Biomedical applications of radioactive ion beams: a new European Research Council advanced grant in particle therapy

The use of charged particle therapy (CPT) is rapidly growing all over the world1, particularly in Europe (1). Due to the favourable depth-dose distribution, more normal tissue is spared with application of CPT compared with conventional X-ray radiotherapy in virtually all sites, leading to high success/toxicity ratios (2). Yet, CPT remains controversial (3). The first reason is the higher cost of CPT facilities compared with those required for X-ray treatment, especially the expensive heavy ion therapy centres. Moreover, CPT is limited in what should be its main advantage, i.e. the high precision that is possible because of the Bragg peak. CPT is less robust than conventional radiotherapy because of considerable uncertainty regarding the particle range and poor image guidance (4). Imaging in radiology very often uses radioactive tracers, and it was proposed many years ago (5) that radioactive ion beams (RIB) had the potential to offer simultaneous treatment and beam visualisation, as is the case with theranostics and radioisotopes. Past efforts were generally hampered by the low intensity of RIB, which are generally produced by nuclear fragmentation of the primary stable isotopes in thin targets (in-flight method). PET-monitoring of CPT is currently used, but this method only exploits the weak signal produced by the fragmentation of nuclei used as projectiles (e.g. 11C for 12C) or as targets (e.g. 15O by fragmentation of 16O). The signal-to-noise ratio for RIB therapy is obviously much higher (Figure 1).

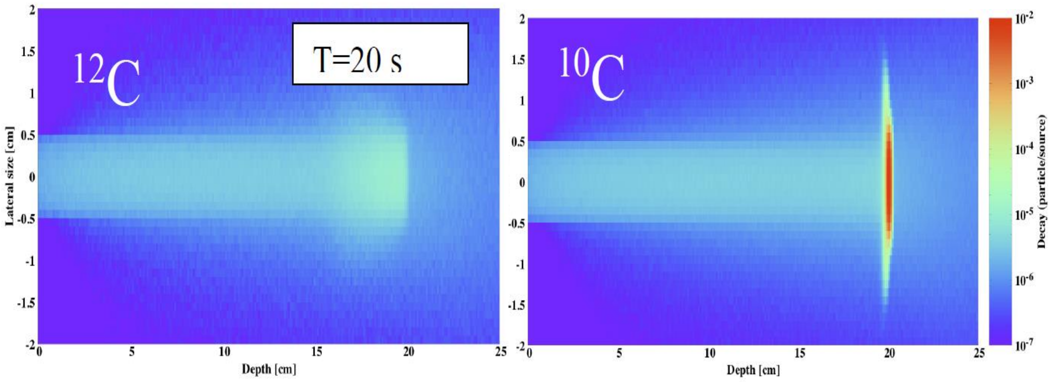

Figure 1. A Monte Carlo simulation of the PET signal that is accumulated in 20s by a stable ^{12}C-ion beam and the β^+-emitter ($t_{1/2}$=19.3 s) ^{10}C-ion beam. Image modified from ref. (6).

The Facility for Anti-protons and Ion Research (FAIR)2 is currently under construction at the GSI Helmholtz Center3 in Darmstadt, Germany. FAIR will use the current GSI synchrotron SIS18 as an injector, and will accelerate heavy ions up to much higher energies and intensities than is achieved currently at GSI or other clinical facilities. The biophysics programme at FAIR aims to exploit the intensity and energy upgrades for therapy and space radiation protection research (6). The intensity upgrade at SIS18 can be exploited to test RIB therapy in the same Cave M (Figure 2) where the pilot therapy project with stable 12C ion beams was performed (7). The researchers involved in the project named biomedical applications of radioactive ion beams (BARB)4 aim to test 10,11C and 14,15O for simultaneous treatment and imaging at FAIR; the goal is to reach sub-mm precision in range verification and to demonstrate the potential of RIB therapy in an animal model. BARB is funded by the European Union within the 2019 European Research Council (ERC) advanced grant call5 (principal investigator (PI), M. Durante; co-PI K. Parodi) and is a five-year project that is due to start in October 2020.

[1] https://www.ptcog.ch/
[2] https://fair-center.eu/
[3] https://www.gsi.de/
[4] https://www.gsi.de/BARB

