ABSTRACTS

of the

NEUTRON THERAPY SYMPOSIUM

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Radiobiology/BNCT

Fermilab neutron therapy facility experience 1976-1995

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Twenty years' experience at the NTF proves that high energy neutrons from a proton linac can be delivered safely in isocentric mode to almost any defined target volume. Skin-sparing, attenuation charactersitics, beam-shaping, and treatment plans with this beam are virtually identical to those obtaining with 8 MeV photons. Response is found to depend on tumor histology and stage rather than site of origin.

Neutrons are primarily indicated for a well-defined subset of tumors in which they have been shown to yield better local control than conventional photon beams. These are mainly locally advanced, unresectable but non-metastatic, "radioresistant" tumors such as
sarcoma (bone and soft-tissue), melanoma, and adenocarcinoma (prostate, salivary gland, thyroid and pancreas), in all of which they have proved more efficacious and less costly than alternative modalities.

Secondary (cosmetic and logistic) indications for technically resectable tumors of head and neck and for metastatic neutron-responsive tumors are discussed. Some new developments are also considered.

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Neutron therapy for head and neck cancer and soft tissue sarcoma: the NAC experience

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A randomised study of neutron versus photon irradiation for headand neck cancer has been active for 7 years and has accured 136patients, with 122 patients available for analysis (follow-uplonger than 6/12). There is no difference in overall survival between the different treatment groups; as far as disease-free survival is concerned, there is a statistically significant difference between the photon arm and the twice-daily neutron arm. However, the patient numbers remain low in each group and the two radiation modalities have been used in a different way. A further analysis based on specific anatomical sites shows no difference in disease-free survival between neutron and photon groups; although there is a trend for better overall survival in the oropharynx group. Although there is no statistical difference in terms of grade 3, 4 late side-effects, there is a trend for more severe side effects in the neutron therapy group, compared to photon therapy. The soft tissue sarcoma study has now accumulated 64 patients with 56 patients having more than 6/12 follow-up, of those 41 were treated with radical intent. The patients with irresectable disease receiving a full course of neutron therapy had a 67% complete response when disease was <10 cm; this dropped to 14% when disease was >10 cm. Our results indicate that patients with small disease, either unsuitable for, or remaining after surgery, are the ones thatwill benefit most from neutron therapy.

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Locally advanced prostate cancer - results of radiotherapy with photons and fast neutrons

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Patients: From 1977 to 1986, 56 patients with locally advanced prostate cancer (stage T2b-4 N0-2 M0) were treated at the Department of Radiotherapy of the University-Hospital Hamburg-Eppendorf. Seven patients were staged B2-3, 36 patients stage C and 4 patients stage D1. In 9 patients treatment started, when local progression of the tumour was stated. All patients were treated with photons (3000 - 4500 cGy) to the prostate and to the locoregional lymphatics and a boost with fast neutrons to the prostate (300 - 740 cGy) in addition to transurethral resection (n=28) and orchiectomy (n=46).
Results: With a median follow up of 7.8 years, the 5- and 8- year local control rate for stage C patients was 84% and 79%. Nineteen out of 56 patients showed local progression of disease. A significant advantage in cause-specific -survival (CSS) and disease-free-survival (DFS) was seen for patients with local control of the tumor (n=37). The CSS-rate for 5- and 8- years for locally controlled patients was 94% and 79% compared with 77% and 51% for patients without local control (p=0.014). For DFS this difference was 32% and 11% vs 73% and 56% (p=0.00014). The CSS for 36 patients staged C for 5- and 8- years was 97% and 90% receptively. Altogether 7 out of 56 patients showed oneform of late side effects for the bladder and the rectum.
Conclusions: Our results seem to indicate that a mixed beam radiotherapy with photons and fast neutrons van favourably affect cause-specific and disease-free-survival in patients withlocally advanced prostate cancer.

