Biomedical Research

The activities of the institute in the field of biomedicine have been devoted to two topics: The continuous operation of positron emission tomography (PET) for quality assurance of heavy ion therapy and the improvement of this method, and as a further application of nuclear physics based technology to a biomedical issue, the preparation of an experimental facility at ELBE for cell radiobiology with quasi-monochromatic X-rays.

During the time period reported here (July 1999 – Dec. 2000) 46 Patients suffering from head and neck tumours received carbon ion therapy at the experimental therapy facility at GSI Darmstadt. All these irradiations have been monitored by means of the Rossendorf in-beam PET scanner BASTEI. It could be confirmed that the modifications of the treatment planning data base, which were initiated by PET observations of carbon ion range deviations especially in highly inhomogeneous target volumes, considerably improved the precision and the reliability of the treatments. This allowed the carbon ion therapy to be extended to more delicate situations. An evaluation of the 45 patients with skull base tumours irradiated with carbon beams between December 1997 and September 1999 was published earlier this year (J. Debus et al., Strahlenther. Onkol. 176 (2000) 211). After a mean follow-up of 9 months it revealed that the irradiations were well tolerated by all patients. Partial tumour remission was seen in 7 patients, one-year local control was 94 %, one patient deceased. No severe unexpected toxicity and no local recurrence within the treated volume were observed. The clinical effectiveness and the technical feasibility of the experimental therapy facility could be demonstrated. To evaluate the clinical relevance, larger patient numbers are necessary and, therefore, the treatments will be continued during three time slots of about 4 weeks a year. Continuing this project a new heavy ion accelerator exclusively for clinical use is planned to be constructed in Heidelberg. The facility will be capable of producing therapeutic beams ranging from protons to oxygen ions, it will be equipped with rotating beam deliveries (gantries) that will be combined with in-beam PET for therapy monitoring. These results and future plans determine the current work on the PET project:

- *To increase the flexibility in treatment planning the GSI therapy facility will be equipped with a chair in 2001 for treating patients in a sitting position. This required to built up a completely new PET gantry which allows the detector heads to be rotated around the beam axis.*

- *It is desirable to quantify deviations between the planned and the applied dose distributions on the basis of PET data. Such deviations are caused by slight mispositioning or by changes of the patient's physical condition during the treatment of more than 3 weeks duration. To prepare for this, improved attenuation and scatter correction methods of the measured data as well as refined models (positron range, photon scattering) for predicting the β^+-activity from the treatment planning have been introduced.*

- *Combining an in-beam PET scanner with an ion beam gantry for multi-field irradiations, as it is planned for the Heidelberg clinical facility, requires new technical solutions, namely new scanner configurations. To predict their imaging properties a versatile PET simulation and reconstruction tool has been developed. Gantry-based multi-field therapeutic irradiations may result in PET scans of rather low counting* *statistics and, thus, an optimization of the signal-to-noise ratio is required. For this we studied the possibility of using the new scintillator material Lutetiumorthosilicate (LSO), which is superior to the currently used Bismutgermanate (BGO) with respect to light output and fluorescence time. We analyzed the influence of the time microstructure of the synchrotron beam to the random coincidence rate registered by the positron camera as the basis for improving the signal-to-noise ratio of the PET images by an effective random coincidence rejection.*

- *The investigation of an extension of our PET technique to proton therapy monitoring has been initiated.*

In preparation of radiobiological investigations with quasi-monochromatic X-rays produced by electron channeling in diamond at ELBE the following activities have to be reported:

- *The radiation physics beam line, where the radiobiological experiments will be performed, has been designed with special attention to an electron beam of low divergence for a high channeling radiation yield. On that basis the majority of the beam line components have been purchased.*

- *By means of Monte Carlo simulations the different radiation components (channeling X-rays, bremsstrahlung, neutrons) contributing to the dose in the cells have been quantified. The beam line configuration has been optimized to reduce the bremsstrahlung and the neutron background. A dedicated channeling radiation production target is under construction. Nevertheless, for energy dependent cell survival studies a further reduction of the bremsstrahlung background is necessary. This will be performed by means of filters of highly oriented pyrolytic graphite.*

- *The equipment for X-ray dosimetry has been purchased and set into operation. Due to the high attenuation of the rather soft X-rays a reliable dosimetry within the cell monolayers requires special care. As a possible solution the application of thermally stimulated exoelectron emission dosimetry has been studied.*

- *The experimental techniques for cell survival studies have been trained and successfully applied to the measurements of the relative biological effectiveness of 25 kV X-rays.*

- *The cell laboratory attached to ELBE has been designed, construction has been started and the main technical equipment (class 2 safety cabinet, incubator, autoclave, centrifuge and microscope) has been purchased.*

Collaborations

Heavy Ion Tumour Therapy

- *GSI Darmstadt*
- *Radiologische Klinik of the Universität Heidelberg*
- *Deutsches Krebsforschungszentrum Heidelberg*
- *Institute for Bioanorganic and Radiopharmaceutical Chemistry (FZ Rossendorf)*

Cell Radiobiology at ELBE

- *Klinik für Strahlentherapie und Radioonkologie of the TU Dresden*
- *Institut für Strahlenschutzphysik of the TU Dresden*
- *Institut für Zoologie of the TU Dresden*
- *Institute for Bioanorganic and Radiopharmaceutical Chemistry (FZ Rossendorf)*

The Redesign of the Positron Camera BASTEI for In-Beam PET Monitoring of Patients Treated with Carbon Ions in a Sitting Position [B,E,G]

