practice (the consistency of the two methods is within few percent).

The definition of the range (energy of the beam) is based on the reproducibility of the tuning of the beam line, is measured also by Hall probes in large magnets and controlled by the position of the beam on the strip monitor in front of the patient. Each tune is regularly checked for consistency with regard to the properties of the beam of the gantry (by

measuring depth dose curves in water, the beam parallelism of scanned beam and the phase space of the beam at different gantry angles and energies).

The calibration of the CT from photon attenuation coefficients into proton stopping power is another item which must be regularly maintained (the calibration is done using both, "tissue equivalent materials" and biological probes from organs of animals).

Concerning treatment planning we can use a specialized Monte Carlo code to simulate dose distributions in complex anatomical structures (effects of density heterogeneities). Procedures to guarantee the integrity of the data are implemented and we continue to improve our dose error algorithms. The dose distribution is regularly recalculated from the steering file using an independent dose calculation. The basic safety is however guaranteed by verification dosimetry applied on each steering file.

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Quality assurance practically applied at new PMRC.

K. Yasuoka, T. Sakae[1], A. Nohtomi[2], A. Maruhashi[1],, Y. Takada[2], M. Sato[3], T. Terunuma[3], Y. Tsunashima[3], and K. Hosono[3]; Institute of Basic Medical Sciences, [1]Institute of Clinical Medicine, [2]Institute of Applied Physics, [3]Proton Medical Research Center, University of Tsukuba, Ibaraki, Japan

Early in this fall, the first patient has been treated in our new proton therapy facility. After completing treatment of at least six patients in the clinical trial in several months, we are required to improve treatment process more efficient so as to make more patients available in daily treatment routine. In the new treatment system, including a treatment planning, a bolus machining, an exposure planning, a beam delivering, a patient positioning, an exposure controlling, and a database managing system, most of important parameters required in each patient treatment are automatically set in each sub system and protected from unnecessary changes against planned values. Human errors in treatment process are strongly reduced with a friendly support of the computer control system in proton therapy. Prior to each patient treatment, three kinds of measurements are required with absolutely-calibrated thimble ionization chambers and imaging plates; 1) daily calibration of main and sub parallel-plate ionization chambers in the nozzle of two individual gantries, 2) range and partial dose distribution, and 3) a rehearsal of patient treatment with a water-equivalent phantom and determination of dose-charge conversion ratio at a certain depth in each exposure target. Detailed comparison of these measurements with predictions, which are calculated from the treatment planning and some simulation programs, makes it available to enhance preventing the proton treatment system from setting undesirable condition. We present here our quality assurance practically applied in the treatment, and usefulness of range detectors and two redundant dose monitors, one set at upstream of the beam delivery system and the other at downstream. In addition, we discuss how accurate we can deliver dose in each patient target and what we really need or not in keeping high quality assurance in the next stage, where we may expect treatment of large number of patients; 2 to 4 patients an hour at each gantry.

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Implementation of Quality Assurance Procedures at NPTC.

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Starting August 2001, a set of quality assurance procedures, which include mechanical and radiation isocentricity tests, proton range measurements, modulation width measurements, beam flatness and dose constancy checks, are regularly carried out in treatment room 1 at NPTC. Procedures for measuring the reproducibility of couch movements, Light field vs. radiation field coincidence, X-ray tube alignment and X-ray/radiation coincidence, laser alignment as well as nozzle ionization chamber checks are currently under development. We will present the first results of the measurements, and report on how the measurements helped to find bugs and problems in the software and hardware of the mechanical patient positioning system and also in the beam modification systems.

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Procedure of calibration of dose monitor at NCC, Kashiwa.

M. Shimbo, T. Nishio, S. Katsuta, S. Kawasaki, T. Ogino, and K. Ikeda, National Cancer Center Hospital East

In our facility, the dose monitor is calibrated against a reference ionization chamber, which is traceable to SSDL in Japan. Output factor should be obtained through this measurements. In this calibration procedure, up-stream devices, for example, first and second scatterer, fine degrador, and so on, should be set as the same as the condition of treatment. There are various discussions about the conditions of the down-stream devices, collimator and compensator. In our canter center, the collimator are set on the irradiation port at the calibration procedure and polyethylene sheet corresponding to the thickness of the patient compensator at center axis. In this report, we will discuss about the accuracy of the calibration procedure adapted in our facility.

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The proton therapy quality assurance program at NAC.