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Androgen ablation followed by external photon irradiation with or without neutron boost in locally advanced prostate cancer: a protcol proposal

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A protocol has been designed by the South African Society of Radiation Oncologists (SASRO) to evaluate the potential benefit of photon irradiation followed by a neutron boost compared to androgen ablation/suppression alone in T3 N0 M0 (C) adenocarcinoma of the prostate. The concept is based on significantly improved 10 year locoregional control rates in T3-4, N0-1, M0 tumours treated with a neutron boost (77%) as opposed to photon irradiation (64%; RTOG 77-04, Laramore et al., 1993) and the cytoreducing effect of primary androgen suppression followed by photon irradiation. This regimen resulted in a significantly higher 3 year locoregional control rate of 84% relative to 71% for external beam irradiation alone (RTOG 86-10, Philepich et al., 1993).

There is also experimental and clinical evidence that early androgen ablation induces a more pronounced delay in tumour growth compared to late hormonal deprivation (Isaacs, 1984; Zagars et al., 1988). Furthermore it has to be recognized that improved locoregional control can only be adequately evaluated for patients with a follow-up time of more than 10 years, since 25-50% of the failures occur after this time (Swanson et al., 1994). Moreover, fewer than 10% of patients with positive nodes are alive at 15 years (Leibel et al., 1994). Therefore it is evident that the combination of an effective local and systematic treatment modality can improve the prognosis of this group of patients. In order to

detect a 15% difference, 150-200 patients need to be recruited. Countrywide, about 800 patients with locally advanced prostate cancer are being treated per year, among them ~ 200 T3, N0, M0 (C) cases. It is expected that approximately 50 patients will be referred by 10 institutions per year, so that the recruitment time would not exceed 4 years.

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Neutron therapy in adenoid cystic cancer of the salivary glands

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Purpose: The slowly growing adenoid cystic carcinomas seem to have a better response to fast neutron irradiation than to photon beam therapy because of the higher relative biological effectiveness.
Materials and methods: In Muenster 64 patients with adenoid cystic carcinomas of the salivary glands were treated with fast neutrons between 1986 and 1994 by a d,T-14 MeV neutron generator. Median age was 54 years. All patients were surgically pre-treated and had either macroscopic tumor left (91%) or recurrences (9%). The dose applied was 15.03 Gy with a single dose of 1.67 Gy given hypofractionated three times a week. Median follow-up was 29 months.
Results: 78% of patients achieved a complete remission after neutron therapy and 22% a partial remission. The survival calculated by the Kaplan-Meier method was 91% after one year, 76% after two years and 32% after five years. The recurrence-free survival was 90% after one year and 69% after two years. The early side effects were skin reactions (57%) Io-IIo (EORTC/RTOG score) and mucositis Io-IIo (32%). Two suffered from radiation induced mucosal ulcers (IIIo-IVo). Late effects were xerostomia in 32%.
Conclusions: Neutron beam therapy seems to be an effective treatment in these negatively selected patients.

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Salivary gland tumours treated with neutron therapy at NAC -an update

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From February ‘89 until March ‘95, 721 patients had been treated on the National Accelerator Centre’s (NAC) p(66)/Be neutron therapy beam. One hundred and sixty seven patients (23%) with salivary gland tumours had been treated. Ninety nine of these were treated with radical intent and are evaluable with 6 months or more follow up. There were 20 patients with macroscopic residual disease after surgery, 61 patients with advanced irresectable disease and 18 patients with resectable disease in whom there was concern about the morbidity that resection would cause to facial nerve or palate. Tumours were in the parotid gland (47), submandibular gland (7), hard/soft palate (16), maxillary

antrum (13), oral cavity (12) and other sites (4). Patients were treated with 20.4 Gy in 12 fractions in 4 weeks (range 18-22 Gy). Complete response was achieved in 69 patients and maintained in 57 patients. The 3 year local control and survival probabilities are 57% and 79% respectively. The effect of tumour stage, surgical status, site and dose on local control was studied in an earlier cohort of 80 patients and found to be significant for stage, ($p=0.02$), macroscopic residual v. resectable ($p=0.01$), macroscopic residual v. irresectable ($p<0.001$), maxillary antrum was worse than other sites ($p=0.025$) and a dose of 20 Gy or more did better than less than 20 Gy ($p=0.054$). Complication rate is 14% (10 out of 72 evaluable patients). Thirty seven patients were treated palliatively and there were 11 complete and 10 partial responses giving a 57% overall response rate. Nine of the complete responses (24%) were maintained at 6-40 months.

