



ELSEVIER

Available online at www.sciencedirect.com

SCIENCE @ DIRECT®

Nuclear Instruments and Methods in Physics Research A 525 (2004) 284–288

**NUCLEAR
INSTRUMENTS
& METHODS
IN PHYSICS
RESEARCH**
Section A

www.elsevier.com/locate/nima

Charged hadron tumour therapy monitoring by means of PET

W. Enghardt^{a,*}, P. Crespo^a, F. Fiedler^a, R. Hinz^b, K. Parodi^a,
J. Pawelke^a, F. Pönisch^a

^a*Forschungszentrum Rossendorf e.V., Institute of Nuclear and Hadron Physics, Postfach 510119, D-01314 Dresden, Germany*

^b*Hammersmith Imanet Ltd., Hammersmith Hospital, London, W12 0NN, UK*

Abstract

Positron emission tomography (PET) imaging of radioactivity distributions induced by therapeutic irradiation is at present the only feasible method for an in situ and non-invasive monitoring of radiooncology treatments with ion beams. Therefore, at the experimental carbon ion therapy facility at the Gesellschaft für Schwerionenforschung Darmstadt, Germany (GSI) a PET scanner has been integrated into the treatment site for quality assurance monitoring simultaneously to the therapeutic irradiation. Although the device has been assembled from components of positron emission tomographs developed for nuclear medicine applications, substantial modifications had to be made for meeting the requirements of ion therapy monitoring. These changes regard the geometrical detector configuration as well as the data acquisition and processing. Since 1997 this technique has been applied to monitor the fractionated irradiation of more than 180 patients predominantly suffering from tumours in the head and neck region. It could be demonstrated that this new PET technique is capable of assessing parameters being relevant for quality assurance of carbon ion therapy, i.e. the particle range in tissue, the position of the irradiated volume with respect to anatomical landmarks and local deviations between the planned and the applied dose distributions.

© 2004 Elsevier B.V. All rights reserved.

PACS: 87.58.Fg; 87.53.–j; 87.53.Xd

Keywords: Positron emission tomography; Charged hadron therapy; Ion therapy

1. Introduction

The high physical and radiobiological selectivity of ions for tumour therapy [1] demands technological solutions for a reliable monitoring of the dose delivery in situ. Since ions—unlike photons—are completely stopped within the target volume, a

technology like electronic portal imaging [2] for controlling the lateral field position is not feasible. Moreover, imaging in the third spatial dimension is required, since in ion therapy the formation of the Bragg maximum at the correct depth is crucial. Shifting the spread out Bragg peak by a few mm may result in severe dose reduction within the target volume or overdosing in organs at risk. The treatment planning of ion therapy [3,4] requires accurate values of the particle range in tissue which are obtained from the Hounsfield units of X-ray computed tomograms (CT) leading to

*Corresponding author. Tel.: +49-351-260-3653; fax: +49-351-260-3700.

E-mail address: w.enghardt@fz-rossendorf.de
(W. Enghardt).

uncertainties of 1–3% in range calculations [4–6]. Furthermore, during the several weeks of fractionated treatment, unpredictable range deviations may occur because of minor inaccuracies in patient positioning or anatomical changes leading to local density modifications with respect to the planning CT [7]. Considering this particular situation, a three-dimensional (3D) non-invasive imaging technique for charged hadron therapy monitoring is required, and at present the only feasible technique for this purpose is positron emission tomography (PET). Therefore, several attempts to utilize PET for treatment control have been undertaken by several groups in the past [8–13]. To evaluate systematically the clinical benefit of the PET method, it has been integrated into the experimental carbon ion therapy unit at the Gesellschaft für Schwerionenforschung Darmstadt (GSI) [14]. This article describes the physical background and the technical requirements of a PET scanner for therapy monitoring, the technical solutions for in-beam PET at the carbon ion treatment facility of GSI Darmstadt as well as the methodology of extracting clinically relevant information from in-beam PET data.