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The proton therapy facility at the National Accelerator Centre (NAC) utilizes the 200 MeV beam from the separated sector cyclotron. A fixed horizontal configuration is used mainly for stereotactic radiosurgical procedures. Treatments are presently conducted on two days per week. The beam delivery system uses standard passive beam modification methods and produces field sizes up to 100 mm in diameter. An automatic system using digital stereophotogrammetric techniques is used for patient positioning in the beam and monitoring patient movement during treatment. Quality assurance of this latter system consists of weekly calibrations of the CCD camera positions and daily checking of the positioning accuracy of the system (± 0.5 mm) with a special calibration frame mounted on the backrest of the treatment chair. Additional daily quality assurance procedures include dose constancy verification (± 2%), patient collimator alignment (±0.5 mm) and axial and lateral laser alignment. Between treatments the beam energy spread is monitored by a multilayer Faraday cup (FWHM < 3.5 MeV) and the beam range by a range ionization chamber (± 0.4 mm). The range is adjusted by inserting or removing plastic trimmer plates 0.07 g/cm^2 thick to achieve the clinical range in water of 24.00 ±0.04 cm (50% level of distal edge of Bragg peak). Other procedures undertaken less frequently include, beam flatness (±5%) and symmetry (±0.05%) measurements [weekly], registration of portal x-ray with proton beam (< 1 mm), absolute monitor calibration (±1%), calibration of ionization chambers in ^{60}Co (with respect to secondary standard), calibration of double-wedge degrader (± 0.1 mm) and calibration of range monitor (± 0.4 mm) etc. For patient treatment a barcode system is used with a laser scanner to ensure that the correct modulation propeller and field-specific collimator are used for each treatment field.

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Quality assurance in the heavy-ion therapy at GSI.

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In the heavy ion tumor therapy project at GSI patients are irradiated with high-energy carbon ions. The carbon ion beam is applied by the raster-scanner beam delivery system and the active energy variation of the accelerator. Therefore the target volume is divided into slices of equal ion ranges. For each of the slices a pencil beam with the energy corresponding to the radiological depth of the slice is requested from the accelerator. Within each of these slices the pencil beam is scanned across the different voxels. The scanning speed is controlled by the applied intensities, this means the scanner moves the beam to the next point whenever the desired number of particles has been directed to one of the voxels. After all of the points within one slice have been irradiated the beam is dumped. The next beam will be requested with an energy corresponding to the next slice.

As a consequence of the novel completely active beam delivery technique dedicated quality assurance procedures have been developed. The main focus of the talk will be about the special QA procedures concerning dosimetry, beam monitoring and treatment planning.

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National Cancer Institute funded Resource Center for Emerging Technologies (RCET) at University of Florida.

J. Palta and V. Frouhar, Department of Radiation Oncology, University of Florida, Gainesville, Florida 32610, USA

RCET has developed an infrastructure for distributed database, visualization and analysis system for collecting, sharing and distributing information generated by institutions participating in clinical trials. The system consists of a centralized database, web server, 3D data visualization, ActiveX and Java browser components and an object transaction server. The software modules enable users to share multidimensional treatment planning and Quality Assurance (QA) data objects, which include 3D visualization and imaging information, as well as conventional database objects.

RCET system provides a set of services for institutions that participate in clinical protocols. Using RCET client software, NetSys, participants of a clinical trial can send required study data for each case. The submitted information becomes readily available for remote review using a Web browser. In addition, users can perform retrieval of original archived data for visualization; modification and analysis similar to a DICOM-RT based PAC system. The RCET system provides a unique opportunity for PTCOG member institutions to participate in cooperative clinical trials and share data electronically for rapid remote review. It also provides the opportunity for remote peer review.

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Network-wide application sharing as part of an electronic patient referral system.

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Introduction. The current state-of-the-art in radiotherapy provides a rich variety of methods by which radiation can be applied to lesions. Patients can currently be treated with either fractionated photons and/or electrons (conventional or IMRT), protons (conventional or IMPT), or with stereotactically guided radiosurgery techniques. Within each of these groups, there are a wide spectrum of possible treatment methods. Taking stereotactic treatments as an example, there is currently the possibility of delivering conformal treatments with a LINAC, using either arc therapy or mini-multileaf collimated static fields, or alternatively with a dedicated radiosurgery system such as the GammaKnife. However, although each particular technique is often aimed at fulfilling a certain role in radiotherapy, it is also not necessarily the case that a particular treatment method will prove to be the most appropriate for *all* patients with a given indication.

Given the current diversity of treatments becoming available, it is extremely unlikely that any one institute can have access to all treatment possibilities. However, different treatment possibilities may well be available at other, possibly widely distributed treatment centres. If the potential of these specialised treatment centres are to be exploited, then it is necessary to put in place methods by which competing treatment methods can be assessed on a patient by patient basis across institutes.

Here we describe the use of network-wide application sharing software, in conjunction with radiotherapy data exchange standards, for the interactive assessment of treatment plans by two or more remotely situated treatment centres.

Materials and methods. At the Paul Scherrer Institute, we are currently treating patients with protons using the spot scanning technique. However, the institute itself is a physics research institute, and as such, we must rely on patients being referred from external radiotherapy clinics, within or outside of Switzerland. To facilitate the selection of patients, we have previously described an electronic patient referral system [1], by which `core' radiotherapy data sets can be transferred between the proton planning system at PSI and a number of commercial planning systems that have installations in clinics within Switzerland. In this system, the results of evaluation plans performed at PSI, in the form of 3D dose distributions, can be electronically transferred back to the referring institute's planning system, where the proton plan can be carefully compared to the treatment possibilities at the local centre. However, there is inevitably still a need to discuss the competing plans and, if a patient is accepted for treatment, the details of the treatment itself, interactively with the referring clinic. For this purpose, we have started to use software for sharing applications over local and wide area networks. With this software, we can make available our proton therapy planning system to remote users, such that they can interact with it exactly in the same way as a user at our institute. That is, both the local and remote users can interact with the same program, thus facilitating meaningful discussions between the different parties.

