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Department of Informatics

Raccolta degli abstract

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The role of Monte Carlo simulations in the characterization of diamond integrated devices for hadrontherapy

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The fast development of new radiation therapy techniques led to a common goal: decreasing the absorbed dose to healthy tissues without compromising the prescribed target coverage. The only conventional dosimetry is not enough for a comprehensive characterization of clinical radiation beams because the absorbed dose is a macroscopic average quantity, while the biological effects of particles are related to the pattern of radiation interactions in the micrometric scale. DIODE project deals with the development and test of a novel detection system based on synthetic single crystal diamond able to perform simultaneously hadron therapy dosimetry and microdosimetry. Monte Carlo simulation plays a crucial role in the characterization of these devices as it permits to predict response in terms of dosimetric and microdosimetric quantities. Through the comparison between the simulation with the experimental data acquired, it will be possible to understand limits and abilities of those new devices.

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Precision of the positron emission activity range during irradiation with radioactive carbon and oxygen beams

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Range verification during heavy ion therapy by means of positron emission tomography (PET) of positron emitting projectile and target fragments has a long history. Presently, stable ions are used, most often carbon ions, for which the PET activity peak only roughly matches the Bragg peak and PET counting statistics is low. These issues can be mitigated by using a short-lived positron emitting ion as therapeutic beam.

We will report on recent studies to determine the precision with which PET can measure the range of positron-emitting C-11, C-10, O-15 and O-14 beams implanted into homo-geneous PMMA phantoms [1,2]. For comparison with stable ion beams, measurements with C-12 and O-16 beams were performed as well. The experiments were performed at the FRS fragment-separator facility of GSI Helmholtzzentrum für Schwerionenforschung GmbH, Germany within the BARB project [3]. Detailed results will be presented, showing that the range uncertainty is fully determined by the PET counting statistics. For the same number of ions, an isotope with a shorter half-life thus allows to reach a certain uncertainty within a shorter time, opening the prospect of quasi-real-time range verification. Amongst the investigated isotopes, C-10 is therefore favoured. However, considering technical aspects of producing beams of therapeutic quality, O-15 is the most feasible candidate among positron emitters of carbon and oxygen for quasi-real-time in-beam range monitoring in ion beam therapy.

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Faster and accurate: probing the biochemical stage of radiation damage with the new TRAX-CHEMxt code

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In latest years, new interest has grown in exploring the chemical effects of ionising radiation. The radical production modelled with Monte Carlo algorithms can provide useful insights but is limited to the microsecond time scale. To extend the range of predictability of the simulations up to the biochemical stage, TRAX-CHEMxt has been implemented. Its predictions have been compared to experimental data and already benchmarked codes on appropriate scales. A three orders of magnitude increase in computing efficiency is achieved, covering meanwhile six additional orders in simulated time, up to 1 s. Moreover, it demonstrated that high LET radiations cannot be treated with algorithms conceived for low LET ones, based on the hypothesis of full homogeneity at 1 μs. TRAX-CHEMxt will be applied to study the impact of radiation-induced radicals on the biological environment (i.e. biomolecules and oxygenation), as a function of beam quality, energy, LET and dose-rate.

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Real-time in vivo range verification using N-12 imaging based on the new Monte Carlo framework for proton therapy

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Purpose: The RIVER (Real Time in Vivo Verification of Proton therapy) project will make a major step towards translating N-12 (half-life of only 11 ms) real-time verification for proton therapy to the clinic. We will have determined its accuracy under clinically realistic circumstances, established its potential clinical benefit in terms of reduced complications for head-and-neck cancer patients, and determined its optimal implementation. Ultimately, this will allow optimal radiotherapy treatment plan design and increase the number of patients benefiting from proton therapy. The N-12 imaging is validated using irradiation of homogeneous and heterogeneous phantoms.

Methods: The distribution of N-12 and other, longer-lived, positron emitters such as O-15 and C-11, from the RayStation output for PMMA, graphite, and head phantoms were used as the input of GATE simulations. The simulated PET scanner is the dual-panel version of a Siemens Biograph mCT PET scanner available in-house.
The irradiation plan consisted of pulsed pencil-beam spots of 120 MeV protons. The irradiation time in PMMA, graphite, and head phantoms was 300 s, 60 s, and 60 s, respectively. The N-12 images were calculated by subtracting the late image (time window from 50-94 ms in the beam-off periods) from the early image (from 4-49 ms), after scaling with the time window width. The experimental and simulation setups of the CIRS 731-HN anthropomorphic head phantom and PET scanner are shown in Fig. 1.

Fig. 1. A) Experimental setup showing the head phantom between the PET scanner panels. B) A CT image of the head phantom is imported into a custom-modified research version of the RayStation treatment planning system. C) GATE simulation setup based on the experimental setup.

Finally, the measured and simulated N-12 images were compared. The production range for N-12 and long-lived isotopes was determined as the point where the N-12 production decreases to 50% of its maximum, which was found by a sigmoidal fit on the cumulative profile.
Results: The N-12 production range for PMMA and graphite phantoms shows a good agreement between simulation and measurement, with measurement values of 94.9±0.3 mm and 69.78±0.29 mm, and simulation values of 94.6±0.3 mm and 70.51±0.26 mm for PMMA and graphite, respectively. The N-12 activity induced in the head phantom shows good agreement with results based on the validated framework. The production range values were at 102.9±3 mm and 103.4±1.2 mm for measurement and simulation, respectively. This is promising for measuring the proton range in real-time in vivo range verification. Due to the large positron range blurring for N-12, its lateral width of a pencil beam image is 4 times larger than that of long-lived isotopes, which is another interesting result from this study.
Conclusion: A Monte Carlo framework based on RaySation/GATE was developed to calculate the N-12 images. The framework was validated by comparison with experiments. Our findings can be a significant step towards translating N-12 real-time in vivo verification to the clinic.