2. Physical background and instrumentation

Two scenarios are possible to provide the positron emitters for therapy control. The most straightforward way is to use positron radioactive ions as projectiles for dose delivery. This approach has been followed at the Heavy Ion Medical Accelerator in Chiba (Japan), where a radioactive beam line delivering ^{11}C or ^{10}C ions has been installed [15]. Such a radioactive beam delivers an activity density within the irradiated volume of 10^3 – 10^5 Bq Gy $^{-1}$ cm $^{-3}$ depending on the half-life of the isotope. However, the method seems to be of minor relevance for practical therapy, since the production rate of secondary radioactive ions is of the order of 0.1–1%, which requires expensive measures for absorbing and shielding the primary beam. Thus, the radioactive beam may be only used for accurate range measurements prior to an irradiation with the stable isotope; this technique has been developed at the Lawrence Berkeley

Laboratory [8]. An alternative to radioactive beams arises from the fact that during therapeutic irradiation with stable ions, e.g. ^{12}C [16] or ^1H [17], a part of the projectiles collides with the atomic nuclei of the irradiated volume and produces β^+ -radioactive fragments, which activate the tissue along the beam path. The radioactivity emerges as a byproduct of each irradiation, which provides the opportunity of a much less expensive solution than a radioactive beam. The activity density is rather low: about 200 Bq Gy $^{-1}$ cm $^{-3}$ for ^{12}C and about 600 Bq Gy $^{-1}$ cm $^{-3}$ for protons. The most abundant positron emitters produced in this process are ^{11}C , ^{15}O and ^{10}C with half-lives of 20 min, 2 min and 19 s, respectively. Considering these short half-lives, the low activity density and finally the rather rapid washout of a large part of the produced activity with time constants of less than 4 min [18] an in-beam PET scanner is the technical solution of choice. The double head positron camera which has been integrated into the carbon ion therapy beam line at the heavy ion synchrotron of GSI is depicted in Fig. 1. In order to avoid interference with the horizontal beam line and with patient positioning, a double head geometry had to be chosen. The two large area (42×21 cm 2) detector heads have been built from components of the ECAT EXACT PET scanner (CTI PET Systems Inc., Knoxville, TN). Each head consists of 8×4 position sensitive scintillation block detectors of bismuth germanate (BGO) with a size of $54 \times 54 \times 20$ mm 3 [20]. The blocks are further subdivided into 8×8 crystals. The two detector heads are operated in coincidence, resulting in 2048^2 lines of response within the camera field of view. The data acquisition (Fig. 2) is based upon the standard solution of the manufacturer [21] with modifications, which are required by the in-beam application. For valid events, i.e. prompt and delayed (by 128 ns) coincidences within a 12 ns wide time window, the identification of the fired crystals is transmitted from the coincidence processor to the data acquisition station [21]. During the off-line tomographic reconstruction only those events are taken into account which have been registered in the pauses between the beam pulses. Coincidences being acquired during the beam pulses are massively corrupted by