Data conferencing standards have been defined by the International Telecommunication Union (ITU) in T.120 and H.323. [2] Software conforming to these standards has become available for a range of computer platforms. We are currently using Microsoft's NetMeeting on Win95/98/NT4.0. [3,4].

NetMeeting conforms to the above mentioned standards and allows application sharing and basic audio/video conferencing over TCP/IP. Data encryption for transfer over public networks is possible. NetMeeting can be downloaded from Microsoft's website along with a Resource Kit containing detailed technical documentation.

In a typical session we want to discuss patient data on PSI's therapy planning system with a remote referring institution [Fig. 1]. At both sites, a Windows PC with NetMeeting installed is connected to the Internet. The therapy planning system is typically running on a separate,-VMS workstation, By running an X server on the PC and directing the workstation's display to it, we are able to take control over the planning system and, through NetMeeting, share it with the remote partner. Sharing in this context means not only that both sites may look at the same picture. Rather, that the remote site may completely take control over the planning application and, for example, modify VOIs.

At PSI we have set up one PC as a dedicated workstation for NetMeeting sessions [Fig. 2]. Along with the required software (Windows95, NetMeeting 3.01 and a X server) it has appropriate hardware (graphics card and a large monitor) to display medical images. A small camera (ViCAM from Vista Imaging, Inc.) transmits video images of the discussion partners. Close to the PC is a telephone with external microphone and loudspeakers. The PC is located in the room used for therapy planning where eventually required additional documents (MRI, CT) are readily available.

Discussion. During 1999, NetMeeting in the configuration described above has been used frequently for the interactive discussion of patient data and therapy plans between PSI, referring clinics and other treatment centres. Inside Switzerland we could mostly rely on the Swiss academic network which offers bandwidths up to 155 Mbps. However, we also conducted interactive sessions over transatlantic links during busy hours or with dial-in links over analog telephone lines without problems.

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Development and approbation of technical means and methods of proton radiation therapy of prostate and oropharynx cancer.

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Basic results are presented of research carried out on the base of the operating Proton Therapy Facility of the Institute for Theoretical and Experimental Physics (ITEP). The research done makes it possible to start clinical approbation in horizontal fixed beams of the proton radiation therapy of malignant tumors of the oropharynx, laringopharynx, oral cavity and pharynx (T2-4NanyMO), and prostate (Tlc-3NO-IMO). In 1996, these tumor localizations were registered in 7.42% of new patients.

In the course of the preparation for the clinical approbation, the following R&D have been carried out: the transfer of pre-irradiation preparation (topometry) results in the required format into the planning system done; problems of patient immobilization and positioning solved, complicated in the case of irradiation of oropharynx tumors by patient inadequate position in topometry (supine position) and in irradiation (seated position); basic dose fields formed, measured and entered into the planning system database, the first home dose planning system for proton therapy developed; technology developed for the on-line manufacturing (with a dosimetry planning system) of individual boluses and collimators, and Radiation Treatment Protocols developed. The design of the treatment units provides for proton irradiation to be done from two or more directions using the chair rotation (irradiation of oropharynx cancer in seated position), and bench rotation (prostate cancer irradiation) with patient about the vertical axis. The Protocols suggest combined (p' and gamma) irradiation of patients and the increase of the tumor dose while retaining the traditional dose level to the regional lymph nodes, prophylactic irradiation zones, adjacent organs and structures. This should lead to the increase of the tumor local control frequency, decrease of recurrences without the increase in the level of post-irradiation complications.

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A New and Dedicated Accelerator and Beam Transport System for the Proton Therapy at the Paul Scherrer Institute (PSI) / Switzerland.

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In 2000 the decision was taken to start a new long-term commitment in the field of proton therapy at PSI. The project PROSCAN was started with the objective to implement and operate at PSI a base technology laboratory for the advancement of proton therapy techniques and clinical applications. Within the project an expansion of the facility and technical infrastructure has to be realized. The new facility has to fulfil particular requirements from the medical and technical point of view. These will be achieved with:

An independent dedicated cyclotron that meets high standard specifications and qualifications for the application of advanced and improved irradiation techniques. Special attention was given to the beam quality, beam stability, extraction efficiency, diagnostics, safety, activation, reliability, operability, maintainability and operation costs.

A beam transport system from the cyclotron to the treatment rooms that meets the requirements such as implementation of a fast raster scanning of the depth dose in addition to that of the lateral dose. For that the beam line has to be adjustable to rapid sequence of different beam energies in short time scales.

A fast beam degrader system that permits a rapid setting of different beam energies, and additionally should be applicable in hospital environments in respect of maintenance and activation. Magnets and power supplies which enable the desired rapid change of the beam setting in order to transport the beam properly in respect to beam quality and position stability needed at the therapy rooms.

A steering and control system that is adaptable to cyclotron, beam lines and treatment facilities, combined with an independent safety system.

On the poster presentation it will be shown how the ambitious goals set are being realized within the frame of the PROSCAN project, including the time schedule.

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Proton 3D-conformal radiation therapy of intracranial tumors: new clinical program at the Dubna proton therapy facility.