Neutron therapy remains the treatment of choice for patients with advanced irresectable salivary gland tumours and for those with macroscopic residual or questionable resectable tumours.

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The Faure experience of neuton irradiation for irresectable malignant melanoma

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Since 1990, 20 patients with irresectable primary or metastatic melanoma lesions have been treated at the p (66 MeV)/Be neutron therapy unit at Faure. 13 were treated radically (18-22 Gy in 12 fractions over 4 weeks).

RESULTS
CR 2
PR 5
NC 4
PD 1
LTFU 1
RR (CC + RR) 85.3%

Med. Survival 14.3 months
Local control 91% at 6/12;
71% at 1 yr

TOXICITY
Acute:
Skin grade 3 = 3
Mucosal grade 3 = 3

LATE:
* Grade 4 bowel = 1

* Grade 4 bone = 1

* same patient, coupled with extensive surgery.

7 were due for palliative irradiation but only 3 completed the treatment (13.5 - 16.8 Gy in 9-12 fractions) with 1 CR.

Neutron irradiation is useful for irresectable lesions, is well tolerated, and these results support continued use of neutrons which appear to be as good, if not more effective as photon irradiation.

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Squamous carcinoma of the maxillary antrum treated with fast neutron therapy at NAC.

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Forty one patients with tumours of the maxillary antrum and adjacent paranasal sinuses have been treated with fast neutron therapy on the NAC's p(66)/Be beam between February 1989 and September 1994 and have a minimum follow up of 6 months. Twenty two of these were squamous carcinoma or transitional cell carcinoma, 11 had tumours arising from minor salivary glands, and there were 3 malignant melanomas, 4 sarcomas and one ameloblastic carcinoma. The 20 squamous carcinomas and 2 transitional cell carcinomas have been evaluated. There were 17 males and 5 females and the ages ranged from 40-79 years with a median of 54 years. There were 1 T2, 5 T3 and 16 T4 tumours and nodes were present in 7 patients. Eighteen patients had stage 4 disease. Tumour size varied from 4.5 x 4.5 cm2 to 11 x 9 cm2. Patients received a median dose of 20.4 Gy in 12 fractions in 4 weeks (range 18-22 Gy).

There was a complete response in 11 patients, 50% occurring in 2-10 months. Three patients relapsed at 8, 22 and 29 months. The median survival of those having a complete response was 24 months (range 8-41 months) and in the others it was 8 months (range 5-22 months). Size and stage did not influence local control and survival. There was a complete response in 6 of the 7 nodal areas treated and one recurred. Overall local control and survival probabilities were 44% and 38% at 2 years (Kaplan-Meier). The results are encouraging for advanced irresectable disease of the maxillary antrum and comparable to other series. The proximity of the brain to the paranasal sinuses limits the dose that can be given to the superior part of the tumour volume. The addition of a proton boost to this lower dose volume close to the brain will allow the tumour to receive the full dose without increasing morbidity.

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The treatment of gynaecological tumours with neutron therapy at NAC

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Introduction: 45 or 6% of patients referred for neutron therapy since 1989 had gynaecological tumours(36 uterine sarcomas of various stages, 7 FIGO stage IIIb cervical cancers, and 2 incompletely resected FIGO stage III vulval tumors). Treatment results and crude complication rates are reported.
Materials and methods: (a)Histology: Uterine: MMMT 17, leiomyosarcoma 13, stromal sarcoma 4, adenosarcoma 1, fibrosarcoma 1. Cervical: Squamous/adenocarcinoma 6, adenoid cystic carcinoma 1. Vulval: Malignant fibrous histiocytoma 1, adenoid cystic carcinoma 1. (b)Radiation: Uterine sarcomas - curative intent: whole pelvis "box", 15.6 Gy in 12 fractions/4w, followed by boost via reduced portals, 2.6 Gy in 2 fractions to vaginal vault if complete resection or 4.5 Gy in 3 fractions to residual tumour. Palliative intent: 12-15.6 Gy in 12 fractions/4w. Cervical cancer: 15-16.5 Gy in 12 fractions/4w, followed by HDR brachytherapy 4 Gy x 4 to Pt A. Vulval tumours: 18 Gy to residual tumour+margin in 12 fractions/4w.
Results:(a)Uterine sarcoma - adjuvant(n=7): 6 evaluable. 1 died of local recurrence, 5 alive and clear, MST=36 months (7-60) (b)Uterine sarcoma - curative intent(n=14): 13 evaluable, CR 9, PR 2, NR 2. Complete responders: distal recurrence 4, local recurrence 1, ie 4/13 = 31% alive and clear, MST=40