W. Enghardt, F. Pönisch, M. Sobiella, P. Crespo[1], D. Schardt[1]

The heavy ion therapy facility at GSI is only capable of delivering a fixed horizontal beam, where the patients have been treated in supine position up to now. This reduces the flexibility in treatment planning for the most frequently treated skull base tumours [1] as a recent analysis of the treatment geometry of such tumours revealed: The heavy ion beam portals giving an optimum dose conformation to the target are found to have an inclination of about 10 to 45 deg with respect to the frontal plane of the patient in supine treatment position [2]. A maximum flexibility for choosing the beam portals as it is usual at medical electron linear accelerators for photon and electron therapy would be achieved with a rotating beam delivery (gantry) [3]. Since such a solution is not feasible at the GSI experimental heavy ion therapy unit, a chair for irradiating patients in a sitting position will be mounted at the therapy site in 2001.
The original design of the positron camera BASTEI [4] was based on the assumption that patients are exclusively irradiated in supine position and thus the detector heads were mounted below and above the table. Evidently they would interfere with a sitting patient. In this case the detector heads have to be rotated into a horizontal or oblique position. Since the positron camera cannot be moved from its park position being 110 cm upbeam to the treatment site before immobilizing the patient, and considering the size of the beam delivery (see Fig. 1), the gap between the heads has to be increased from 83.2 to 115 cm before rotating. After this the camera can be moved downbeam to the patient position and the heads are radially removed to their standard imaging distance of 83.2 cm. To meet these requirements the PET gantry had to be completely rebuilt (Fig. 1).
The gantry reconstruction has been coordinated by Dr.-Ing. Haderthauer, nukmed konstruktion, Tülau-Fahrenhorst, mechanical engineering was carried out by Bernd Flach, Maschinenbau & Kunststoffverarbeitung, Schönheide under the technical leadership of K. Spitzner, and the control system based on the SPS process control units of SIEMENS including the position readout via network by the PET workstation has been developed by Automatisierungstechnik Egbert Neuschulz GmbH, Salzwedel. The reliability of the new gantry was demonstrated during the therapy of Nov./Dec. 2000, when 535 PET scans have been performed.

Fig. 1 *The new PET gantry in treatment position. (Photo: A. Zschau, GSI Darmstadt)*

[1] *Gesellschaft für Schwerionenforschung Darmstadt*

References

[1] J. Debus et al., Strahlenther. Onkol. 176 (2000) 211
[2] O. Jäkel, J. Debus, Phys. Med. Biol. 45 (2000) 1229
[3] K.D. Gross, M. Pavlovic (eds.), Proposal for a dedicated ion beam facility for cancer therapy, GSI Darmstadt, 1998
[4] W. Enghardt et al., Strahlenther. Onkol. 175/II (1999) 33

A Realistic Description of Positron Ranges Based on GEANT Simulations [G]

F. Pönisch, B. Naumann[1], W. Enghardt

The monitoring of dose localization at carbon ion tumour therapy at GSI Darmstadt by means of BASTEI [1] requires the comparison between the measurement and a model calculation of the positron activity distributions [2]. For this a realistic description of the positron range distribution in tissue is required. For that purpose a new model is developed and an improved numerical implementation to the code is used.

Up to now the probability distribution of the positron emitter range is supposed to be a bilinear exponential function [3] with three parameters depending on the maximum positron energy. These parameters have been estimated for β^+-endpoint energies up to 3.5 MeV, which is sufficient for PET applications to nuclear medicine. However, in the nuclear fragmentation reactions between the therapeutic carbon ion beam and the atomic nuclei of the tissue β^+-emitters of much higher endpoint energy (up to 16.7 MeV) are produced for which the parametrization of [3] is not proved. Therefore, the positron range distributions have been calculated by means of GEANT [4] simulations for all positron emitting isotopes that may be produced by the fragmentation of ^{12}C ions in tissue. The geometry used in the GEANT calculations consists of an isotropic point-like source in the centre of a water cube being sufficiently large for stopping all the positrons. The initial positron energy values were deduced from the β^+-energy spectra. In Fig. 1 the projection of the 3D spatial distribution on an arbitrary oriented axis (denoted with x) obtained by GEANT is compared with those of Hasch [2] and Derenzo [3]. A much more realistic description of the positron transport in the calculation of the β^+-activity distribution is expected if the 3D positron range distribution (Fig. 2) is applied. Now the distribution function method is used for sampling the range values. A cumulated distribution function (cdf) is constructed from the positron range distribution, which was derived from the GEANT results. The inverse function of cdf is stored in a lookup-table. This database is used for the sampling of the random quantity positron range by means of chosing equally distributed random numbers within the interval [0,1].

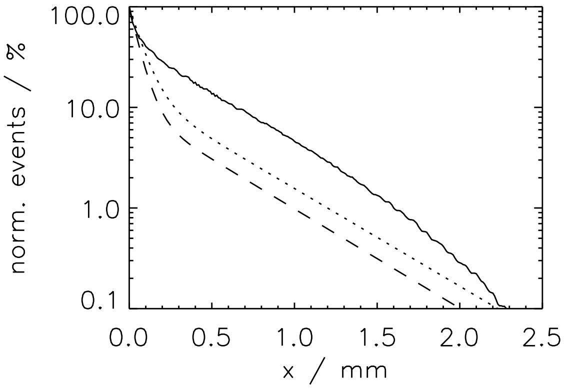

Fig. 1 *Projected point spread function by Derenzo (dashed), Hasch (dotted) and GEANT (solid) for ^{11}C.*

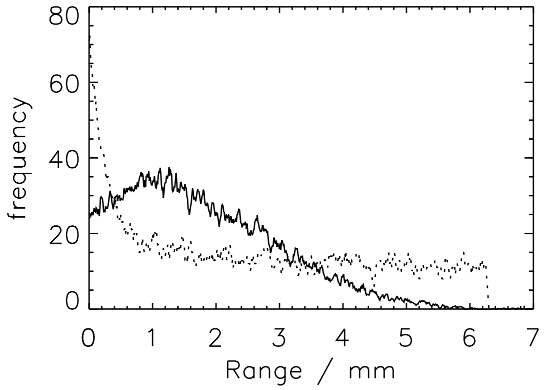

Fig. 2 *Positron range distribution of random quantities implemented by Hasch (dotted) and by GEANT (solid) for ^{15}O.*

[1] *TU Dresden, Institut für Kern- und Teilchenphysik*

References

[1] W. Enghardt et al., Annual Report 1999, FZR-271 (1999) 89
[2] B. G. Hasch et al., Annual Report 1996, FZR-179 (1997) 87
[3] S. E. Derenzo, IEEE Trans. on Nucl. Science, Vol. 33, No.1 (1986) 565
[4] GEANT-Detector Description and Simulation Tool, CERN Prog. Lib. W 5013 (1994)

An X-ray CT Based Attenuation Correction Method for PET [G]