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Introduction. One of the most suitable target locations for conformal proton irradiation are intracranial lesions. Proton conformal radiation therapy proved to be safe and effective treatment method for various critically located, complex shape intracranial tumors such as skull base chordomas and chondrosarcomas, meningiomas (especially atypical and anaplastic), gliomas, metastasis and some others. Large irregular shape arteriovenous malformations are also good candidate for proton radiosurgery.

Hardware and equipment. During last 18 months one of the procedure room at the Joint Institute of Nuclear Research (JINR) have been modified to satisfy requirements for precision radiation treatments. Room is equipped with horizontal proton beam line with particles energy of 150 MeV. Depth penetration of the beam in water is 149-151 mm depending of the used ridge filter. Beam has 6x6 cm rectangular shape. Recently, size of the beam has been increased up to 8x8 cm. Final collimation of the beam in accordance with target shape is performed by micro-multileaf collimator for 6x6 cm beam (leaf width - 0.5 cm) and 0.7 cm leaf-width collimator for 8x8 cm beam. Several ridge filters with plateau region 2-5 cm can be used for beam modulation. Patient positioner represents the treatment chair with 4 degrees of freedom. Head of the patient immobilized by the perforated thermoplastic mask and X-ray translucent head holder. System for target alignment and beam centration includes orthogonal laser beams and X-ray tube for introscopic alignment. Films of the skull during treatment are double exposed by X-ray and treatment proton beam.

Treatment planning. We are using three-dimensional treatment planning system "TPN" that has been developed at the Loma Linda University Medical Center. This is early version of the "OptiRad-3D" system that is now presented at the market. The system was modified to incorporate the Dubna proton beams. The series of dosimetry experiments have been performed to verify calculation algorithm with good coincidence of calculated and measured dose distributions. At the same time treatment plans have been duplicated with local planar planning system.

Technological chain. After individual mask manufacturing treatment planning CT with up to 70 narrow slices have been performed. "Siemens" "Somatom" CT was calibrated to reflect proton stopping power of the CT-pixel. Physician outlines target, critical structures, alignment bone landmarks. 3D structure models are calculated by "TPN". Three to six beams located at the axial plane are calculated. Beams features are individual shape with multyleaf collimators and beam's eye-view function, complex shape boluses to conform distal contour of the beam to the target shape. Digital reconstructed radiographs (DRRs) with projection of target, isocenter and bone landmarks were calculated and printed. Alignment Rxfilms were compared with-DRRs during. irradiation sessions. Alignment accuracy was about 1-2 mm. This is first experience in Russia of using 3D treatment planning and beam formation for proton radiation therapy.

First clinical experience. Since April 2001 eight patients with ten targets received proton conformal radiation therapy at JINR. There were 6 meningiomas (2 benign, 3 atypical, 1 anaplastic), 2 malignant gliomas, 2 metastasis. Hypofractionated regimen of 12-14 fractions have been used, depending on the time of accelerator run, usually 2.5 weeks. 3-4 GyE with traditional for proton RBE = 1.1 were delivered for one fraction. Total equivalent doses were calculated by the linearquadratic formula and were equal to 56-60 GyE-a/b to the target margin. Early results demonstrated that developed technique of irradiation allow to deliver proton dose to the target volume precisely. On metastasis completely disappeared, one glioblastoma demonstrated gradual decreasing in size during 1 and 3 month MRI follow-up, another malignant glioma shows localized planning necrosis exactly at the place of location of dose distribution. Meningioma patients need longer follow-up to evaluate the results.

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Requirements and opportunities of mass hadron-therapy development.

B. Astrakhan, Russian Cancer Research Center (RCRC RAMS)

Therapy with hadron beams remains extremely expensive. Value of Modern Proton Therapeutic Complex (PTC) is $90120 million, and the Therapeutic Complex for heavy ions (ITC) - some hundred million $. The lion's share of charges falls to its medical-technical part, and is connected to use of engineering GANTRY. Meanwhile, in Russia annually 110000 new oncological patients require hadron-therapy. It is impossible to satisfy these needs due to installations with GANTRY, - owing to their huge cost. Such position is kept everywhere in the world. For example, USA have only two large Hadron Therapeutic Complexes now, while their general need is about 100 copies. We offer essentially new <<AntyGANTRY>>-SYSTEM (<<AG>>) for realization of rotatory-scanning proton therapy of malignant tumors. The patient it is fixed in a thin-

walled capsule with the vacuumed bags filled with plastic grains. Patients are prepared for an irradiation in several Preliminary Procedural rooms simultaneously. The computer aided transport system controlled by computer, delivers the next patient from Preliminary to Radiating room and back without breaking of fixing quality. During a therapeutic irradiation the vertically located patient is rotated under narrow horizontal scanning beam of hadrons. "AG"-SYSTEM is universal and may work with any accelerators of any heavy particles. Replacement GANTRY by "AG"-SYSTEM will lower PTC cost in tens, and ITC cost - in hundreds times. Serial PTC (1200 patients/year) with the miniature accelerator (p+ 250-320 MeV) and "AG"-SYSTEM should cost $ 3,5-4 million. For less developed countries it is possible to come into mass proton therapy not only thout additional financing, but also with simultaneous reduction of the inevitable expenses in 1,5 times. It can be made if the telegamma-units (which have served its time and become archaic) will be replaced not with linear electron accelerators (as they do usually), but with our cheap PTC.