months. Overall MST of group=7 months (4-46). (c)Uterine sarcoma - palliative intent(n=15): 14 evaluable, PR 5, NR 7, PD 2. 1 patient alive with stable disease at 12 months.MST=11 months responders: local recurrence 1, distal recurrence 1, 2/7 = 28% alive and clear at 7 and 21 months.(e) Vulval tumours (n=2): CR 1 - maintained for 37 months, died distal recurrence. PR 1 - stable disease at 22 months.(f) Crude complication rate: 2/42 evaluable patients RTOG>grade 2 = 5% (1 patient previous pelvic RT).
Conclusions: Small patient numbers in this unrandomised study prevent defining a role for adjuvant neutron therapy in uterine sarcomas; further accrual of such patients are invited. Of those with recurrent, irresectable or incompletely resected sarcomas treated with curative intent, 9/13 (70%) showed CR, though distal recurrences is a constant reminder of the behaviour of these tumours. Additional chemotherapy may extend the DFI. The 4/13 (31%) currently alive tended to have tumour diameters <5 cm. Only 35% of patients treated palliatively had PR with control of symptoms.With cervical cancer, no benefit over photons is apparent. 2 patients with unusual vulval tumors responded favourably. Treatment was well tolerated up to 20 Gy and the crude serious complication rate of 5% is acceptable; it is hoped more data on neutron therapy in uterine sarcomas can be accrued.

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Specification of dose and radiation quality for reporting neutron therapy

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The dose distributions achieved in neutron therapy are very similar to those in photon beam therapy. Therefore, the same approach can be followed for dose specification for reporting the treatment. In 1993, the ICRU (International Commission on Radiation Units and Measurements) published Report 50 “Prescribing, recording and reporting photon beam therapy”. The recommendations contained in this Report can also be followed in fast neutron therapy.

In therapy with fast neutrons, protons or heavy ions, a specific problem requires to be taken into account due to the fact that their RBE is significantly different from unity. The RBE of fast neutrons varies within wide limits depending on neutron energy spectrum, dose, biological system and endpoint. For proton beams, the RBE ranges within smaller limits (about 1.0 to 1.2). Clinical benefit is not expected from RBE differences. However, the RBE problem cannot be ignored, since dose differences of about 5% can be detected clinically in some situations and the prescribed dose is directly related to the selected “clinical RBE”. The situation is most complex with heavy ions since the RBE variation, as a function of particle type and energy, biological effect and dose, is at least as large as with fast neutrons. In addition, the RBE varies considerably with depth in the particle beam.

Radiation quality thus has to be taken into account when reporting a treatment and when prescribing the dose to the patient. This can be done in different ways:

a) Description of the beam production. For fast neutrons, nuclear reaction and energy of the incident particles. For protons, incident particle energy and width of the spread out Bragg peak. For heavy ions, type and energy of the particles and width of the spread out Bragg peak.

b) Computed LET spectra and/or measured microdosimetric spectra at one (or more) relevant point(s).

c) RBE determination. RBE determinations are currently performed using biological systems which are well codified and suitable for this type experiment. The most relevant data are those obtained for late tolerance of normal tissues with a fractionation of 2 Gy (equivalent) per fraction. This leads to the

concept of “reference RBE”. In general, the “clinical RBE” selected by the radiation-oncologist when prescribing the treatment will be the “reference RBE” or close to it. However, other factors, such as the dose distribution may influence the selection of the “clinical RBE”. Combination of microdosimetric spectra and experimental RBE values improves the confidence in both sets of data.