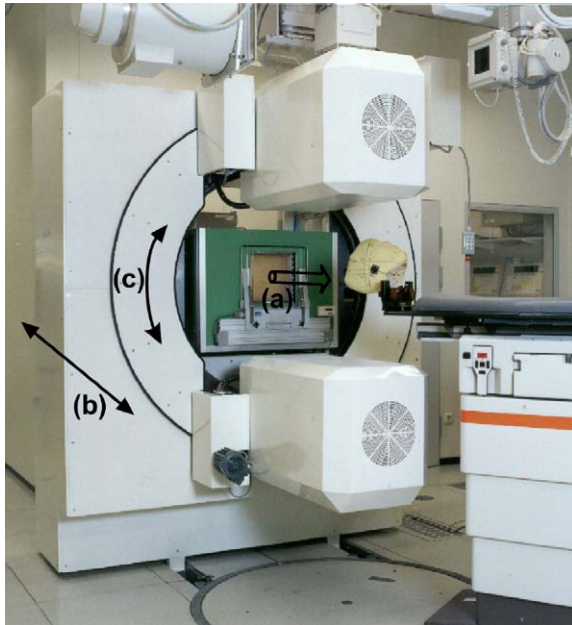


Fig. 1. The double head positron camera at the treatment site at GSI Darmstadt. The horizontal carbon ion beam escapes the beam pipe through a $20 \times 20 \text{ cm}^2$ window visible in the centre (a). To provide sufficient space for patient positioning, the PET scanner can be moved parallel to the beam between the measuring position displayed and the parking position upbeam (b). For irradiating patients in supine position the detector heads are fixed below and above the patient couch, whereas for future treatments of sitting patients [19] the detectors can be rotated around the central beam (c).

random events caused by the γ -ray background from projectile induced nuclear reactions in combination with the time microstructure of the beam on a sub- μs scale [22]. Therefore, each data word is completed by the information on the synchrotron beam status (extraction on or off) which is derived from the output of an ionization chamber which the beam passes before reaching the patient. Usually the data are stored in list mode, where a time tag is inserted into the data stream every 10 ms. This allows a flexible setting of time frames for reconstruction, since the target activation during dose delivery by raster scanning [23] is a dynamic process that has to be resolved in some critical therapeutic situations. For data evaluation (Section 3) the beam energy, intensity and diameter of each beam pulse are needed. Therefore, the accelerator control unit is con-

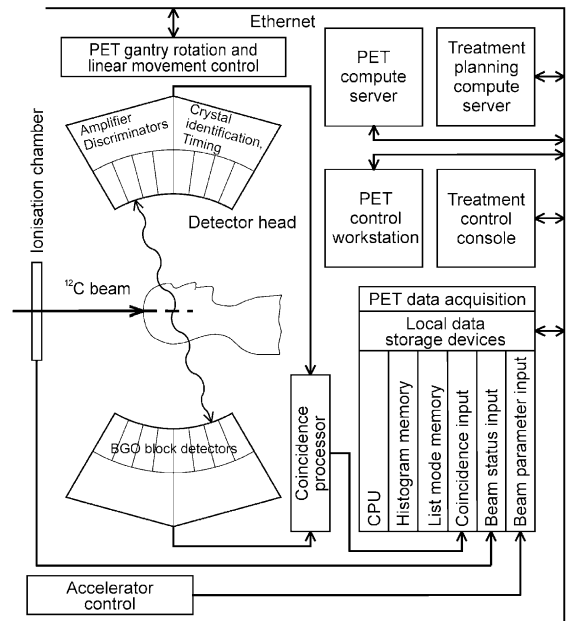


Fig. 2. Data processing scheme at the in-beam PET facility.

nected with the PET data acquisition and these parameters are recorded. For correlating the reconstructed PET images with the patient CT, the position of the camera is read via Ethernet from the PET gantry rotation and linear movement control unit. The PET data acquisition is controlled via a dedicated workstation, or alternatively during the patient irradiation from the treatment control console. The time consuming off-line PET data processing up to 1 h per patient is performed on a Linux Cluster with Intel Xeon processors, 2 GHz. In particular situations access to the compute server running the treatment planning is necessary.

3. Clinically relevant data from in-beam PET imaging

Neither for tumour irradiation with stable nor with radioactive beams the spatial distributions of β^+ -activity and dose are congruent [24]. Thus, for the extraction of clinically relevant parameters such as particle range, lateral field position or local dose values from the radioactivity distribution a

dedicated procedure has been developed. The basis of PET data evaluation is the comparison of the spatial distribution of β^+ -activity reconstructed from the measured PET data with that calculated from the treatment plan as well as from the time course of the irradiation, which can be retrieved from the registered beam parameters. These predictions are obtained by a realistic model of all the processes eventually leading to the PET signal: the stopping of the primary ions and the fragments in tissue, the nuclear reactions, the decay of the positron emitters, stopping and annihilation of the positrons in tissue and propagation and detection of annihilation γ -rays [25]. The necessary anatomical information (density, stoichiometric composition of tissue) is extracted from the planning CT. Particle fluences are provided by the treatment planning. The calculations are implemented as a Monte Carlo event generator, which delivers list mode data sets in the same format like the PET hardware. This allows the source distributions from the measured and predicted data to be reconstructed by means of the same Maximum Likelihood Expectation Maximization algorithm [26]. The PET images are super-

imposed onto the CT, to relate them to anatomical information.