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Accelerator Facility PATRO at Hyogo Ion Beam Medical Center.

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Hyogo prefecture government has started a design and construction of accelerator facility PATRO (Particle Accelerator for Therapy, Radiology and Oncology) for hadrontherapy (Particle therapy) in 1995. Our medical center is located in Harima Science Garden City of Hyogo prefecture, about 75 km northwest of Kobe. The facility consists of two 10GHzECR ion sources, IMeV/u RFQ linac, 5MeV/u Alvarez linac (200MHz operation frequency), synchrotron with 93.6m circumference, high-energy beam transport system and patient irradiation system. Beam is extracted from synchrotron by slow extraction scheme and can be gated by human breezing motion. Beam particles for patient treatment are proton (230Mev, 30cm range in human tissue) and carbon (320MeV/u, 20cm range). We have 5 treatment rooms:

A. Oblique (45-deg) beam port,

B. Horizontal and Vertical beam ports,

C. Horizontal port with patient seated position, (A -C, for carbon and proton) and G1 and G2. Two isocentric gantry ports for proton beam.

Beam test was started from 2000 and. we have now a full intensity beams, with a dose rate about 5GyE/min. We have now 150, 190 and 230 MeV extracted proton beams and 250 and 320 MeV/u extracted carbon beams to cover the clinical requirement. Transverse dose uniformity is obtained by the wobbling method. The ridge filter is used to obtain a spread out Bragg peak (SOBP.

Clinical trial by proton beam has successfully started this May 2001. On weekday beams are delivered to the treatment rooms from 9 to 17 o'clock for patient treatment. In September, 15 patients are treated per day. Typical proton beam intensity is 7.5 nA. Dosimetry is checked every day for each patient and also at all treatment ports to obtain statistical data on stability and reproducibility. Clinical trial by carbon beam is expected to start this year after the completion of the proton trial.

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The survey for building proton therapy facilities in Yokohama.

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We are planning to build a hospital based proton center in Yokohama City. Yokohama City located in eastern Kanagawa Prefecture. It will be 25 minutes travel from Tokyo station to Yokohama station by Tokaido line. Yokohama, the second largest city in Japan, has a population of just over 3.4 million. The city extends approximately 33.1 km from north to south and 23.6 km from east to west. Yokohama's total land area is 434.71 km'.

The survey was done by sending questionnaire forms to the radiation oncologists of 10 facilities in Yokohama. Number of patients treated with radiation therapy in Yokohama city was 2700 between January 1999 and December 2000. We estimated annually 500-600 patients in Yokohama city would be good candidate for proton therapy.

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Present Status of Proton Therapy Project at The Wakasa Wan Energy Research Center.

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Proton cancer therapy project has been proceeded at The Wakasa Wan Energy Research Center (WERC), Japan. Three parts of the whole system (therapy beam line with accelerator, patients' positioning part with X-ray CT, and treatment planning part) are finished and now being verified.

The construction of the therapy beam line with two fixed irradiation ports has been completed, following to the completion of an accelerator complex with a 10 MeV p tandem injector and a 200 MeV p synchrotron. -The synchrotron can now deliver 80, 90, 100, 120, 140, 160, 180 and 200 MeV p with the maximum intensity of 7 nA (at 200 MeV). This accelerator system can produce the diameter of 100 mm x 60 mm SOBP

(Spread Out Bragg Peak) irradiation field with the flatness of 5%-at the dose rate of 3 Gy/min, using two wobbler magnets and scatterers. Some of obtained data are shown.

Two other parts of the system, which are positioning and treatment planning, are also being tested whether they are enough accurate for the medical use. The obtained data are shown. The first clinical trial is planned after some developments and more measurement opportunities are processed.

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Treatment System in Hyogo Ion Beam Medical Center.

T. Akagi, A. Itano, and A. Higashi, Accelerator managing section, Hyogo Ion Beam Medical Center

Hyogo Ion Beam Medical Center has been constructed for proton and carbon therapy. Clinical trial for proton therapy has started from the end of May. Beam delivery system and treatment planning system are introduced in this presentation.

We have four fixed beam lines and two gantry beam lines of six beam lines, and 5 treatment rooms. Wobbling beam delivery is adopted for spreading proton and carbon beam laterally, and stationary bar-ridge filter for SOBP. We prepare SOBP's between 30c m to 120 cm in 1 cm step. Uniformity of the radiation field is around +-2.5%. The uniformity was checked with dosimetry system. The system can measure three dimensional dose profile as well as absolute dose.

Treatment planning system has also been constructed. The TP system consists of information server, two planning terminals, and image fusion terminal. While MR image is good for drawing target outline, CT image is essential for planning. The image fusion makes drawing target on MR image possible by fusion CT and MR images. For dose engine, pencil beam code is adopted to consider the scattering effect in patient. The information server manages all data for treatment and communicate with HIS/RIS to accomplish smooth treatment.