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Status report from the superconducting cyclotron neutron therapy facility at Harper Hospital

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Routine patient treatment commenced at the Harper Hospital superconducting cyclotron neutron therapy facility in March 1992. During the second year of operation the facility was available for 80.8% of the scheduled time, while in the third year availability was 91.6%, and so far in the fourth year (March - September) it has averaged 92.7%. Since March 1993 (when record keeping started) major sources of downtime have been identified as the RF system which accounts for 17.0% of all downtime, the magnet/cryogenic system (12.8%), operator errors (11.2%), the multirod collimator (8.8%), the ion source (5.9%) and the therapy console (5.7%). Downtime due to operator error has dropped significantly as operating experience increases; in the last year it accounts for only 2.2% of the annual downtime. Strategies for minimizing downtime have included carrying as many direct replacement spare parts as possible; these include spare rotary and turbo molecular pumps, power supplies (including magnet power supply), target assembly, gantry drive motor, computer/accelerator interface unit and electronics components. Spares of the custom-made electronics modules and a spare ion source assembly are under construction. A 24 hour alarm is for power interrupts and failures and for vacuum failures through the hospital security office.

In the first year of operation (March 1992 - February 1993) 711 fields were treated in 299 treatment sessions, the corresponding numbers for the 2nd and 3rd years of operation are 3910 fields in 1392 and 3425 fields in 1124 sessions respectively. So far this operational year (March 1994 thru September 1995 - 7 months) 3451 fields were treated in 932 sessions; this projects to approximately 5900 fields and 1600 treatment sessions for the full year. Of the 369 patients treated so far with neutron therapy at the Harper Hospital facility, 255 have been patients with adenocarcinoma of the prostate. Many of these patients have been treated using 3D conformal therapy and non-coplanar fields. The non-coplanar technique involves two lateral fields, a right anterior inferior superior oblique field (RAISO) and a left anterior inferior superior oblique field (LAISO); patients treated with this technique receive 10 Gy equivalent of neutrons in 10 fractions plus 38 Gy of photons (2 Gy/fraction). Preliminary results based on post treatment biopsies and PSA levels suggest that this treatment with photons using twice ad day (BID) treatment may achieve a comparable result.

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Neutron kerma assessments in a d(48.5)+Be therapy beam

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The neutron kerma ratio of tissue to A-150 plastic was experimentally determined for the d(48.5)+Be therapy facility at Harper Hospital, Detroit. Low pressure proportional counters with different walls made from A-150 plastic, graphite, zirconium oxide and zirconium served to measure ionization yield spectra. The absorbed dose in the wall of each counter was determined and rendered the A-150 and carbon kerma directly whilst that for oxygen was deduced from differences between the matched metal oxide and metal pair. This enabled the evaluation of an effective kerma ratio as a function of radiation field size and hydrogenous filtration. Although filtration was observed to harden the beam the application of a single kerma ratio for the various irradiation conditions investigated was found appropriate. A kerma ratio of 0.94 ± 0.02 was assessed for the beam and agrees with previous independent estimates for a similar clinical source and supports continued use of the recommended value of 0.95.

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Microdosimetric studies in the Harper Hospital fast neutron therapy beam.

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The proportional counter microdosimetric technique has been employed to quantify the variation in the quality of a d(48.5)+Be fast neutron beam passing through a homogeneous water phantom. Single event spectra have been measured as a function of central-axis depth and lateral position at field size between 5 x 5 cm^2 and 20 x 20 cm^2. The measured microdosimetric spectra have been analyzed in terms of the gamma ray dose component, the recoil proton and the heavy ion (including all ions beyond the proton edge) dose components. the RBE of the neutron beam is assumed to be proportional to the microdosimetric parameter y* (the saturation corrected mean lineal energy) for doses of the magnitude encountered in fractionated radiation therapy. The relative variation in y* within the phantom is assumed to be representative of variations in the RBE as function of field size and position in the phantom. A variation of about 4% was observed in y* for points within a 10 x 10 cm^2 field and an 8% variation was seen for points outside the field. The variation in y* within the beam result form the increase in the gamma dose component with depth in the phantom. An increase in y* of about 4% is observed with increasing field size and this is attributed to a change in the neutron phantom. The measured spatial y* (RBE) variations are not considered significant enough to be incorporated into the treatment planning system. These variations are small in comparison to the uncertainties in the prescribed dose associated with uncertainties in the clinically assigned RBE, the variation in the RBE between various tissues/organs and the other dosimetric uncertainties such as patient inhomogeneities, patient set-up errors, patient motion etc.