F. Pönisch, W. Enghardt, K. Lauckner[1]

As reported [1] a maximum likelihood algorithm was adapted for the reconstruction of images from data taken by the limited angle double head camera BASTEI at the heavy ion therapy facility of GSI Darmstadt. The necessary attenuation correction algorithm differs from the one which is used in nuclear medicine. The information on tissue composition and densities within the camera field of view (FOV) are derived from X-ray computed tomograms (CT) which are taken for each patient for treatment planning. Additionally, a CT of the head rest is used. These two CT are automatically merged by means of our MERGECT IDL-code. The correct positioning of these CT with respect to the positron camera is derived from stereotactic coordinates used during the diagnostic CT scan and the tumour irradiation with simultaneous PET measurement. The created data set contains all information on the spatial distribution of matter within the positron camera FOV and is the basis for the calculation of attenuation correction factors. The Fig. 1 shows that there is a significant influence of absorption by the head rest on the detector response. The dashed lines denote the acceptance cone of the tomograph. By means of the HU-density calibration curve (Fig. 2) for a given Hounsfield unit (HU) the corresponding density is obtained. Due to the dependence of the mass attenuation coefficients on the tissue composition a segmentation of the HU range into air, soft tissue and bone is applied. The attenuation factors along each coincidence channel (4 millions) are calculated by a forward projection. From Fig. 3 the improvement is evident; whereas without attenuation correction spurious activity is observed inside the nasal cavity it is nearly completely removed after introducing the attenuation correction.

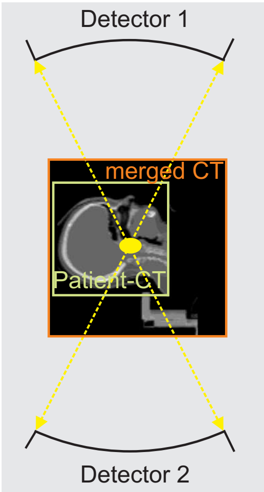

Fig. 1 *PET detector with a sagittal slice of a patient and head rest extended CT.*

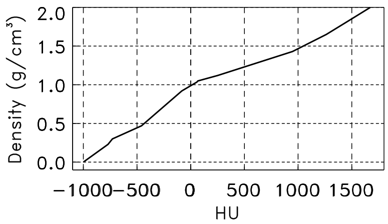

Fig. 2 *Density-Hounsfield unit calibration curve from Zaers [2].*

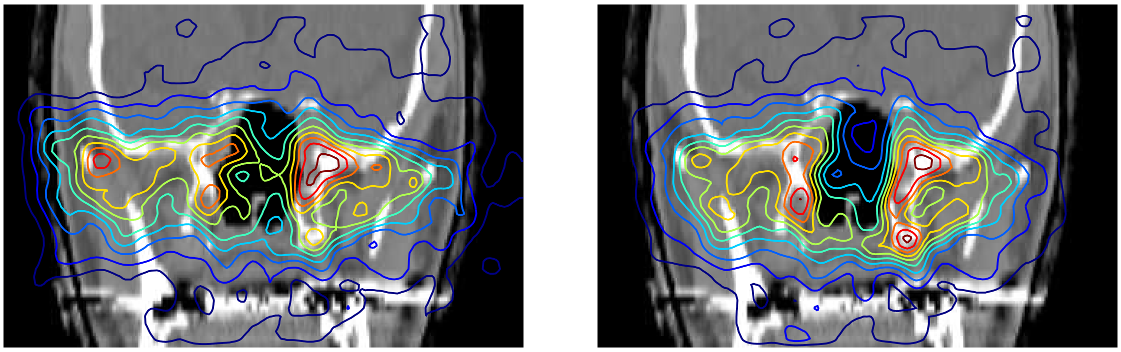

Fig. 3 *Comparison of β^+-activity distributions obtained without (left) and with (right) attenuation correction for a beam portal that is typical for treating skull base tumours. The beam enters the patient from the right side (left on the figure). The β^+-activity isolines are superimposed onto X-ray CT.*

[1] *Gesellschaft für Schwerionenforschung Darmstadt*

References

[1] K. Lauckner et al., Annual Report 1997, FZR-215 (1998) 70

[2] J. Zaers, DKFZ Heidelberg, priv. communication

The Description of Photon Scattering on the Basis of X-ray CT data [G]

F. Pönisch, W. Enghardt, J. Henniger[1]

The process of photon scattering considerably influences the image quality in positron emission tomography (PET): for head and neck imaging only about 20 % of the annihilation photons escape the patient without any interaction with the tissue. About 25 % of the registered true coincidences are influenced by Compton or Rayleigh scattering, which may destroy the correspondence between the source and the reconstructed radioactivity distribution, especially in highly inhomogeneous regions of the human body. In the PET application for quality assurance of carbon ion therapy [1] the scatter problem has to be considered not only with respect to the reconstruction of the source distributions from the measured data but, furthermore, to the prediction of the β^+-activity distribution from the treatment plan and the time course of the irradiation [2]. Since the decision on the correctness of an irradiation is based on the comparison of this prediction with the β^+-activity distribution reconstructed from the data acquired during the patient treatment, both data sets have to be processed the same way. Therefore, the first step of the prediction is a Monte Carlo calculation [2] that describes the stopping of the therapeutic ion beam in tissue, the decay of the β^+-emitters, the propagation of positrons and the annihilation photons and finally the γ-ray detection. This code produces a list mode data set like a measurement and thus it can be reconstructed in the same way as measured data. However, in the original Monte Carlo code photon scattering was processed in a simplified way by assuming a homogeneous scatter volume ($400 \times 200 \times 200\,\mathrm{mm}^3$, $\rho = 1.18\,\mathrm{g/cm}^3$) centered in the field of view (FOV) of the positron camera. Thus, the simulated data had to be reconstructed without attenuation correction. Obviously this approach is quantitatively incorrect and neglects the large tissue inhomogeneities of the head and neck region, as the typical target for carbon ion therapy at GSI. Therefore, a more comprehensive scatter description has been developed. It requires an attenuation map obtained from the X-ray computed tomograms (CT) of the patient and of the equipment for patient positioning within and nearby the camera FOV [3]. The positron and annihilation photon propagation is modelled by means of a Monte Carlo code that takes also into account multiple scattering. To reduce computing time the following approaches that do not influence the accuracy have been introduced: 1) Positron annihilation in air is neglected. 2) The points of interaction are determined by means of the Delta Scattering Photon Transport algorithm of ref. [4], leading to a run time being independent on the voxel size of the CT. 3) The processing of annihilation photons is stopped either after hitting a detector, after escaping the CT image stack or after reducing the photon energy below 250 keV (the lower energy threshold of the positron camera). 4) Due to the coincidence condition it is not necessary to follow the second photon of the annihilation pair if the first photon is not detected. The computing time is reduced by a factor of 4 in comparison with the original method. This CT based photon scatter estimation allows the reconstruction algorithm to be applied to the measured and simulated PET data sets in a similar way. This is, furthermore, the condition for including a scatter correction algorithm in the reconstruction in order to evaluate both simulated and measured data quantitatively.