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Features of Hitachi Proton Therapy System

K. Hiramoto, K. Suzuki and K. Moriyama, Hitachi, Ltd.

Hitachi has proposed and developed a proton therapy system, which consists of a slow cycle synchrotron with maximum beam energy of 250 MeV, beam transport and rotating gantries with irradiation nozzles. The present system has several features needed in daily treatments, one of which is highly stable and reproducible proton beam with simple operation. For example, the beam position change in the irradiation nozzle is kept in 0.5 mm without feedback control in daily treatments. This characteristic, which is especially important for irradiation due to double scattering or pencil beam scanning, is realized by Hitachi's new techniques of the RF driven slow extraction scheme, stable power supply and magnets, etc. Another feature is flexible operation for patient's respiration synchronized treatment, that is, the timing of synchrotron operation and beam extraction is varied according to patient's respiration signals. We consider that these features are essential and indispensable for reliable, precise and economical operation in proton therapy of cancer.

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Operational experience of a medical ion accelerator HIMAC.

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HIMAC has been providing carbon beams to medical treatment for seven years. Performance of beam delivery and irradiation systems will be presented. It will include stability and reproducibility of the accelerated beam, beam monitor, and alignment of the patient positioning system. Possible improvement will be discussed also.

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Beam Optics for a Scanned Proton Beam at Loma Linda.

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The next nozzle at Loma Linda will use two scanning magnets, which will be installed on one of the three Loma Linda gantries. This will require a small beam at isocenter, which can be swept across the tumor with the scanning magnets. The accelerator group has developed magnetic quadrupole solutions in the gantry beam lines which can deliver a small beam (less than 6 mm diameter) to isocenter. The strategy has been to find a solution for one energy, at one gantry angle, in one room and then find a general solution, which can be used for all energies, all gantry angles and any gantry room. The simulation program TRANSPORT, first developed at Stanford Linear Accelerator Center, was used to find magnetic quadrupole strengths along the beam lines, which must satisfy multiple constraints including a small beam at isocenter. Starting with the first gantry, we present a small beam solution for 155 MeV and compare TRANSPORT predictions with beam size measurements at nine positions along the beam line. Due to passive scattering systems in the nozzles, a small beam measurement at isocenter in the gantry rooms is not possible at this time. However, the research room has been instrumented with scanning magnets and allows for small beam measurements at the appropriate distance to the patient. Small beam measurements and two dimensional patterns using the scanning magnets will be presented in this report.

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The Accelerator and Beam Transport System of PMRC, Univ. of Tsukuba.

M. Umezawa, Collaboration of Hitachi, Ltd. and PMRC, Univ. of Tsukuba

The proton therapy system of PMRC employs a synchrotron with a maximum energy of 250 MeV and two rotating gantries. The proton beam was successfully accelerated to 10 energy levels and transported to the irradiation nozzles through the gantries. Each gantry can be rotated ±190 degrees. Since each rotating gantry has sufficient stiffness, the measured mechanical iso-center precision was found to be inside a cube of 1 mm sides for all rotating angles. The position of the beam extracted from the synchrotron and transported to the irradiation nozzles was confirmed to be very stable and reproducible, which is sufficient for formation of a flat irradiation area by using the dual ring double scattering method developed at University of Tsukuba. The present system is being applied to clinical trials with satisfactory reproducibility and stability.

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Specific design peculiarities of proton synchrotrons for hadron therapy.

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Proton synchrotrons for hadron therapy can be divided into two groups according to an operation mode. The first group is a low-cycling accelerator and the second one is a rapid-cycling machine. The first group combines machines with the repetition rate less or equal to 1 Hz. The second group presents synchrotrons with the fast repetition rate. The repetition rate of the medical proton accelerator defines main parameters of the beam, which should meet first of all the medical requirements to treat different kind of cancer tumours. From the other side a compact design is the common feature of the medical machines. The

presented report is devoted to study of specific design peculiarities of the low-cycling proton synchrotron, in particular the effects of the space-charge of the low-energy high-intensity proton beam and non-linear magnetic field distribution near the edge of the quadrupole and dipole magnets of the synchrotron. In the case of the proton synchrotron the high-intensity beam itself without any magnetic field imperfections can excite the high-order resonances, that could lead to increasing of the beam emittances. To avoid the blow-up of the transverse emittances during the multiturn injection process the parameters of the machines should be optimized, particularly the working point position on the betatron tune diagram and the parameters of the RF system. Moreover, the non-linear effects of the fringe fields can increase the chromatic tune shift and reduce the dynamic aperture of the compact synchrotron significantly. Combination of these effects can limit the beam intensity of the medical machine. To avoid it the proper choice of main machine parameters should be based on detail analysis of these effects. The report presents the simulation results for the low-cycling proton synchrotron of PMRC (University of Tsukuba).

The work was performed under support of Japan Society for the Promotion of Science (JSPS).

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Implementation of a Voxel-Based Monte Carlo Code for Direct Dose Planning in Proton Therapy, Including Inelastic Scattering.

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For simulation of proton transport we introduce a voxel based Monte Carlo algorithm which includes inelastic scattering in detail. The aim of this work is threefold: obtaining pencil beam kernels for a semi-analytical planning algorithm (s. paper in addition); direct Monte Carlo dose planning, and also for quality control of the semi-analytical model; tackling questions concerning real proton fluence, boundaries, inhomogeneous media, and secondary particle transport.