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Potential therapeutic gain from using p(66)/be neutrons.

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Neutron therapy will be beneficial to patients with tumour types which are resistant to photons but relatively sensitive to high-LET radiation. In this work 15 different cell types, mostly of human tumour descent, were exposed in vitro to Cobalt-60 and p(66)/Be neutrons. Micronuclei frequencies in binucleated cells and surviving fractions were determined for each cell type. Following exposure to either 1 or 1.5 Gy neutrons, micronuclei frequencies were significantly correlated with that observed from 2 Gy photons. A strong correlation between mean inactivation doses determined for these radiation modalities from survival curve inactivation parameters, was also noted. In spite of this a significant correlation between the variation in neutron RBE values and photon resistance was established. It is concluded that although neutron and photon sensitivities are related in the group of cell types studied, the use of this high energy neutron source may constitute a potential therapeutic gain for some tumour types.

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The role of cell cycle kinetics and dna content in the radiosensitivity of human tumour cells to photons and neutrons.

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Large variations of intrinsic radiosensitivities between patients with identical tumour types make it very difficult to select patients for specific radiotherapeutic schedules. Radiosensitivity assays could therefore considerably improve the current success rate of radiotherapy. Cells in the different stages of the cell cycle differ in radiosensitivity with
S-phase cells the most radioresistant and G2/M cells most radiosensitive, and the DNA content of the cells in these different stages also differ. DNA content and cellular proliferation kinetics could therefore have an influence on intrinsic radiosensitivity and could serve as predictors of radiation response. This prompted us to investigate the relationship between DNA content, cell kinetics and the intrinsic radiosensitivity of 15 human tumour cell lines to photon and neutron irradiation. This study was done in the hope to establish radiobiological criteria which could help in the selection of patients for photon and neutron therapy. DNA content and cell cycle kinetics were analysed by single- and multi-parameter flow cytometry techniques involving BrdU antibody labelling. Survival parameters were obtained by exposing cells to either (60)Co gamma rays or P(66)/Be neutron irradiation. Survival data were fitted to the linear quadratic model and a mean inactivation dose was calculated for each cell line. Linear regression analyses showed a correlation between %S-phase, Tpot (potential doubling time) and mean inactivation doses for photons (r=0.63). No significant correlation was found between neutron mean inactivation doses and cell kinetic parameters. DNA content showed no correlation with either of thetwo radiation modalities. It is concluded that high %S-phase and short Tpot have potential value as predictors of photon response. It is suggested thatcertain tumour cell vs. normal cell proliferation rates might benefit fromneutron irradiation. In such cases the analysis of cell cycle kinetics might play a role in patient selection for neutron therapy.

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Neutron capture therapy: status and prospects

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With the advent of powerful neutron sources (high-flux reactors or spallation sources) new possibilities appear for use of filtered slow-neutron beams. This situation, and important recent chemical and biological developments, contribute to the renewed interest in the classical idea, 'neutron capture therapy' (NCT) based on the special characteristics of some nuclei with very high neutron capture cross-sections, notably ^{10}B. Since this modality, evidently, is dependent on the ability of used boron compounds to penetrate into tumor tissue, it is very likely to be more useful for treatment of small local metastases and infiltrating tumor cells than in radiotherapy for solid tumors. There is thus a need for development of improved boron-carriers, and important progress is being made.