[1] *TU Dresden, Institut für Strahlenschutzphysik*

References

[1] W. Enghardt et al., Annual Report 1999, FZR-271 (1999) 89
[2] B.G. Hasch et al., Annual Report 1996, FZR-179 (1997) 87
[3] F. Pönisch et al., „An X-ray CT based attenuation correction ...“, this Annual Report
[4] C.H. Holdsworth et. al, IEEE NSS Conference Record 1999, M10-66

Possible Effect of the Carbon Ion Beam Microstructure on In-Beam PET Measurements at GSI Darmstadt [B]

K. Parodi, W. Enghardt, H. Eickhoff[1], T. Haberer[1], P. Moritz[1], P. Forck[1], A. Peters[1]

The data acquired by the positron camera during the beam spills delivered by the heavy ion synchrotron SIS at GSI Darmstadt are affected by high noise level and are useless for the image reconstruction. A reason could be a wrong correction of random coincidences. The standard method of random correction, identifying random coincidences with delayed ones (delay time of 128 ns and coincidence window 12 ns wide), properly works in nuclear medicine, where the random background seen by the scanner is rather constant in time. In the therapy case, a background correlated in time with the beam microstructure on a time scale comparable to the delay time could lead to an underestimation of random coincidences and hence to the observed increase of noise. In Fig. 1 we sketch the background model used in our simulation approach for reproducing the experimental random (i.e. not related to β^+-activity) prompt and delayed coincidence rates acquired by the camera in spill. The periodical repetition of the bunch Gaussian shape represents the background radiation directly following the beam appearance, whereas the bias c introduces a delayed γ-ray component, due to isomeric de-excitations or radioisotope decay with half-lives longer than several ns.

Our model with FWHM and period values given by in-ring measurements of the beam microstructure at flat top voltage $U_{ft} = 2\,\text{kV}$ (which is applied for a more homogeneous beam structure in time) could not explain all the experimental PET data. Therefore, the microstructure was measured after the extraction in the beam line of the medical cave. At $U_{ft} = 2\,\text{kV}$ the time occurrence of the ions in one RF period (Fig. 2) revealed bunches of lower FWHM than in the accelerator ring. With the new measured T and w values, all the experimental prompt and delayed coincidence rates could be reproduced by simulation, provided that a bias c of some percent with respect to the Gaussian modulation was added. However, at $U_{ft} = 0\,\text{kV}$ the microstructure vanished (Fig. 2), while the in spill PET data could be explained by a loss but not a completely suppression of time correlation at $U_{ft} = 0\,\text{kV}$. Nevertheless, the disagreement could come from slight self-bunching effects, due to the higher beam intensity ($I \simeq 10^7 - 10^8$ ions/s) in the PET acquisitions than in the microstructure investigation ($I \simeq 10^5 - 10^6$ ions/s). On the basis of all these considerations, we want to measure the background radiation seen by the positron camera. If the experiment will confirm our model and hence prove the beam microstructure influence on the in spill PET acquisitions, the last step will be to destroy the microstructure or to find a new method of random correction, overcoming the limitations given by frozen software and hardware features of the scanner installed at GSI.

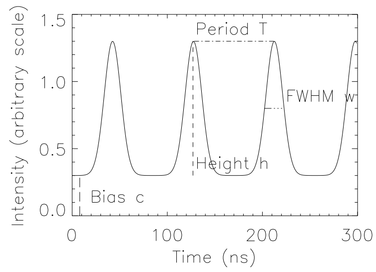

Fig. 1. *Model of the background radiation reaching the scanner during the beam spill.*

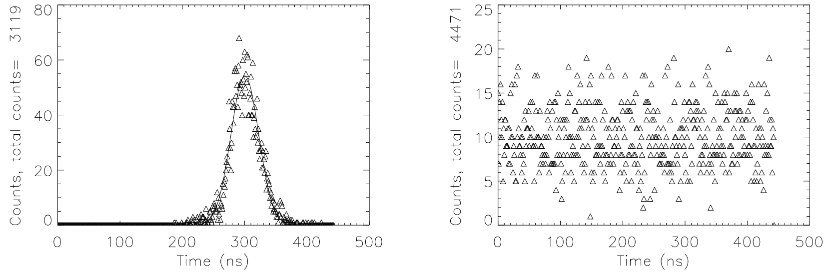

Fig. 2. *Left: example of beam microstructure at $U_{ft} = 2\,kV$. A Gaussian fit is superimposed onto the data. Right: example of not correlated time distribution measured at $U_{ft} = 0\,kV$.*

[1] *Gesellschaft für Schwerionenforschung Darmstadt*

Potential Extension of PET Technique to Proton Therapy Monitoring [B]