Our algorithm is based on PTRAN. Unlike to it we calculate the non-elastic interactions with the atomic nuclei on event by event. Together with the condensed random walk the procedure yields a more realistic outcome in respect to the dose distribution for protons. In addition the algorithm is real 3D and voxel-based.

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Light CT ---- 3D Proton Dose Distribution Measurement. ---

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The Light CT was designed and developed in order to make the measurement of the proton 3-d dose distribution easy and reliable. It is composed of a scintillation part that emits light according to the proton dose distribution and a CCD camera that can detect the emitted light from arbitrary direction. The principle of Light-CT is basically similar to that of Xray CT. The proton 3-d dose distribution was reconstructed by the filtered back projection method. The evaluation of its performance was made using the proton radiation field that has four different residual ranges. This demonstrated that LightCT could measure the proton 3-d dose distribution in use of the principle of the Light CT. However, it also showed some problems such as reduction of resolutions due to the light scattering in the scintillation part. We plan to investigate its effect using the numerical phantom.

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Dosimetry of pulsed clinical proton beams by a small ionization chamber.

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Response of a micro volume (0.01 ml) ionization chamber has been studied with pulsed proton beams which are used for clinical purposes and has been compared with those of some JARP ionization chambers (0.6 ml). All chambers used had been calibrated by standard 60Co beams at the Electrotechnical Laboratory (ETL) and exposure calibration factors, Nx, were obtained on advance. Two methods are used to compensate the general recombination which occurs during pulsed beam irradiations : theoretical correction by a Boag's formulation and a modified two-voltage technique. An evaluation of absolute absorbed dose-to-water is performed on the basis of the protocol provided by ICRU report 59. The results imply that, to a first approximation, both chambers indicate the almost same result within 2% when unknown chamber-dependent parameters of the micro chamber are tentatively assumed to be identical to those of the JARP chamber for the calibration with 60Co beams. The about 1.5 % discrepancy observed in the response of both chambers is not discussible due to presumably 1-2 % uncertainty of the protocol of ICRU report 59 which does not include any chamber-dependent corrections for the perturbation effects in proton beams.

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Beam quality measurements of the gantry beam at new PMRC, Tsukuba.

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Dose distributions of the gantry beam at the new Proton Medical Research Center (PMRC), University of Tsukuba have been extensively measured using a silicon semi-conductor sensor scanned in a water vessel. A uniform fluence distribution is formed by a double scattering method using a uniform first scatterer and a dual-ring second scatterer. Depth-dose distributions of the broad beam have been measured for beam with ten different energies. Based on the measured Bragg curves, we designed ridge filters. We prepared two series of ridge filters. Whereas the one series are optimized for 200MeV protons, the other series are optimized for 155-MeV protons. Depth-dose distributions of the range-modulated beam are measured and compared with calculations. Basic quantities such as lateral penumbras and distal falloffs are measured and compared with calculations. We found that measurement results agreed well with the calculations. As expected from calculations, dose distributions of beam with lower incident energy were found to be largely affected by insertion of a ridge filter and a range shifter. Dose distribution measurements using a water vessel with a movable cross-type array of parallelplate ionization chambers

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Dose distribution measurements using a water vessel with a movable cross-type array of parallel-plate ionization chambers.

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A detector has been fabricated to measure proton dose distributions in water efficiently. It is a cross-type array of forty parallel-plate ionization chambers (twenty chambers in each direction) movable in a water vessel. A reference chamber is prepared to compensate time variation of beam intensity. Since the assembly can be rotated manually around an axis of rotation, dose distributions can be measured for many rotational angles of the gantry. The pitch of the ionization chambers is 10 mm and the effective volume of individual chambers is about 0.1 cc (5.6 mm x 4 mm). Calibration of sensitivities of ionization chambers was made by locating each chamber at the center of beam field and by measuring the electric charge in the chamber. A transmission ionization chamber along the beam line is used for compensating the beam-intensity variation during the measurements. Since the device enables us to measure lateral dose distribution in x- and y-axes simultaneously, it serves to reduce the measurement time of dose distributions. Depth-dose distributions of forty lateral positions can be obtained at once by moving the array remotely.

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Experimental Evaluation of Proton Dose Calculations in Heterogeneities.

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We have developed a method of dose calculation based on the pencil beam algorithm (PBA) and the simplified Monte Carlo (SMC) dose calculation method with the new concept. In order to verify the accuracy of calculations by the PBA and the SMC, we manufactured heterogeneous phantoms which were made of Tough Water and Tough Lung, and dose distributions in heterogeneities were measured. The results of the measured dose distributions agreed with the measured ones within several percent since the PBA could not predict the edge scattering effect. On the other hand, the calculated results by the SMC agreed considerably with the measured ones. In conclusion, Care must be taken to apply the PBA to dose calculations in heterogeneities and the dose-calculation method by the SMC will be applicable to actual treatment planning of the proton therapy.

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Development of a Multi-layered Ionization Chamber for Heavy Ion Therapeutic Beam.