It is worth noting that few neutrons are induced in the irradiated tissue during ion therapy. Not so with fast neutrons, however. The situation has still to be studied, from scratch, but it is instructive to review the prerequisites for the use of NCT in fast neutron therapy. It has been observed that the low energy neutrons present in fast neutron therapy may be used for dose enhancement in tumors that can be selectively loaded with ^{10}B. Since the probability of tumor control is a steep function of dose, even prospects of a few per cent increase in the biologically effective dose, in tumor cells, would provide motive for NCT-assisted fast neutron therapy. For an efficient therapy of tumor cells near the edge of the radiation field, uptakes of >100g ^{10}B/g of tumor ought to be strived for.

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Activation of soda-lime glass spheres for Boron Neutron Capture dosimetry in a fast neutron therapy beam

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The fast neutron therapy beam (FNB) from the Seattle cyclotron facility has been investigated for the possibility of a concomitant BNC dose boost with the goal to selectively increase the tumor dose while sparing normal tissue.

The FNB dose distribution for various beam geometries was measured with a tissue equivalent ion chamber, while the expected BNC dose was determined by neutron activation of the ^{23}Na in 5 mm diameter soda lime glass spheres. A standard material for activation studies of this nature is gold. Typically gold foil measurements require two runs: with and without cadmium shield. Sodium has the advantage that its low energy capture cross section runs parallel to the 10B cross section up to about 100 eV compared to 1 eV for gold. There is only little dose contribution from higher energy capture events and for a general dose survey it is not necessary to include runs with cadmium shielded activation material. The glass spheres have proven to give reproducible results at the 3% level.

Based on the activation results a test set-up was chosen for a first experimental irradiation of a human melanoma patient. Two skin nodules were irradiated one before and one after administering a ^{10}B containing drug. The results were encouraging and the studies are expected to continue.

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Plans for Gd-NCT at Moscow TTR reactor: facility, radiobiology, clinical aspects

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Considering encouraging results of Gd- NCT assay carried out on tumor-bearing rats, a planning work is now under way at the Thermal Testing Reactor (TTR), Moscow. The project is based on Gd-related NCT with certain clinical prospective. Biomedical beam is under construction with improved characteristics, namely: diameter of the beam from 30 to 150 mm; thermal neutron fluence rate 109 n/cm2/s; core gamma dose 0.002 Gy/sec. Dosimetric studies at the beam are planned in phantoms irradiated by both thermal and epithermal neutrons using Gd-DTPA complexes. The goal for radiobiologic assays is comparison of Gd NCT and X-ray effects on the cells in vitro and tumor-bearing rats models. Clinical effects of Gd-related NCT could be related to the treatment of (i) surface-seated tumours, and, (ii) high grade gliomas. Gd-complexes for tumour visualisation and demarcation are widely used in patients with high grade glioma at the Burdenko Institute for Neurosurgery, Moscow, and are estimated as being of potential value for purposes of NCT.

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Neutron capture therapy with Gd-DTPA in tumor-bearing rats

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Aim: Does Gd-DTPA intratumorally administered prior to the n-irradiation have a therapeutic benefit due to the high neutron cross section of Gadolinium (Gd)?
Materials and Methods: Rats with a Jensen sarcoma were irradiated with thermal neutrons of the TTR reactor, Moscow, at two fluences (3.6 x 10+11 and 5.4 x 10 + 11 n/cm2) in the presence or absence of high Gd-DTPA concentrations (13,750 ppm Gd/g tumor). The results of the treatment were monitored by observing the clinical status of the animals and measuring the tumor size as function of time post irradiation. Four groups were studied: two controls ((Gd-n-), (Gd+n-)) and two irradiated ones ((Gd-n+), (Gd+n+)).
Results: The non-irradiated controls showed a continuous tumor growth. 20 min irradiation alone resulted in a transient growth inhibition, while the intratumoral administration of Gd-DTPA prior to the neutron irradiation led to a significant decrease of the tumor volume with four times as much total regressions as obtained with the n-irradiation in the absence of Gd-DTPA. At 30 min irradiation the Gd-specific effects are less pronounced due to the high -background and the drainage of the Gd-DTPA from the tumor.
Conclusion: Gd-DTPA (Magnevist) intratumorally administered prior to the neutron-irradiation has therapeutic gain and considerable potential for the clinical treatment of tumors. The total body dose of the Gd-DTPA administered is about six times the diagnostic dose routinely used in MRI.

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