therapy (hadron MBRT). The technique is based on the well established tissue-sparing effect of arrays of parallel, thin or small beams, observed in studies performed with synchrotron radiation [1-2]. In parallel, significant tumor growth delay was observed in highly aggressive tumors by using interlaced irradiations [1-3]. Hadron MBRT combines the advantages of MBRT with the high dose conformability and the remarkable biological effectiveness of hadrontherapy. This novel strategy might guarantee tissue recovery and reduce the side effects of radiation in healthy tissues. The main goal of this study was to explore this new approach from a dosimetric point of view and to verify its technical feasibility at a clinical center (HIT, Germany). In particular, carbon and oxygen minibeam were studied.

Materials/methods: Carbon and oxygen minibeam were generated through a tungsten multi slit collimator with line apertures of 700 μm separated by 3500 μm. Scanned 12C and 160 pencil beams were used to cover a given irradiation field size (1x1 cm2) and a spread out Bragg peak (SOBP) region of 5 cm at 8 cm-depth in water. Radiocromic films (EBT3) were placed at several depths in a solid-water slab phantom to evaluate dose distributions. Quenching effects of these films were also assessed and results were accordingly corrected. As a figure of merit, the ratio between the central dose of one minibeam (peak dose) and the dose in the middle of two consecutive beams (valley dose) was evaluated. This magnitude, named peak-to-valley dose ratio (PVDR), is a very relevant magnitude in such spatially fractionated techniques.

Results: The measured lateral dose profiles in carbon and oxygen MBRT consisted in a pattern of peaks and valleys, which prove the technical feasibility of this approach. This first dosimetric study showed PVDR values around 10-20 in the first centimeters of the phantom. PVDR values progressively decrease up to around 5 at 8-cm-depth. These PVDR values are in the order of the ones obtained in x-rays MBRT, for which biological effectiveness has already been proven.

Conclusions: This is the first exploratory study that experimentally proves the technical feasibility of hadron MBRT at a clinical center. The PVDR values obtained showed the potential of this radiotherapy approach, which might allow reducing side effects in the healthy tissues. Animal experiments are warranted.

Keywords: minibeam radiation therapy, hadron therapy, experimental dosimetry

References:

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Infrared study of the biochemical effects in glioma cells induced by x-rays and Gd nanoparticles: first studies at SESAME synchrotron (Jordan)

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Purpose: One strategy to improve the clinical outcome in radiotherapy (RT) is to increase the dose effects in the tumor. This can be achieved by using specific nanoparticles (NP). Numerous studies have shown an enhanced effectiveness of tumor cell killing when NP were associated to irradiation [1-3]. However, the mechanisms of action are not yet clear. In addition to the damage due to a possible local dose enhancement, the interaction of NP with essential biological macromolecules could lead to changes in the cellular function, such as cell arrest at radiosensitive phases [4]. These effects, which could be amplified with a subsequent irradiation, might increase their anticancer effectiveness. Along this line, in this study we used F98 glioma rat cells as an in vitro model to evaluate the intracellular biochemical changes induced by x-ray irradiations in combination with Gadolinium NP by using Fourier transform infrared microspectroscopy (FTIR). FTIR allows in situ chemical structure determination of intracellular biomolecules. In addition, this technique has significantly contributed to study apoptosis, as well as cell cycle and cell death modes.

Materials/methods: FTIR measurements were performed using the internal source of infrared radiation at SESAME synchrotron (Jordan). Principal Component Analysis (PCA) was performed to show the variances between the different sets of spectra.

Results: Noticeable spectra alterations in the presence or absence of NP were detected in the proteins, DNA and lipids regions, indicating changes in the cellular function (even in the absence of radiation). In particular, biochemical changes related to apoptosis were detected. These include a shift toward the low wavenumbers in the amide I and II bands, relative amplitude changes in the CH2 and CH3 stretching modes, along with DNA chromatin condensation indications [5]. The figure below shows an example of PCA analysis in the DNA region of the infrared spectral range in the presence and absence of NP for a dose deposition of 10 Gy.

Conclusion: This is one of the first research studies performed at the Emira laboratory of the SESAME Synchrotron (Jordan). This infrared work provides new insights on the biochemical effects induced by nanoparticles and nanoparticles, for which the full mechanisms of interaction are not well known up to now. Results will be discussed in relation to cell viability studies.

Keywords: Fourier Transform Infrared Microspectroscopy, radiotherapy and nanoparticles, F98 glioma cells.

References:

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Construction and first tests of a PET-like detector for hadrontherapy beam ballistic control

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We present the first results obtained with a detector, called Large Area Pixelized Detector (LAPD), dedicated to the beam ballistic control in the context of hadrontherapy. The purpose is to control the ballistics of the beam delivered to the patient by in-beam and real time detection of secondary particles, emitted during its irradiation. These particles could be high energy photons (γ prompt), or charged particles like protons, or 511 keV γ from the annihilation of a
Visualization of target inhomogeneities in carbon ion radiotherapy using nuclear fragments

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Purpose: Ion beams are used for highly precise radiotherapy, making an accurate dose deposition in tissue crucial. However, this accuracy can be compromised by unpredictable changes of the patient. Therefore an online monitoring of the beam within the patient is of large interest. The main challenge is given by stopping of the entire beam inside of the patient. Our group investigates the possibility to collect and reconstruct the information about the beam extension in the patient by detecting light ions emitted from the irradiated object, suggested in [1]. Exploiting the directions of secondary ions measured, a method for visualization and quantification of the carbon ion beam profile in a homogeneous phantom was published in [2]. In this contribution, the capability of the method to detect inhomogeneities in otherwise homogeneous phantoms is presented.

Materials & methods: The experiments were performed at the Heidelberg Ion Beam Therapy Center (HIT) in Germany. Narrow carbon ion beams of therapy-relevant energies, were directed onto homogeneous plastic phantoms with a typical head size. Secondary ions emerging from the phantom during the irradiation, were detected by a Timepix detector [3] developed by the Medipix Collaboration at CERN. A multilayered detector, consisting of 3 parallel Timepix detectors, was used to measure their tracks in 3D. The track distributions acquired with a full phantom were compared with cases when parts of the phantom were missing at several positions, simulating cavities in the body.

Results: It was found that exploiting the information carried by secondary ions enables to visualize cavities in the irradiated volume at different positions of the Bragg curve. The method was found to be sensitive also to cavities situated behind the Bragg peak (in the fragment tail). Moreover, a three-dimensional image reconstruction based on maximum likelihood expectation maximization (MLEM) exploiting the measured secondary particle tracks was developed. In the resulting images, air cavities and inhomogeneities with density differences down to 0.3 g cm⁻³ to the surrounding material are clearly visualized for the first time.

Conclusions: Our experimental results demonstrate that this novel imaging modality enables clear visualization of down to 1 cm-sized air cavities in head-sized phantoms, under clinical irradiation conditions. Therefore we conclude that secondary ions, being a by-product of the irradiation, are an attractive source of information on the actual beam extension in the irradiated body.

Keywords: carbon ion radiotherapy, in-vivo beam monitoring, secondary charged particles

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References:

The effect of fractionated administration of thalidomide at γ-ray irradiation on tumor response and lung metastasis

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