K. Parodi, W. Enghardt

In perspective of the proposed proton and heavy ion (up to oxygen nuclei) therapy facility at Heidelberg [1] and on the basis of the positive impact of positron emission tomography to quality assurance of carbon ion therapy at GSI Darmstadt [2], we investigated the potential of PET for proton therapy monitoring [3]. We simulated by means of the FLUKA Monte Carlo code the β^+-activation of a $9 \times 9 \times 30\,\mathrm{cm}^3$ PMMA target ($C_5H_8O_2$, $\rho = 1.19\,\mathrm{g/cm}^3$) irradiated by monoenergetic pencil-like proton beams (FWHM = 10 mm) in the energy range of interest for therapy (70 − 200 MeV). The selected target contains the most abundant elements of the human body and is very suitable for experimental investigations. The simulated yield of β^+-emitters of main relevance for the PET monitoring, namely ^{11}C, ^{15}O and ^{10}C, and the outcoming activity in 5 minutes (as a typical irradiation time) were found one order of magnitude lower than those induced by carbon ion irradiation at the same range and number of projectiles. But keeping into account the $\simeq 20$ times higher fluence of protons required in order to deliver the same physical dose and, furthermore, the lower relative biological effectiveness of protons in comparison to carbon ions, the activation induced by protons is expected to be at least twice as intense than for carbon ions. However, the spatial correlation between the positron emitter distribution and dose is poorer for protons, since they cannot experience the projectile fragmentation reaction leading to the sharp activity peak close to the dose maximum in the carbon ion case (Fig. 1, right). Nevertheless, the range and Bragg peak position of protons are still correlated to the distal edge of the β^+-emitter depth distribution (Fig. 1, left), depending on the energy threshold of the fragmentation reactions and on the O/C ratio of the irradiated target. Therefore, an important check of particle range and dose localisation seems to be possible for proton irradiation, too.

In practical clinical cases a strategy could be to compare the measured activity with a simulated pattern based on the treatment plan, as already done in the carbon therapy case [2]. Moreover, an in-beam PET scanner is required in order to exploit the quantitative gain in the activity signal, dominated by the contribution of ^{15}O ($T_{1/2} = 121.8\,\mathrm{s}$) according to our estimations in typical mean irradiation times. On the basis of these simulated results and of their agreement with a previous set of off-line PET measurements [4], sensitive only to the activity contribution coming from ^{11}C, a new experiment has been performed with the FZR in-beam PET scanner at GSI Darmstadt in December 2000. The data analysis is currently in progress.

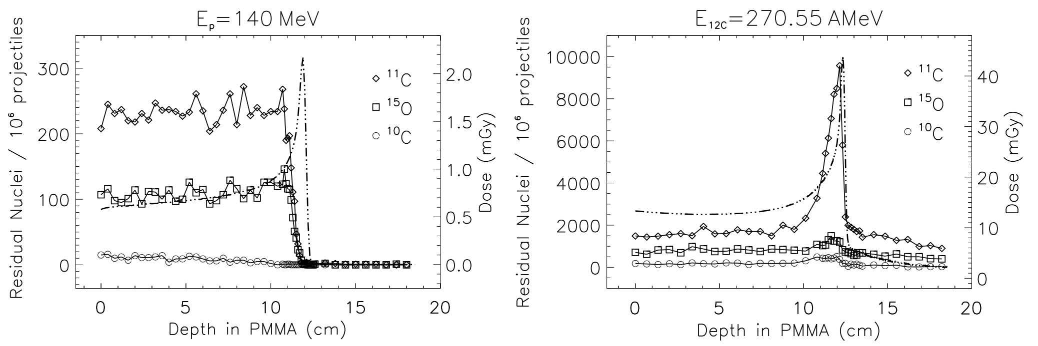

Fig. 1 *Simulated spatial depth distribution of β^+-emitters produced by 10^6 proton and carbon ion projectiles. The dashed-dotted line displays the dose profile. The factor of about 20 between the amount of dose delivered by the same number of primary particles can be seen.*

References

[1] K. D. Gross and M. Pavlovic (eds), Proposal for a dedicated ion beam facility for cancer therapy (GSI Darmstadt, 1998) pp 43-6
[2] W. Enghardt et al., Strahlenther. Onkol. 175 (1999) 33
[3] K. Parodi and W. Enghardt, Phys. Med. Biol. 45 (2000) N151
[4] U. Oelfke et al., Phys. Med. Biol. 41 (1996) 177

Feasibility Study for an LSO-Based In-Beam PET Scanner B,E

K. LAUCKNER[1], P. CRESPO[1], W. ENGHARDT, J. PAWELKE

Over the last 3 years in-beam PET has proven its capability of quality assurance in carbon ion tumour therapy at the pilot project of cancer therapy at the Gesellschaft für Schwerionenforschung (GSI) in Darmstadt, Germany [1]. It is planned to integrate a new positron camera into the proposed dedicated hospital-based facility for ion beam therapy in Heidelberg, Germany [2]. We have investigated the possibility of using LSO as the scintillation material for the next generation of in-beam PET cameras.

We address the issue of background coincidences arising from the natural radioactivity of LSO. Natural lutetium contains the radioactive isotope ^{176}Lu with an abundance of 2.59 %, causing a background activity of 280 Bq per cm^3 of LSO. ^{176}Lu undergoes β^--decay feeding excited levels of ^{176}Hf at 597 keV and 998 keV with probabilities of 99.66 % and 0.34 %, respectively. These levels are de-excited via a prompt γ-ray cascade of 307, 202 and 88 keV, which is topped by a 401 keV transition in the case of the 998 keV level. This results in undesired true coincidences when the electron and low-energy γ-rays deposit enough energy in the crystal, where the β^--decay takes place, and the γ-rays of higher energy escape and deposit their energy in an opposite crystal. Because the true count rate measured with the BGO-based dual-head positron camera BASTEI during the cancer treatment averages at only 100 coincidences/s we studied the influence of the LSO background on realistic in-beam PET images.

Therefore, we have estimated the background coincidences expected for the detector geometry of BASTEI assuming LSO as detector material. The estimation takes into account the energy distribution of the electron resulting from the β^--decay, together with all γ-ray combinations that lead to a background coincidence. This has been done for energy windows of 250 - 850 keV, 350 - 650 keV and 400 - 600 keV, two γ-ray combinations that are possible within the energy windows and an energy resolution of 15 % FWHM. Furthermore, the attenuation of the escaping 307 or 401 keV γ-rays due to the presence of the patient has been taken into account.

The analysis [3] shows that the major component of the background of true coincidences caused by ^{176}Lu originates from the escape of the 307 keV γ-ray and subsequent detection by another detector of the positron camera. If, however, an energy window between 350 - 650 keV or narrower is applied these background coincidences are effectively rejected and an influence on the reconstructed β^+-activity distribution can be avoided (Fig. 1).

