Advance in in-beam PET*

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Abstract Tumor radiotherapy was a promising modality and over 100 years. Beams of heavy-charged particles show high RBE advantages and become the optimum tool for tumors therapy. Newly, along with the development of accelerators, scintillators, micro-electronics and computers, the heavy ion tumor therapy has been recognized more and developed.

Key words tumor therapy, TOF-PET, in-beam PET

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1 Tumor therapy with heavy ions

Shortly after the discovery by W.C. Roentgen in 1895, X-rays were applied in tumor therapy. Due to an exponentially decreasing depth dose distribution of X-, γ-rays, the healthy tissue in front of the target volume was radiated overly for the treatment of deep-seated tumors.

Compared with photons, ^{12}C particle show an inverse dose profile with increasing penetration depth the dose increases up to a sharp maximum (Bragg peak). Beyond this so-called Bragg peak the dose decreases within a few millimeters to a small value which consists of nuclear fragments of the carbon beam. Through energy variation the dose maximum can be shifted over the depth of the target volume. It allows highly conformal treatment of deep-seated tumors with millimeters accuracy, giving minimal doses to the surrounding healthy tissues. And the carbon ions have high RBE in tumor volume. Fig. 1 Comparison of the depth dose profiles of X-rays, ^{60}Co γ-rays and photos of 18 MeV with ^{12}C ions of 250 and 300 MeV/u[1]. It is very evident that beams of heavy-charged ions represent the optimum for the treatment of deep-seated inoperable tumors in contrast to the conventionally photons.

The first trials of tumor therapy with protons and heavier ions were performed at Berkeley in 1954. By 1990s the tumor therapy with heavy ions developed fleetly. The dedicated medical facilities were constructed at Germany, Japan, France, Italy and Austria. The superficial tumor therapy unit was also set at IMP of China in 2006[2].

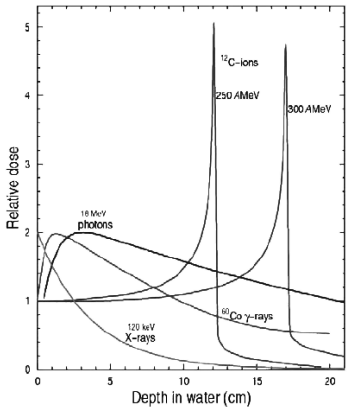

Fig. 1. Comparison of the depth dose profiles of X-, γ-rays with ^{12}C ions[1].

With ^{12}C ions penetrate a thick absorber, a small amount of the ^{12}C particles will undergo nuclear fragmentation. A very frequent process of fragmentation is the stripping of one or two neutrons, converting the stable ^{12}C isotope into the positron-emitting isotopes ^{11}C and ^{10}C that decay with half-lives of 20 min and 19 s, respectively. These lighter fragments have nearly the same range as the primary particles,

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and the detection of the decays allows to deduce the maximum penetration rang and the distal edge of the dose distribution with high accuracy. It also offers a unique possibility for the in-situ beam monitoring by In-beam PET.

Figure 2 shows layout of heavy ion tumor therapy facility using the rasterscan technique. It basically composed of a magnetic deflection system in x-y direction, MWPC and IC gas detector system and in-beam PET beam monitoring system.

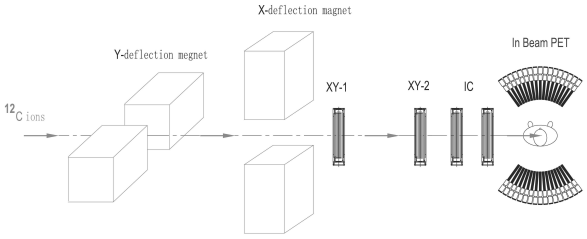

Fig. 2. Layout of heavy ion tumor therapy facility using resterscann technique.

2 In-beam PET

In-beam PET is currently the only method for an in-situ monitoring of highly tumor-conformed heavy ions therapy In 1975 the in-beam PET research in Berkeley was abandoned due to BGO activation arising most probably from passive beam shaping contaminations.

The dual-head BGO in-beam PET installed at the carbon ion tumor therapy facility of GSI by 1997. It consists of two detector heads with 42 cm×21 cm front area each. A total of 8×4 BGO block was implemented in each head, with each detector block consisting of 8×8 6.75 mm×6.75 mm×20 mm BGO crystals with 54 mm×54 mm front surface each and 2 cm depth. Each head form a spherical calotte with a radius of 41.5 cm. In these detectors, a block of BGO is coupled to four PMT and read with a modified anger logic. The position resolution obtained with a fixed point source ^{22}Na was 6.5±0.2 mm FWHM. The coincidence time resolution is 12±0.2 ns FWHM. Since December 1997 over 180 patients with radio-resistant tumors in the head and neck region were treated with high energy carbon ions with very promising clinical results achieved.