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In heavy ion radiotherapy, it is strongly desired to measure dose distributions for individual patients, and to compare them with the results of calculated dose distributions. So we are developing a multi-layered ionization chamber (MLIC) for the measurements of the dose distributions. It can take the data of depth dose distributions at once.

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Measurements of charge-changing cross sections for carbon and neon beams.

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High-energy ion beams exhibit a flat depth-dose distribution near the end of their range, where there is a marked increase in dose, called the Bragg peak. In cancer therapy using high energy ion beams, energy absorbers are usually set in front of a patient in order to superimpose the Bragg peak over the whole target volume. These absorbers cause attenuation of the beams through nuclear fragmentation and may possibly change the beam fluence which is planned for patient irradiation. Nuclear fragmentation cross sections are therefore of particular interest in heavy ion radiotherapy.

Although fragmentation reactions have been studied for many years from the viewpoint of nuclear physics, there is still a lack of experimental data, especially for light ions such as are used in therapy, and there are in some cases large differences between data and model calculations. We have measured the survival of 400 MeV/u carbon and neon beams as a function of the absorber thickness with dE-type plastic scintillators. The total charge-changing cross sections of several materials for those beams were deduced from the measured survival data. We will show comparisons between our data, theoretical predictions and other experiments.

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Study of acoustic signals generated by pulsed proton beam irradiation.

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In proton therapy, a location of the high-dose volume must be controlled very accurately. However only few studies have been tried to measure a dose distribution inside a patient's body. All radiation beams, especially a pulsed proton beam, generate an acoustic wave inside a medium. This phenomenon may have a possibility of being used to verify dose distributions during treatment, since shapes of acoustic signals have a 3-D dose information. Based on dose measurements with 1.6 mm resolution using imaging plates, we calculated expected acoustic signals at different locations in water with 1 sec resolution. In the calculating model we made two assumptions. Firstly, for each point of dose distribution the micro pressure was generated by the adiabatic expansion and the amplitude of pressure is proportional to the dose. Secondly, the pressure signal travels to the detector with a delay proportional to the distance (r) and with an attenuation proportional to 1/r. Results of the calculations agreed well with the measurement results detected by the hydrophone in a water tank.

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Microdosimetric Characteristics of the JINR, Dubna Clinical Proton Beams.

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Proton clinical beams contains particles with high linear energy transfer (LET). Secondary heavy charged particles and degraded protons at the Bragg peak region are particles with high LET. The contribution of the high LET particles to the dosimetric and microdosimetric characteristics of proton beams was experimentally studied by track etched detectors.

The method of the LET spectra measurement with track etched detectors allows one to determine the contribution of high LET particles to the dosimetric characteristics of proton clinical beams, absorbed dose, equivalent dose and the value of the Relative Biological Effectiveness (RBE). For the RBE calculation from the measured LET spectra the Biological Weighting Function r(y) proposed by T. Loncol was used.

Track detectors were irradiated in the various depth of proton clinical beams with the primary energies of 155 and 200 MeV at the JINR (Dubna) phasotron. The LET spectra between 10 and 700 keV/μm were measured by means of the CR-39 track etch detectors and automatic optical -image analyzer LUCIA at the NPI (Prague). Due to the increased fraction of high LET particles with a depth of proton beam penetration, radiobiological characteristics of the clinical proton beam changed with the depth as well.

The relative contribution of the high LET particles to absorbed dose increases from several percent at the beam entrance to several tens of percent at the Bragg peak region. The value of the RBE increased from about 1.0 at the beam entrance to about 1.25 at the Bragg peak. These values undoubtedly must be taken into account during beam production and using.

In future it will be interesting to make the same measurements of RBE values at the Bragg peak region of the modified proton and heavy ions clinical beams, where this effect is more significant.

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Progress on DICOM Standard for Ion Beam Therapy.

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The increasing number of different beam delivery and planning systems that are now or soon to be on line for proton therapy will require a large effort in developing communications protocols. These protocols are necessary not only to pass beam information from the planning system to the delivery system but also to compare treatments within inter-institutional trials. A sub-committee of the DICOM-RT working group has been formed to propose a communication standard for ion beam therapy. A progress report on the activities towards this standard will be presented.

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RBE values of 180 MeV proton beams at the Wakasa-Wan Energy Research Center an interim report.

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Prior to the start of clinical use, we are investigating the relative biological effectiveness RBE of 180 MeV therapeutic proton beams for the following objectives; 1) to confirm RBE for the medical course of synchrotron installed in the Wakasa-Wan Energy Research Center, 2) to accumulate data of RBE values for proton beams, 3) to check the apparatuses such as dose monitors by comparing with RBE which was measured in another facility with an accelerator. The biological systems used were HSG cell human salivary glands for in vitro experiment and mouse intestinal crypt cells for in vivo experiment. The dose responses by irradiation at the entrance plateau and a middle portion of a Spread-Out-Bragg-Peak (SOBP) of 6-cm width were compared with those by X-ray irradiation of a linac at 4 MV. RBE values of in vitro experiments were 1.14 and 1.08 at entrance plateau and SOBP, respectively. RBE values of in vivo experiments were 1.00 and 1.12 at entrance plateau and SOBP, respectively, showing similar RBE values previously reported. We are currently repeating measuring those RBE values of the beams for more reliable values.

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