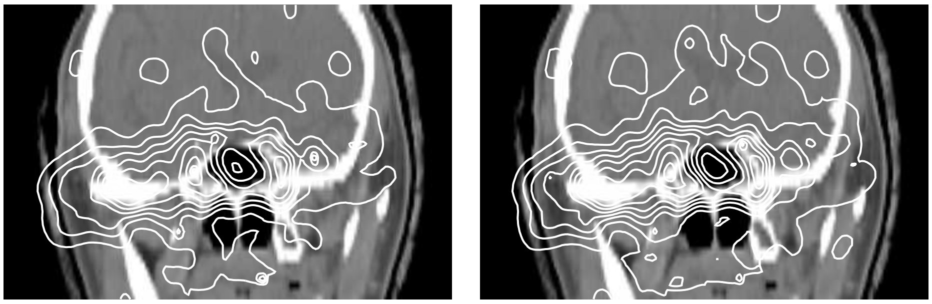

Fig. 1 *The left Figure shows a typical β^+-activity distribution as it was measured by the BGO-based positron camera BASTEI. The image on the right shows the same measured β^+-activity distribution but with background coincidences added to the original PET scan as they would be expected for an LSO-based BASTEI assuming an energy window of 350 - 650 keV.*

[1] *Gesellschaft für Schwerionenforschung Darmstadt*

References

[1] W. Enghardt et al, Nucl. Physics A 654 (1999) 1047c
[2] K.D. Gross, M. Pavlovic (eds.), Proposal for a dedicated ion beam facility for cancer therapy, 1998
[3] K. Lauckner et al, An LSO-based scanner for in-beam PET:
A feasibility study, IEEE NSS/MIC Conf. Rec., 2000

The Combination of an In-Beam PET Scanner with a Rotating Beam Delivery for Ion Tumour Therapy [B,E]

P. Crespo[1], K. Lauckner[1], W. Enghardt

Over the past three years the PET camera installed at the tumour therapy facility in GSI has proven its capability of contributing to the quality assurance of ^{12}C radiotherapy [1]. In this report, we present the first studies concerning the PET camera design and implementation onto a dedicated hospital-based ion beam facility for cancer therapy, proposed to be built in Heidelberg [2] due to the promising results achieved with the GSI pilot project [3]. In the proposed facility, due to the presence of a rotating gantry which will deliver the heavy ion beam - thus satisfying an important medical need [4], the flexibility of the PET camera must be enhanced so that it does not collide with the patient or the couch nor with the beam gantry, as well as it allows a fast access of the physicians to the patient.

Figures 1 and 2 depict possible PET scanner implementations. In Fig. 1, the scanner moves along the patient couch and, thus, can be positioned around the region being irradiated. An aperture on the tomograph ring allows the beam to pass through without touching the γ-ray detectors. This configuration can provide a full coverage of the volume under observation if the scanner rotates 180° around its axial direction (Z_{PET}) during the beam extraction cycle (spill off, ~ 2 s). This detail, besides being relevant for the image quality, is also important for a quantitative analysis of the measured β^+-activity. If typical dimensions of a PET scanner are applied, an aperture of 30 cm for the beam is considered (param. 7) and the distance between the scanner and its support ring is 40 cm (param. 10), the map plotted in Fig. 3 is obtained. The black and dark grey areas correspond to beam gantry and patient couch angle combinations not suitable for therapy because the beam penetrates the patient through the trunk of the body (caudo-cranial direction). The angle combinations mapped in light grey are free for irradiation only if the beam leaving the target volume does not activate substantially the scanner support structure. In this configuration the scanner never approaches the patient.

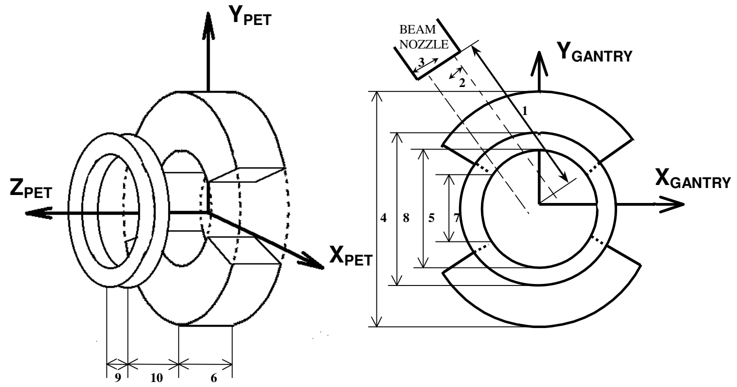

Fig. 1 *PET scanner connected with the patient couch. The couch lies along Z_{PET} and the camera rotates, before the beginning of the treatment, facing the beam with its aperture (not shown).* ***Legend:*** *1) Nozzle distance to isocenter, 2) Beam radius, 3) Nozzle radius, 4) Scanner outer radius, 5) Scanner inner radius, 6) Scanner width, 7) Scanner aperture for beam, 8) Support ring outer radius, 9) Support ring width and 10) Distance between scanner and its support ring.*

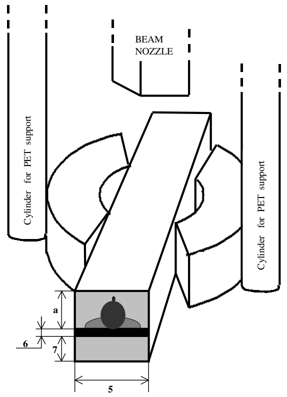

Fig. 2 *PET scanner connected with the gantry, placed perpendicular to the beam nozzle. The central parallelepiped represents the volume reserved for patient and couch.* ***Legend:*** *1) through 4) as in Fig. 1. 5) Couch width. 6) Couch thickness. 7) Vertical range. a)* $\frac{couch\_width}{2}$

In Fig. 2 the PET scanner is depicted, which is assumed to be connected to the gantry and to be placed parallel to the beam nozzle (the beam does not collide with the scanner or its support structure in any situation). A collision study yields a minimal scanner aperture of 75 cm in order for no physical collisions to occur between scanner and patient/couch. If the scanner is placed parallel to the beam nozzle the minimum aperture needed decreases to 65 cm (the present dual-head PET scanner at the GSI therapy facility has 63 cm aperture). These collision studies did not take into account the movement of the scanner into the measurement position.