Due to the very promising clinical results achieved at GSI, a hospital-based tumor therapy facility with heavy ions is constructed at the Heidelberg University Clinics, Germany in 2007[4]. It was equipped a dedicated dual-head LSO in-beam PET system. The finger-like LSO crystals ((2.34±0.14) mm× (2.30±0.15) mm×(15±1) mm) coupled one by one to pixels of avalanche photodiode detector arrays (APDA). The mean energy resolution obtained both with a line source (^{68}Ge, fixed and scanned) and a fixed point source (^{22}Na) was 15.5±0.4 % FWHM with the coincidence time resolution 6.2±0.2 ns FWHM[4].

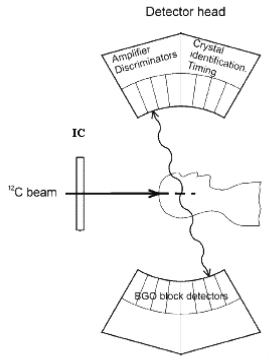

Fig. 3. The sketch of dual-head BGO in-beam PET at GSI[3].

3 TOF-PET

Simple theory predicts that the statistical noise variance in PET can be reduced by an order of magnitude by using TOF information. In conventional PET, the location of an individual positron is constrained to lie along a LOR, and tomography reconstruction algorithms then determine the three-dimensional (3D) source distribution. In TOF PET, the 3D location of each positron could be determined by accurately measuring the difference in arrival times of the two annihilation photons (see Fig. 4). However, the position along the LOR is localized to

$$\Delta x = \frac{c}{2}\Delta t \ , \qquad (1)$$

where Δx is the position error, c is the speed of light, and Δt is the error in the timing measurement. With current detector and electronic technologies, TOF timing resolution has only achieved the level of 200—300 ps FWHM at best. It constrains the positron position to a line segment 3—4.5 cm long at LOR. This does not improve the spatial resolution, but it does reduce the statistical noise in the reconstructed image if the line segment is shorter than the size of

the emission source. This reduction factor f (corresponding to the reduction in noise variance) is given

$$f = \frac{D}{\Delta x} = \frac{2}{c} \cdot \frac{D}{\Delta t} \ , \tag{2}$$

$$SNR_{\rm TOF} = f^{\frac{1}{2}} \times SNR_{\rm Conv} \ , \tag{3}$$

where D is the size of the emission source. SNR is signal-to-noise ratio.

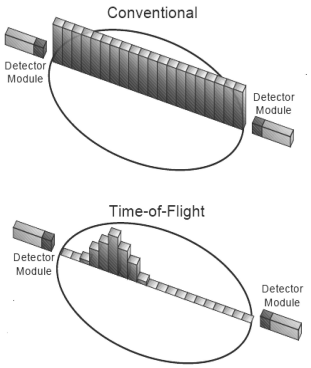

Fig. 4. Imaging reconstruction algorithms compaction of TOF-PET and conventional PET[5].

If $D = 30$ cm, $\Delta t = 300$ ps, $f \approx 6.6$, $\dfrac{SNR_{\rm TOF}}{SNR_{\rm Conv}} \approx 2.6$. As demonstrated, a 300 ps time resolution TOF-PET can improve image signal-to-noise by as much as 2.6 and should allow much-improved images.

4 In-beam TOF-PET

Recent scintillators with high light yield and very fast fluorescence time constant were discovered. Best examples are LaBr3 CeBr3, with light yields twice that of LSO and decay times of 35 and 17 ns, respectively. These scintillators offer the possibility of using the time difference between the moment of detection of the two opposed γ-rays. This so-called time-of-flight (TOF) difference allows to restrict the location of the positron annihilation point within the LOR formed by the two hit detectors.

P. Crespo present the advantages of direct TOF-PET imaging for monitoring carbon ion tumor therapy[6]. If the coincidence time resolution lies below 200 ps FWHM, the TOF-PET like as Heidelberg's PET provides useful images for in-beam PET. If a coincidence time resolution of 100 ps FWHM or better can be measured, the quality of the images obtained with a dual-head PET with large gaps like as GSI PET is only slightly inferior to that obtained with a closed-ring PET. But the most impressive results are expected if direct TOF-PET detectors with very high coincidence time resolution, below 200 ps FWHM, become commercially available. The image becomes available to the radiotherapist for online. Since the time to obtain an image is smaller than the typical irradiation time, direct TOF-PET would allow the image to be processed and shown to the oncologist during the course of the irradiation, i.e. in-beam PET could become real time in-beam PET. If a coincidence time resolution of ~30 ps FWHM, the location where the positron annihilation occurred can be directly compute, on event by event basis.

C. T. Chen proposes an initiative to apply the techniques of High Energy Physics for particle detectors, fast electronics, data acquisition, and 'end-to-end' simulation to biomedical imaging[7]. It includes ps-TDC ASIC Chip, ps-TOF and the SiPM. Due to its small size (1—10 mm^2), high gain (10^6—10^7), fast timing (10—100 ps), and low cost, this novel SiPM device presents an opportunity for novel PET technologies for cancer imaging. In particular, direct coupling of the SiPM device to the PET scintillating crystals would enable the next-generation PET imagers to achieve ultra-high resolution, high-sensitivity, high-throughput, low cost, and compactness.

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