The INSIDE project: online range monitoring in hadrontherapy with in-beam PET

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The INSIDE in-beam PET scanner has recently monitored in-vivo two fractions of a hadrontherapy treatment.
Hadrontherapy is based on the delivery of beams of charged particles, such as protons or heavier ions, to the patient. Charged particles beams lose energy in matter with a trend that exhibits the so-called Bragg peak at the end of range, where the majority of the energy is released. Moreover charged particles can be shaped in a narrow beam, which can be deflected by scan magnets so as to paint the whole volume to be irradiated. In order to exploit at best the features of hadrontherapy, online treatment monitoring and verification is highly desirable.
PET-based monitoring consists in the measurement of the $\beta+$ activity induced by beam-tissue interactions. In-beam PET monitoring, when data are acquired during the treatment, presents the highest correlation of the measured activity distribution with the deposited dose, since it is little influenced by biological washout effects. Furthermore, after a short initial acquisition time necessary to collect enough statistics for image reconstruction, in-beam PET can provide on-line in-vivo treatment monitoring.
The INSIDE collaboration has developed a bimodal in-vivo online treatment monitoring for hadrontherapy, installed at the CNAO (National Center of Oncological Hadrontherapy) in Pavia, Italy. The INSIDE scanner features a dual-head in-beam PET and a charged particles tracker to be used as a dose profiler. This work focuses on the in-beam PET results.
The INSIDE PET scanner is based on small Lutetium Fine Silicate scintillator elements (3x3x20 mm^3) coupled 1:1 with Hamamatsu Multi-Pixel Photon Counters; its front-end features the TOFPET ASIC and its data acquisition is based on Xilinx Spartan-6 FPGAs. The system has been thoroughly characterized during the irradiation of PMMA phantoms with both protons and carbon ions, in order to assess its acquisition performance and stability, coincidence finding and image reconstruction capabilities. The acquisition can be performed all along the treatment during both irradiation (spill) and pauses between different energy layers (inter-spill). Coincidence finding is performed in real-time with a multi-threading optimized software running on a multi-core CPU, an implementation that allows the development of innovative fast data analysis solutions. The image reconstruction is performed on-the-fly with a multi-

core MLEM algorithm, and its results are provided on-line during the treatment. An extensive work has been done to optimize the acquired image features and to optimize a 3D comparison technique so as to evaluate the treatment compliance with a gold standard (e.g., a prior session).
The first in-vivo test of the INSIDE in-beam PET has been performed during two consecutive treatment fractions of a patient affected by lachrymal gland carcinoma, being treated with proton beams. The results indicate that the INSIDE in-beam PET scanner is able to perform on-line treatment monitoring and to provide significant results after about two minutes of a 2.2 GyE four-minutes long treatment.