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Feasibility of in-beam time-of-flight SPECT/PET gamma imaging based on Silicon Photomultipliers for high precision hadrontherapy

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Hadrontherapy is an emerging technology toward personalized high precision medicine, a vital instrumentation, especially in a cancer treatment. Success in the treatment critically depends on the precision of gamma imaging in general and absorbed dose profile monitoring in particular. PET and SPECT are well-established modalities of gamma imaging, and both of them have specific advantages and specific drawbacks with respect to hadrontherapy applications. Therefore, EU R&D activities in this area (ENLIGHT network, ENVISION project, INSIDE collaboration) are mostly focused on in-beam imaging, and a necessity to combine PET and prompt gamma imaging (in fact, SPECT) is already foreseen as the next major step in hadrontherapy improvements. However, this combination hardly could rely on conventional approaches to PET and SPECT, first of all, because slit-based SPECT contradicts with PET imaging technology.

Authors consider another approach in a development of in-beam in-vivo bimodal imaging for high precision hadrontherapy –a combination of time-of-flight (TOF) PET and recently proposed Prompt Gamma-Ray Timing (PGT, in fact, TOF SPECT). In contrast with slit-based SPECT, TOF SPECT allows encoding information on a hadron absorption spatial profile by the hadron transit time and the prompt gamma transit time using a reference time signal of a beam monitoring system without any collimation and compatible with TOF PET modality. To uncover its full potential, the combined TOF SPECT/PET imaging should utilize cutting-edge advances in accelerator beam monitoring, profiling and timing and in fast scintillation detectors with Silicon Photomultipliers (SiPM). Feasibility, benefits, challenges, and possible implementation of the TOF SPECT/PET approach to be considered and discussed.

Summary

Hadrontherapy is an emerging technology toward personalized high precision medicine, a vital instrumentation for a cancer treatment. Success in the treatment critically depends on the precision of gamma imaging in general and absorbed dose profile monitoring in particular. PET and SPECT are well-established modalities of gamma imaging, and both of them have specific advantages and specific drawbacks with respect to hadrontherapy applications. Therefore, EU R&D activities in this area (ENLIGHT network [1], ENVISION project[2], INSIDE collaboration [3], [4]) are mostly focused on advances in in-beam gamma imaging.

PET still is the only technically feasible and clinically proven method for a volumetric non-invasive verification of the ion treatment during or shortly after daily dose delivery [5]. However, with respect to conventional PET, in-beam PET imaging in hadrontherapy has specific features and limitations [6]:
Typically, the activity induced by the nuclear reactions between the incident beam and the patient tissues is 3 orders of magnitude less than those injected in a conventional clinical PET scan;
The created isotopes during the irradiation are short-lived isotopes and these isotopes diffuse inside the patient tissues because of the human metabolism;
There is a large amount of background because of the other secondary particles, particularly the gamma-prompts also produced by the nuclear reactions and affecting the 511 KeV measurements;
The geometry of the detector is also specific, as it cannot be a complete ring-like conventional clinical PET.

In a hadrontherapy, prompt gammas are a more intense source of information on absorbed irradiation then inter-spill or delayed positron annihilation gammas of PET imaging, it yields 22% of secondary radiation vs.

0.02% for positrons [4]. In spite of higher intensity, an in-spill prompt gamma imaging (PGI) has large spatial spread around the primary particle deposition point while for an inter-spill acquisition, the spread is much smaller [4].

Passively collimated gamma camera is a conventional approach for a PGI. However, it has low efficiency because most of the gammas are absorbed or scattered in a collimating grid. Electronically collimated systems such as Compton cameras require a tremendous electronic expense and still lack in the low efficiency of useable events. Overall, the PGI has not yet been demonstrated to be successful in clinical environments, there are still unsolved technical challenges [7], [8].

A necessity to combine PET and PGI (in fact, SPECT) is already foreseen as the next major step for the best estimations of dose placement in hadrontherapy [8], [9]. However, this combination hardly could rely on conventional approaches to PET and SPECT, first of all, because a passively collimated (slit-based) SPECT contradicts with non-slit PET imaging technology.

Authors consider another approach in a development of in-beam in-vivo bimodal imaging for high precision hadrontherapy –a combination of time-of-flight (TOF) PET and recently proposed Prompt Gamma-Ray Timing (PGT, in fact, TOF SPECT) [7] –to resolve the contradiction pointed above. In contrast with a slit-based SPECT, the TOF SPECT allows encoding information on a hadron absorption spatial profile by the hadron transit time and the prompt gamma transit time using a reference time signal of a beam monitoring system without any collimation and compatible with TOF PET modality.

Silicon Photomultipliers (SiPMs) are widely recognized as the most appropriate detectors for various TOF applications, especially for TOF PET, due to their unique performance in photon number and time resolution [10], [11], [12]. Recently SiPM-based TOF PET scanners have been successfully developed by Philips and General Electric, and very active ongoing R&D on SiPM development and applications provide sustainable competitiveness of this emerging technology and further advances in SIPM performance.

Therefore, the universal non-collimated scintillator-SiPM-based detector system for TOF SPECT/PET imaging is assumed to operate as follows:

1. Advanced beam monitoring provides reference time for TOF SPECT as well as a spatial distribution of hadrons in the beam [13], [14];
2. TOF SPECT modality provides distribution of detection events (typically 4.3 –4.5 MeV) accumulated during beam-on time. Improvement in precision of a dose profile monitoring is expected to be good enough because time resolution of 4.5 MeV gammas with SiPM could be about 3 times better than that for 511 KeV gammas (˜ 150 ps for LSO/LYSO-SiPM detectors) just because of ˜ 9 times higher number of scintillation photons for 4.5 MeV gammas;
3. TOF PET modality operates during beam-off time in a time coincidence window and in an energy window around 511 KeV (conventional way);
4. Scintillator–SIPM block detector should be optimized for both modalities, and it could be rather challenging task;
5. TOF SPECT/PET detector design is assumed to be a monolithic scintillator block for higher efficiency and faster timing of photon detections as considered in [11];
6. Absorbed dose profile reconstruction is to be based on utilization of temporal and spatial distribution of the hadrons for TOF SPECT/PET image post-processing (deconvolution of output time distribution with measured beam spatial profile).

To reveal its full potential, the combined TOF SPECT/PET imaging should utilize cutting-edge advances in accelerator beam monitoring, profiling and timing on-the-fly and in fast scintillation detectors with advanced SiPMs.

Challenges to be evaluated and resolved for TOF SPECT/PET imaging:
1. Implementation of precision beam profile and beam time monitoring;
2. Development of TOF SPECT modality for high time resolution PET-compatible detection;
3. Optimisation of TOF PET modality for low-dose high-sensitivity SPECT-compatible detection;
4. Development of advanced fast timing SiPMs;
5. Optimisation of monolithic scintillator block detector performance;
6. Development of processing/modelling algorithms for precise dose profile reconstruction.
Feasibility, benefits, challenges, and possible implementation of the TOF SPECT/PET approach to be considered and discussed.
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Author: S. VINOGRADOV, LEBEDEV PHYSICAL INSTITUTE, MOSCOW (Lebedev Physical Institute)

Co-authors: WELSCH, Carsten (Cockcroft Institute / University of Liverpool); POPOVA, Elena (National Research Nuclear University MEPhI (RU))

Presenter: S. VINOGRADOV, LEBEDEV PHYSICAL INSTITUTE, MOSCOW (Lebedev Physical Institute)

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