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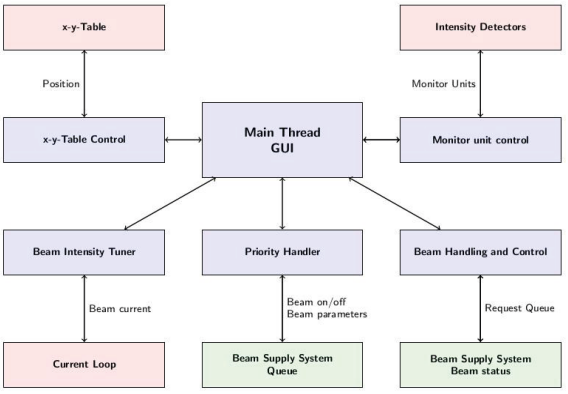

Figure 1: Schematic structure of beam control system. Software components are drawn blue, hardware components red and the IBA Beam Supply System (BSS) green.

Figure 1.

Keywords: Proton Therapy, Instrumentation, Software Development

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Radioisotopes: the "fuel" for nuclear medicine

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Nuclear medicine provides essential and in many cases even unique tools for diagnostics and therapy of a large variety of illnesses. Every year over 30 million nuclear medicine procedures are performed worldwide and new promising applications are under development.

Radioisotopes are the key ingredient for any radiopharmaceutical and can be considered as the "fuel" that is driving all nuclear medicine applications. The choice of a radioisotope with appropriate nuclear decay characteristics and chemical properties can be decisive for the outcome of the procedure.

Today the vast majority of all diagnostic procedures is performed with ^{99m}Tc (for scintigraphy and SPECT) and ^{18}F (PET) respectively. ^{18}F is produced in a decentralized way by a fleet of over 800 medical cyclotrons. For the last 30 years the supply of ^{99m}Tc relied exclusively on a centralized production chain distributing convenient ^{99}Mo/^{99m}Tc generators. However, recent ^{99}Mo supply perturbations triggered several projects that try to implement alternative production schemes of ^{99}Mo or ^{99m}Tc respectively.

Due to their excellent nuclear decay properties and their chemical versatility, ^{99m}Tc and ^{18}F will undoubtedly maintain their leading role in the future. They are complemented by other radioisotopes that are advantageous in specific diagnostic applications. In particular the generator-derived PET isotopes ^{68}Ga and ^{82}Rb, as well as longer-lived PET isotopes like ^{44}Sc, ^{64}Cu, ^{89}Zr, etc. are experiencing a rapidly rising demand.

For long time therapeutic applications of nuclear medicine were dominated by ^{131}I, used in the treatment of hyperthyroidism and thyroid cancers. However, with the advent of new targeted therapies such as radio-immuno-therapies (RIT) and peptide receptor radionuclide therapies (PRRT), radiometals were found to be more appropriate than radioiodine. Today ^{177}Lu is considered as the "gold standard" for such applications, but for particular applications radioisotopes emitting radiation with even shorter range are sought. The recent FDA approval of Xofigo (^{223}Ra-chloride) for the treatment of bone metastases is now paving the way for the large scale clinical use of alpha emitters.

The demand and supply prospects of important medical isotopes will be discussed. A particular emphasis will be put on examples where nuclear and particle physics laboratories can support the radioisotope supply with their special infrastructure or technologies.

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Beam monitoring and dosimetry tools for radiobiology experiments at the cyclotron ARRONAX

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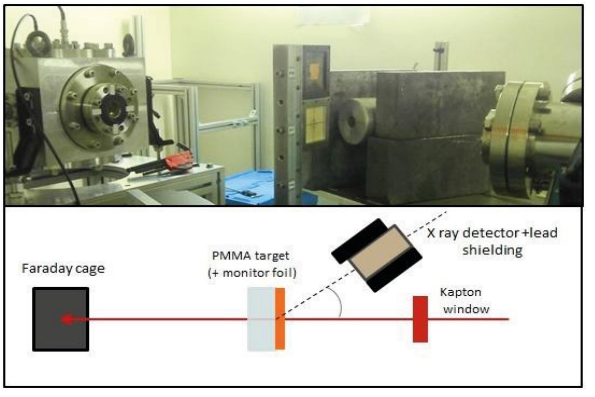
Purpose: The ARRONAX (Accélérateur pour la Recherche en Radiochimie et Oncologie à Nantes Atlantique) cyclotron in Saint Herblain - France is a facility delivering α particles at 68 MeV ([1]). One of its purposes is to become a platform for radiobiological studies. The radiobiological studies evolve around two axes: the low energy range (<10MeV) in order to optimize radio-immunotherapy (RIT) treatments, and the high energy range (30-68 MeV) in order to puzzle out the fundamental mechanisms generated by cells in response to ionizing radiations.

The ARRONAX platform for radiobiology is currently preparing to use a time lapse fluorescence confocal microscope suitable for the irradiation of cell wells. This platform should contain tools for beam intensity checks to enable accurate and repeatable irradiation conditions and a device to monitor the delivered dose.

Materials and Methods: A system has been developed to monitor the beam intensity using an X-ray spectrometer. It is based on the online measurement of the bremsstrahlung (>1keV) produced by the interaction of the incident particle with the medium. Experiments were made using PMMA targets bombarded with 63MeV alpha particles, in order to characterize this continuous X-ray spectrum. A simulation code of the bremsstrahlung has been built.