In addition to the collision studies summarized, we have developed the tools to quantify the spatial resolution degradation as one moves from a closed ring to an open ring PET camera configuration: (i) a simulation capable of treating several camera geometries and (ii) a flexible image reconstruction routine being capable of reading the output from the simulations. The reconstruction uses an iterative procedure based on the maximum likelihood estimation maximization algorithm. Due to the enormous amount of crystal combination possibilities (over 150 million), dynamic memory allocation is used in conjunction with a developed factorization scheme, which obliged the routine to differ substantially from the one presently used at the GSI therapy unit [5].

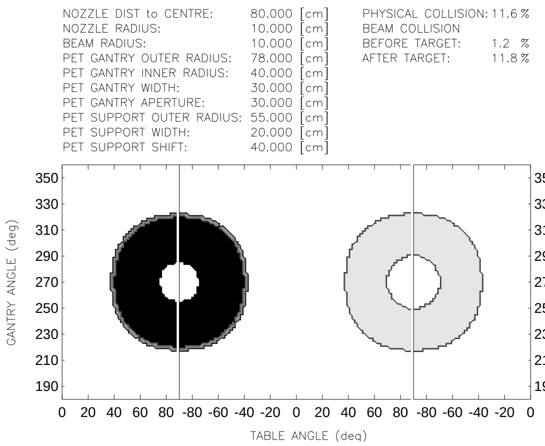

Fig. 3 *Collision study for the case PET connected with the patient couch. Black area: physical collision between beam gantry and scanner. Dark grey area: beam collides with scanner support ring* ***before*** *the target volume. Light grey area: as dark grey but* ***after*** *irradiating the target volume.*

In Fig. 4 we depict the first results on the spatial resolution degradation if one moves from a closed ring to an open ring detector assembly. No Compton scattering effects on the detector were simulated yet, the attenuation of the γ-rays in the crystals and thus the depth-of-interaction influence on the spatial resolution was taken into account. The degradation in spatial information experimentally observed for detector crystals coupled to photomultipliers according to the modified Anger principle was also not included.

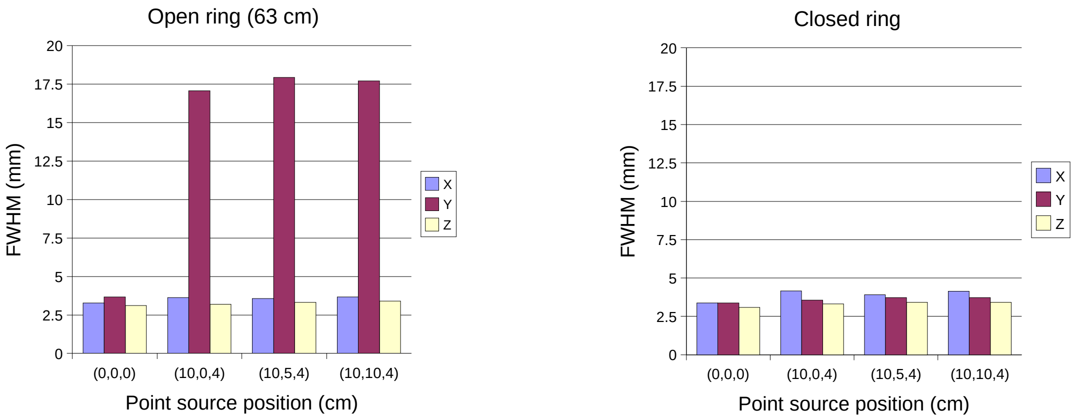

Fig. 4 *Comparison between the spatial resolution achieved with a closed ring versus an open ring positron camera (diameter: 82.3 cm, aperture: 63 cm, Fig. 1), built up of crystals of* $5.0 \times 4.5\,\mathrm{mm}^2$ *frontal surface and 30 mm depth.*

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References

[1] W. Enghardt et al., GSI Scientific Report (1999) 164-5
[2] K.D. Gross, M. Pavlovic (eds.), Proposal for a dedicated ion beam facility for cancer therapy, GSI Darmstadt, 1998
[3] J. Debus et al., Strahlenther. Onkol., 176 Nr 5, (2000) 211-6
[4] O. Jäkel and J. Debus, Phys. Med. Biol. 45 (2000) 1229-41
[5] K. Lauckner, Ph.D. Thesis, Dresden University of Technology, 1999

TSEE Dosimetry of Soft X-rays

J. Pawelke, A. Panteleeva

The measurement of RBE by cell irradiation requires precise determination of dose, delivered to the cell target. Absolute dose measurements are usually done by an air-filled ionisation chamber. However, in the case of low energy X-rays (below 10 keV) it does not sample the cell target because of the high attenuation. Detection based on thermally stimulated exoelectron emission (TSEE) allows to sample the depth dose distribution in a cell monolayer ($\approx 5\,\mu$m thick), because the thickness of the sensitive detector layer is of the order of ~ 10 nm [1]. A TSEE prototype system (Dr. Holzapfel Messgerätelabor, Teltow) consisting of 3 types of thin-film BeO (100 nm) detectors and a counter based on a spherical anode Geiger-Müller methane gas-flow counter was tested. The irradiation was performed with a high-activity beta-source (^{90}Sr), a calibrated gamma-source (^{137}Cs) and a soft X-ray source (^{55}Fe). Highest response as well as stability were shown by detector type I (fig. 1, table 1, same results were obtained with ^{55}Fe source), which proves that the 200 nm Au layer contributes for better mechanical attachment of the BeO layer as well as for electrical stability. The saturation in the dose response (fig. 2) due to the limited pulse resolution of the gas-flow counter results in an upper detection limit of about 0.1 Gy and is far from the requirements of the cell survival studies (≤ 10 Gy). Therefore it cannot be used as online monitoring system. In order to determine the dose delivered to cells, measurements must be done in the presence of cell culture medium. Irradiations were made after wetting the surface and showed no change in the detector response due to any tribo-effect [2]. As expected detector response after irradiation of detectors covered with about 0.5 mm propanol with low energy X-rays from ^{55}Fe source and high energy photons from ^{22}Na source was reduced only due to attenuation in the liquid layer. However, the dependence of the detector response on photon energy and dose rate must still be studied.