4. Results from in-beam PET imaging

The fused PET-CT images (Fig. 3) are further evaluated by comparing the measured data with the predictions from the treatment plan. This procedure has been applied to the in-beam PET monitoring of the fractionated carbon ion therapy of about 180 patients, most of them with head and neck tumours [27]. According to this experience, in-beam PET is capable of revealing deviations in the maximum particle ranges due to (i) inaccuracies of the physical beam model in treatment planning, (ii) minor positioning errors and (iii) particle range deviations due to local modifications of the density distributions relative to the planning CT. Reasons for these modifications are, e.g. the filling of nasal or paranasal sinuses with mucus or tissue reduction during the healing process after surgery. Whereas the problem (i) can be solved by refining the physical models of treatment planning [28], it is highly desirable to quantify the impact of

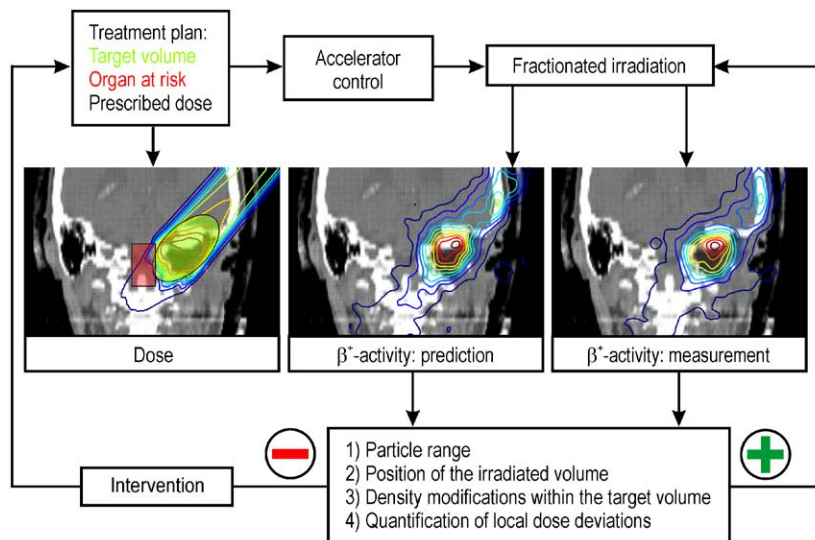


Fig. 3. Scheme of the clinical implementation of in-beam PET. As an example, the irradiation of a skull base tumour is shown. As seen from the dose distribution superimposed onto the CT the carbon ions must not reach the brain stem as an organ at risk. The comparison of the predicted with the measured β^+ -activity distributions shows that this requirement has been fulfilled during the treatment. The isodose and isoactivity lines are decoded in rainbow colours and denote levels of 5%, 15%, ..., 95% of the maxima.

the unpredictable deviations (ii) and (iii) on the dose. For this an interactive procedure has been developed [7], where the patient CT is iteratively modified until the predicted activity distribution resembles the measured one. Finally the dose distribution is recalculated for this modified CT using the projectile fluence distribution administered to the patient.

5. Conclusions

Five years of clinical application have proven the technical feasibility of operating an in-beam PET scanner for monitoring therapeutic irradiation with ion beams. Since the PET data are acquired during the therapeutic irradiation, treatment times are prolonged only marginally. It could be demonstrated that on the basis of PET data the field position can be controlled in 3D and local dose deviations with respect to the treatment plan can be quantified.