Keywords: Proton therapy, N-12 imaging, RayStation, Monte Carlo simulation.

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"IN VITRO SPARING EFFECT OF ULTRA HIGH DOSE RATE RADIOTHERAPY ON HPV-NEGATIVE HEAD AND NECK SQUAMOUS CARCINOMA"

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Aims:
Ultra high dose rate (FLASH) radiotherapy (RT) has experimentally highlighted the possibility of increasing the therapeutic window in vivo models. Concerning head and neck cancers, due to the complex anatomy of the region, several critical structures in and around the area receive radiation treatment. Reducing the incidence and severity of damage to surrounding noble organs could enable the intensification of RT enhancing the probability of tumor control. However, the results from in vitro studies are mixed and the biological mechanisms underlying FLASH-RT remain unclear. The purpose of this study is to compare the effect of FLASH and CONV-RT modalities on Human Dermal Fibroblast (HDF) and Human Oral Squamous Carcinoma (SCC-25) cells viability at increasing doses of radiation.
Methods:
HDF and SCC-25 were irradiated with doses ranging from 4 to 16 Gy using FLASH (average dose rate >200 Gy/s) or CONV dose rates (7 Gy/min), with a 10 MeV electron beam from Sordina Low energy Electron LINAC. Irradiation was delivered under normoxic conditions at room temperature with the plates lying flat on 1 cm of solid water and irradiated from beneath (beam angle 180 degrees). HDF cells were cultured in Dulbecco's Modified Eagle Medium (DMEM), while SCC-25 cells in a mixture of DMEM and Ham's F12 medium (1:1). The medium was supplemented with 10% fetal bovine serum (FBS), 1% L-glutamine, sodium pyruvate, and penicillin-streptomycin. For SCC-25 medium, 400 ng/mL of hydrocortisone was also added. The cells were maintained at 37℃ in a humidified incubator with 5% CO2 atmosphere. MTT assay was performed after 24 h, 72 h, 6 and 8 days to explore cell viability.

Results:
Cell viability was more marked in HDF FLASH-RT group at 8 days after irradiation with lower doses. Both CONV and FLASH irradiation showed a late cytotoxic effect on SCC-25 cells, resulting in a significant decrease in viability to 50% within 6 days.
Conclusions:
Our preliminary experimental evidence points to a protective effect of FLASH-RT on HDF cells with iso-effecacy on cancer cells.

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Hadrontherapy at CNAO

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Positron emitting Radioactive ion beams for simultaneous treatment and imaging.

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Dosimetric study of lung modulation and motion effects in carbon ion therapy for lung cancer

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Carbon ion therapy has the potential to deliver the most effective treatment for non-small cell lung cancer (NSCLC) patients. Nevertheless, motion related uncertainties and lung tissue heterogeneities can highly jeopardize the dose distribution.
In particular, lung tissue microstructures are responsible for the modulating effect, resulting in the broadening of the Bragg curve, and thus in an increased dose in the distal fall-off and a lower target dose (Fig.1 a,b). By implementing the modulation mathematical model in the treatment planning system TRiP98, it is possible to predict and compensate both for physical and biological dose degradation. With carbon ions, because of the fragmentation spectra, linear energy transfer (LET) and relative biological effectiveness (RBE) maximum shift in depth, which might lead to an increased normal tissue toxicity behind the target (Fig.1 c,d).
This effect will be studied experimentally in cell survival experiments, for which plans are presented. Treatment planning studies will investigate the potential clinical impact as well as compare it to motion related dose degradation

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Optimisation and setup for quantitative in vitro/vivo experiments with low energy UHDP electron in FLASH RT

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The emergence of Ultra-High dose-per-pulse (UHDP) pulsed beams, capable of inducing the Flash effect, has garnered substantial scientific interest. This radiobiological phenomenon presents a potential breakthrough in clinical applications by minimizing healthy tissue side effects while ensuring efficacy against tumors. The journey toward clinical implementation of FLASH treatments involves several steps. Firstly, specialized linear accelerators like the ElectronFlash, installed in Pisa, are essential, requiring modification of specific beam parameters. Secondly, precise dose monitoring is critical. Current dosimeters, especially ionization chambers, are inadequate for UHDP regimens, prompting exploration of new dosimeters. The third step involves conducting quantitative in vitro/vivo radiobiological experiments. These experiments provide crucial insights into Flash effect-triggering parameters, emphasizing the need for accurate dosimetric setups. In particular, in vivo experiments necessitate dedicated Treatment Planning Systems for optimized internal dosimetric distribution, integrated positioning, centering and imaging systems and dose calculation station.

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New image reconstruction approach for in-vivo range verification of multiple field carbon ion treatments by means of in-beam PET system

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In-beam PET is one of the most advanced non-invasive techniques for in-vivo range verification in particle therapy.
Following the promising results of proton therapy monitoring within the INSIDE clinical trial (ClinicalTrials.gov NCT03662373), a novel PET image reconstruction approach was developed for carbon ion beams, which suffer a severe reduction of positron emitters.
Since most of the activity is related to 11C isotopes from projectile fragmentation, most of the positron emitters decay in the Clinical Target Volume, which is always included in the PET field of view. Therefore, the new proposed method aims to reconstruct multiple field irradiations in a single PET image to gain statistical significance and image quality.
The reconstruction relies on a Maximum Likelihood Expectation Maximization algorithm and a patient-tailored response model.
A Voxel-Based Morphometry method was applied to PET images simulated on CT scans of patients where morphological changes occurred, proving the possibility of detecting them. The analysis of experimental images and the integration with the Dose Profiler measurements are in progress.