For relative dosimetry, experiments were performed to get Gafchomic EBT3 films response to alpha particles (1 – 30 Gray). To quantify the alpha darkening, the relative efficiency (*RE*) defined as the delivered dose ratio between photons and alpha particles for the same optical density was used. The same EBT3 lot was used and an identical protocol for scanning and analysing was applied.

Results: A good agreement has been found between experimental and simulated spectra of bremsstrahlung. The intensity of the bremsstrahlung spectrum allow the beam monitoring with an accuracy <3% for 1 Gray delivered dose. The measured spectrum presents variations with the target thickness, showing a good sensibility for thin target (<1000µm) and a saturation for thicker ones. Bremsstrahlung

spectrum also shows a sensibility with the chemical composition of the target.
For EBT3 study, an effect of polymerization saturation has been observed compared to a photon response curve. The (RE) factor found was about 0.7.
Conclusions: Tools for a radiobiological platform are developed at ARRONAX. Bremsstrahlung measurement would allow a control of the beam intensity on the target directly without the use of an additional medium disrupting the beam. Sensibility on the chemical nature can be used for precisely modelling the dose evolution in medium with the beam direction.
The data of EBT3 response to an irradiation with alpha particles is new and necessary. We will run equivalent experiments using different beams available at ARRONAX to compare the EBT responses by varying the LET, the ionization density, the charge of incident particle.
Keywords: Beam monitoring, dosimetry

References:
[1] F. Haddad et al., Eur. J. Med. Mol. Imaging 35, 1377-1387 (2008)

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New challenges for biologically adapted ion beam treatment planning: single and multi-ion approaches

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Purpose: Ion beam radiotherapy, in addition to the well known physical and radiobiological benefits of particular ion species like 12C, offers unique additional advantages in terms of effective dose shaping.
Multimodality, i.e. the use of multiple fields of different ion species in the same treatment plan, introduces additional degrees of freedom, allowing to distribute high- and low-LET radiation arbitrarily. This is particularly attractive in order to selectively target hypoxia and potentially other types of intra-tumour biological heterogeneity. In order to exploit these advantages, specific treatment planning tools are required.
Materials and methods: To this end, we have extended the TRiP98 code, the first treatment planning system for particles, in several directions.
The optimization engine has been modified to allow the inverse planning of different ion modalities simultaneously.
The biological effect calculation was extended beyond the RBE-weighted dose, including the oxygen enhancement ratio (OER).
An experimental in-vitro survey at NIRS with the irradiation of specific hypoxic targets with various ions supports this approach with the benchmarking of the OER-LET model newly implemented in TRiP98.
This way the first complete database for the OER-LET dependence in the region of intermediate pO2 has been generated.
Additionally we performed extended target irradiation of an inhomogeneous target to test the model in realistic geometries.
Results: Biological dosimetry measurements performed at NIRS and GSI revealed a good agreement of the model developed to handle OER in treatment planning.
Physical and radiobiological base datasets for ion beam modalities from protons to oxygen have been established.
Treatment plans with single and multiple ion species have been produced allowing to restore the prescribed survival level across the entire target in the presence of hypoxic subvolumes.
The impact of different fractionation schemes for different ion beam modalities is also critically evaluated.
Conclusions: We present the first treatment planning system optimizing several ion species as well as allowing biological effect painting across inhomogeneous targets. The OER model is validated experimentally. TRiP98 is effective in restoring a given uniform cell killing, by scaling and redistributing beam components accordingly.
We give an outlook on the possibilities of ion beams in this respect.

Keywords: (Particle therapy, biological dose optimization, hypoxia)

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Biomarker for stratification in radiotherapy - preclinical and early clinical models

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Within the last centuries, major advances have been achieved in radiotherapy technique as well as in combined radiation treatments. Thereby, tumour control and survival of patients improved. However, it is known for a long time that radiation response varies from patient to patient, even in the same tumour entity and stage. Predictive biomarkers that have always been used in radiation oncology are tumour site and histology, stage, differentiation and tumour size. With increasing knowledge in tumour biology, genetics and pathophysiology the tools are now available to establish more precise biomarkers that can in future help to define groups of patients for individual interventions like radiation dose escalation, decision between radiochemotherapy or radiotherapy with molecular targeted drugs or the application of hypoxic cell radiosensitisers. The talk will give an overview on the current status of knowledge on potential biomarkers e.g. of tumor hypoxia, tumor cell metabolism, DNA repair and biomarkers for combining radiotherapy with inhibition of the epidermal growth factor receptor using monoclonal antibodies.

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Real-time monitoring of the ion range during hadrontherapy:
An update on the beam tagging hodoscope

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Purpose: For an improvement of the quality control during hadrontherapy an online monitoring of the ion range is highly desired. For this purpose several modalities are under development, using the detection of emitted prompt gamma rays [1,2,3] or secondary protons (IVI) [4,5,6] in the case of incident carbon ions.
For all modalities, the nuclear interaction vertices (whose distribution is strongly correlated with ion ranges) are determined by intersecting the incident ion trajectory with various geometries provided by secondary radiation, e.g. planes (collimated cameras), cones (Compton cameras) or