Acknowledgements

We would like to thank all colleagues of the German Heavy Ion Therapy Project for the fruitful collaboration. This work has been supported by the German Federal Ministry of Education and Research (BMBF).

References

- [1] G. Kraft, *Strahlenther. Onkol.* 166 (1990) 10.
- [2] L.E. Antonuk, *Phys. Med. Biol.* 47 (2002) R31.
- [3] M. Krämer, O. Jäkel, T. Haberer, et al., *Phys. Med. Biol.* 45 (2000) 3299.
- [4] O. Jäkel, M. Krämer, C.P. Karger, et al., *Phys. Med. Biol.* 46 (2001) 1101.
- [5] G.T. Chen, R.P. Singh, J.R. Castro, et al., *Int. J. Rad. Oncol. Biol. Phys.* 5 (1979) 1809.
- [6] B. Schaffner, E. Pedroni, *Phys. Med. Biol.* 43 (1998) 1579.
- [7] K. Parodi, W. Enghardt, *FZ Rossendorf FZR-341* (2002) 98.
- [8] J. Llacer, *Nucl. Sci. Appl.* 3 (1988) 111.
- [9] K. Yoshikawa, T. Tomitani, M. Kanazawa, et al., *J. Nucl. Med. Technol.* 24 (1996) 167.
- [10] G.W. Bennett, J.O. Archambeau, B.E. Archambeau, et al., *Science* 200 (1978) 1151.
- [11] S. Vynckier, S. Derreumaux, F. Richard, et al., *Radiother. Oncol.* 26 (1993) 275.
- [12] A.M.J. Paans, J.M. Schippers, *IEEE Trans. Nucl. Sci. NS-40* (1993) 1041.
- [13] U. Oelfke, G.K.Y. Lam, M.S. Atkins, *Phys. Med. Biol.* 41 (1996) 177.
- [14] G. Kraft, *Nucl. Instr. and Meth. A* 454 (2000) 1.
- [15] E. Urakabe, T. Kanai, M. Kanazawa, et al., *Jpn. J. Appl. Phys.* 40 (2001) 2540.
- [16] W. Enghardt, W.D. Fromm, H. Geissel, et al., *Phys. Med. Biol.* 37 (1992) 2127.
- [17] K. Parodi, W. Enghardt, T. Haberer, *Phys. Med. Biol.* 47 (2002) 21.
- [18] H. Mizuno, T. Tomitani, M. Kanazawa, et al., *Phys. Med. Biol.* 48 (2003) 2269.
- [19] P. Heeg, D. Schardt, J. Störmer, GSI Darmstadt, *GSI 2002-1* (2002) 166.
- [20] M.E. Casey, R. Nutt, *IEEE Trans. Nucl. Sci. NS-33* (1986) 460.
- [21] W.F. Jones, M.E. Casey, L.G. Byars, et al., *IEEE Trans. Nucl. Sci. NS-33* (1986) 601.
- [22] K. Parodi, P. Crespo, W. Enghardt, et al., *FZ Rossendorf FZR-372* (2003) 77.
- [23] T. Haberer, W. Becher, D. Schardt, et al., *Nucl. Instr. and Meth. A* 330 (1993) 296.
- [24] J. Pawelke, W. Enghardt, T. Haberer, et al., *IEEE Trans. Nucl. Sci. NS-44* (1997) 1492.
- [25] B.G. Hasch, Ph.D. Thesis, Dresden University of Technology, 1996.
- [26] F. Pönisch, W. Enghardt, K. Lauckner, *Phys. Med. Biol.* 48 (2003) 2419.
- [27] D. Schulz-Ertner, T. Haberer, O. Jäkel, et al., *Int. J. Rad. Oncol. Biol. Phys.* 53 (2002) 36.
- [28] E. Rietzel, O. Geiss, T. Haberer, et al., *GSI Darmstadt, GSI 2000-1* (2000) 166.