

signals from a pulsed proton beam (about 5 pC/pulse, 6 μ s FWHM) and detector shifts down to 2 mm. The measured relative shifts of the Bragg peak position of 2.3 mm for 1 MeV energy change and 173.25 mm for 82 MeV are in perfect agreement with Geant4 predictions. However, the low signal amplitude below 1 mV required an averaging with 1024 acquisitions.

Conclusion: Measuring the ionoacoustic signal at the IBA synchro-cyclotron, the detectability of 2 mm range shifts could be demonstrated. Experimental upgrades will be discussed, from which we reasonably assume to improve the resolution to 1 mm and below. In order to determine an absolute ion range in water in future ionoacoustic experiments, a method using an additional ultrasound transducer to measure the distance of the hydrophone to the water surface was developed. Remaining challenges on signal detectability for clinical dose rates as well as perspectives of future setup improvements will be discussed.

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Keywords: Ionoacoustics, Range Verification, Ultrasound

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Monte Carlo simulation of prompt- γ emission in proton therapy using a track length estimator

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Purpose: Online in vivo control of the ion range in a patient during proton therapy is a major challenge for quality assurance of treatments. After measurements showed that prompt- γ emission is correlated to the ion range (Min *et al* 2006, Testa *et al* 2008), prompt- γ imaging emerged as a promising method (Verburg *et al* 2013). Fast methods are required to compute accurate prompt- γ emission maps to design and predict the camera response from treatment plans. An analytic computation method based on the structure of the dose calculation engines in treatment planning system has recently been proposed (Sterpin *et al* 2015). An alternative technique based on variance reduction in Monte Carlo (MC) calculations is developed here for computing prompt- γ emission maps in proton therapy.

Materials/Methods: The track length estimator (TLE) method is a standard variance reduction technique in voxel-based dose computation in the kerma approximation (Williamson 1987), and similar approaches have also been developed for positron emitter distributions in proton therapy (Parodi *et al* 2007). A specific track length estimator has been developed here to design a continuous process along the proton track

that locally deposits the expected value of the prompt- γ emission (induced by proton inelastic scattering) that would have occurred if a large number of protons with the same incident energy had followed the same step (i.e. track element). First an elemental database of prompt- γ emission spectra is established in the clinical energy range of incident protons for all elements in the composition of human tissues. This database of the prompt- γ spectra is built offline with high statistics. Regarding the implementation of the prompt- γ TLE MC tally, each proton deposits along its track the expectation of the prompt- γ spectra from the database according to the proton kinetic energy and the local material density and composition. All software developments have been carried out with the Gate/Geant4 toolkit.

Results: A detailed statistical analysis is reported to characterize the dependency of the variance reduction on the geometrical (track length distribution) and physical (linear prompt- γ spectrum database) parameters. Benchmarking of the proposed technique with respect to an analogous MC technique is carried out. A large relative efficiency gain is reported, ca. 10^5 . Such an efficiency gain could reduce the MC computing time of a full treatment from some weeks to less than one hour. Implementation issues are also addressed.

Conclusions: This MC-based technique makes it possible to deal with complex situations such as heterogeneities for which proton straggling and secondary protons may have a decisive contribution. When considering translation to clinic, measurements for the prompt- γ spectrum database, or at least a sound calibration protocol of the simulated prompt- γ spectra, will have to be carried out.

Keywords: prompt- γ imaging, Monte Carlo simulation, variance reduction

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Preclinical imaging and radiotherapy of prostate cancer using the theranostic twins (⁶⁸Ga/¹⁷⁷Lu)-radiolabeled peptides

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Since the gastrin-releasing peptide receptor (GRPR) has been shown to be overexpressed in prostate cancer, bombesin which is the ligand of GRPR has been investigated to be a successful candidate for the peptide receptor radiotherapy (PRRT)[1]. The present study describes the imaging and therapeutic efficacy of the theranostic twins (⁶⁸Ga/¹⁷⁷Lu)-labeled bombesin derivatives for the PRRT of GRPR-overexpressing prostate tumors.

A series of DOTA-conjugated bombesin derivatives were synthesized using a solid-phase synthesis. Competitive binding studies were performed for selecting a GRPR-targeting peptide with high affinity. The selected peptide was labeled with ⁶⁸Ga using the NaCl method for imaging[2], and labeled with ¹⁷⁷Lu which was produced by the HANARO research reactor (thermal neutron flux of 1.8×10^{14} n·cm⁻²·s⁻¹) for therapy. The labeling yield was evaluated by iTLC-SG, and the PET/CT imaging and therapeutic efficacy of the radiolabeled peptides were evaluated using nude mice bearing PC-3 human prostate carcinoma xenograft.

Hydrophilic-modified bombesin derivative showed a nanomolar binding affinity for GRPR. The peptide was labeled with the both radionuclides in high incorporation yields (>98%). ⁶⁸Ga-labeled peptide was quickly cleared from the blood and clearly visualized in PC-3 tumors at 1 hr p.i. ¹⁷⁷Lu-labeled peptide were also rapidly accumulated in a PC-3 tumor, and the % ID/g of the tumor was 12.42 ± 2.15 1 hr p.i. The radio-peptide significantly inhibited the tumor growth