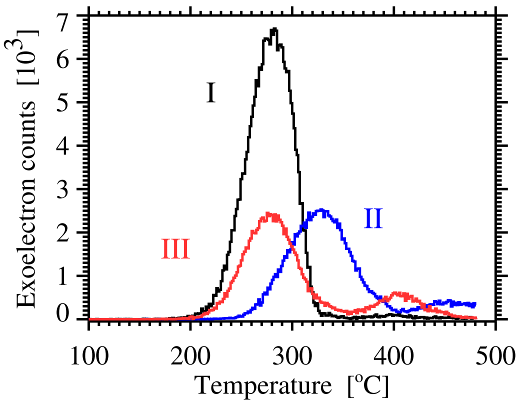

Fig. 1 *Typical glow curves of thin-film BeO detectors.*

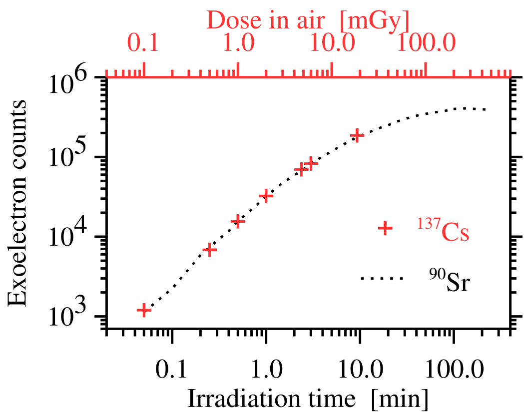

Fig. 2 *TSEE response of detector type I to electron (^{90}Sr) and photon (^{137}Cs) irradiation.*

Table 1 *Main detector properties.*

Detector type	Layer structure	Sensitive area [mm^2]	Peak range [^{o}C]	Reproducibility^a [%]	Sensitivity^b [counts/mGy]
I	BeO-Au-C	43.0	180...360	1.8	15538
II	BeO-C-Al	146.4	200...410	2.6	7603
III	BeO-C	146.4	180...360	9.6	6137

^{a}) average error of the mean for a series of 8 measurements with ^{90}Sr ^{b}) ^{137}Cs, dose in air

References

[1] J.S. Durham et. al., Radiation Protection Dosimetry, Vol. 39(1991), No 1/3, pp. 67-70
[2] H. Eichenüller, Radiation Protection Dosimetry, Vol. 4(1983), No 3/4, pp. 281-285

The Determination of RBE of Soft X-rays

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The superconducting electron linear accelerator ELBE, at present under construction at Forschungszentrum Rossendorf, is going to be used to produce various types of secondary radiation, among which are X-rays in the energy range 100 eV - 100 keV. At the first stage, monochromatic X-rays in the energy range 10 keV - 50 keV will be obtained by means of planar channeling of high-energy electrons in a diamond crystal. Such an unconventional X-ray source is rather compact, tuneable and allows the possibility of delivering a beam in picosecond pulses [1]. The relative biological effectiveness (RBE) of the X-rays in this energy range will be determined by studies of cell survival and cytogenetic damage. Precise RBE values are required for risk assessment in diagnostic radiology, such as mammography, and radiotherapy with soft X-rays (brachytherapy). It has been previously shown that soft X-rays are more effective in cell killing [2] and chromosome abberations induction [3]. In preparation of radiobiological studies at ELBE, experiments were performed with a 25 kV soft X-ray tube and a 200 kV reference X-ray tube at TU Dresden. The cell line NIH/3T3 mouse fibroblasts was chosen because it is widely used, easy to handle, and contact-inhibited. The cells were cultured in DMEM supplemented with 10 % bovine serum, 10 mM HEPES buffer, 1 mM Sodium Pyruvate, 1 % non-essential aminoacids, 100 U/ml penicillin and 100 μg/ml streptomycin (all from Biochrom Seromed) at 37^{o}C in air containing 5 % CO_2. Exponentially growing cells were irradiated in 25 cm^2 polystyrene flasks at dose rates 1.22 Gy/min (200 kV, 20 mA, 0.3 mm Al filter) and 1.67 Gy/min (25 kV, 20 mA, 0.5 mm Cu filter). After irradiation the cells were harvested, counted and seeded at appropriate densities (6-8 replicates per dose point). After 12 days, colonies having at least 50 cells were scored as offspring from 1 surviving cell.

The RBE value at 10 % survival, determined by a linear-quadratic model fit was found to be 1.28 ± 0.5. As the photon energy is decreasing, the secondary electron spectrum becomes dominated by low-energy electrons and this leads to higher localisation of damage. The comparison of the energy spectrum of the 25 kV X-ray tube (measured with a Si PIN photodiode) and the 200 kV X-ray tube (modelled) revealed that in the first case the main contribution to the dose is coming by the photons of energy 10 - 20 keV, whereas in the second case, photons of this energy range contribute to the absorbed dose only by 4 %. Although the results obtained are not in contradiction with published data, there is a demand for accurate determination of RBE photon energy dependence.

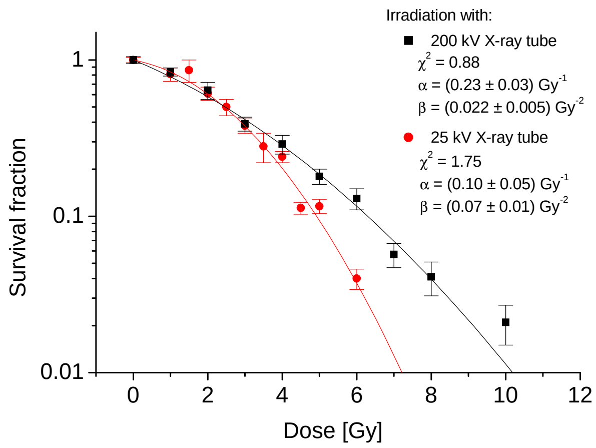

Fig. 1 *Clonogenic survival of NIH/3T3 cells after 25 kV and 200 kV X-ray tube irradiation.*

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[2] *Centre of Oncology, Krakow, Poland*

References

[1] W. Enghardt et. al., Acta Physica Polonica, Vol. 30 (1999), No. 5, pp. 1639-1645
[2] M. Bistrovic et. al., Radiother. Oncol., Vol. 7 (1986), No. 2, pp. 175-180
[3] R.P. Virsik et. al., Radiat. Environ. Biophys., Vol. 14 (1977), No. 2, pp. 109-121