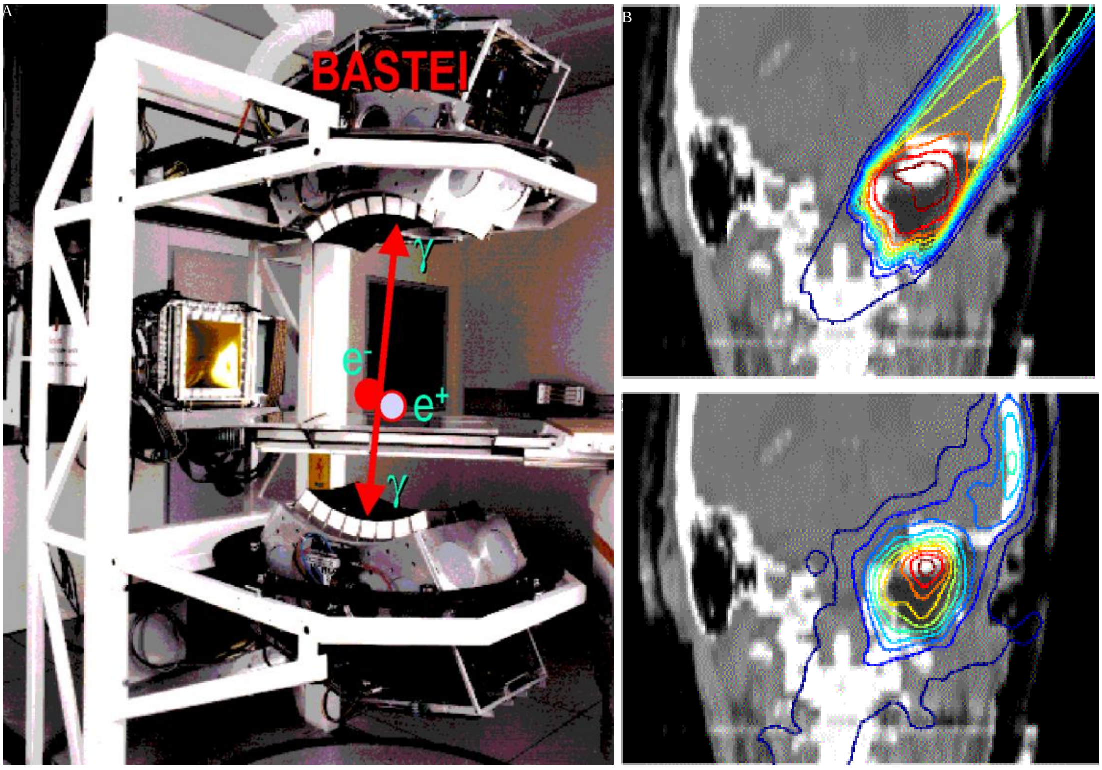

Figure 2. A) The PET camera (without housing), developed and operated by the Forschungszentrum Rossendorf (now Helmholtzzentrum Dresden-Rossendorf), installed at the GSI treatment room (cave M) and used during the therapy pilot project, as shown in the clinical case in panels B (prescribed dose according to treatment planning) and C (measured activity distribution, modified by the washout). Image by the GSI library, courtesy of Wolfgang Enghardt.

In BARB, the radioactive ions of interest will be produced by fragmentation (one or two-neutron removal, respectively) of relativistic primary beams (12C, 16O) in reaction targets (beryllium, carbon) that are placed at the entrance of the SIS18 fragment separator (FRS) and separated in-flight. Cave M is equipped with an online PET machine (Figure 2), but even online PET can only register in-between the synchrotron beam spills, because the signal is obscured by the large prompt γ-ray signal during the irradiation. An improved detector should be able to exploit the prompt γ-ray emission during beam extraction, in addition to the PET acquisition (and concomitant third-g emission in the cases of 10C and 14O) in-between the synchrotron spills. BARB will build a hybrid detector, the aim of which is to exploit both the prompt γ-rays emitted in nuclear interactions during the beam-on time of the synchrotron pulsed delivery, and the delayed emission of the (g-)β+-emitting primary beam (superimposed to a minor contribution of positron emitting projectile and target fragments) in the beam pauses (8). The new detector concept will be based on an advanced version of the γ-PET design originally proposed at Ludwig Maximilians Universitat (LMU), Germany, (9) and further developed in the framework of the International Open Laboratory and International Research Initiative between LMU and the National Institute of Radiological Sciences (NIRS) of Japan (10) (Figure 3).

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[5] https://erc.europa.eu/funding/advanced-grants

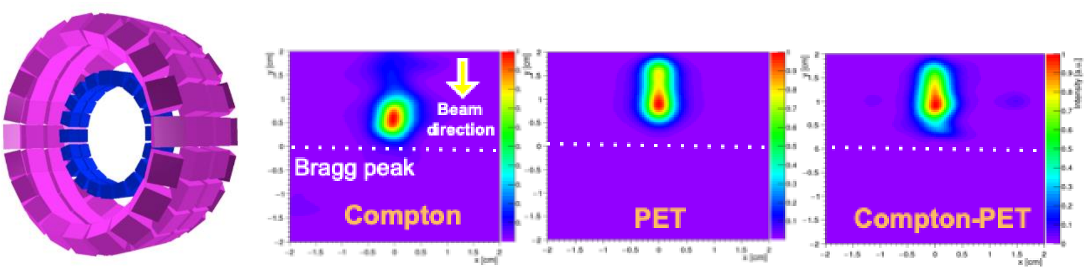

Figure 3. From left to right: example of hybrid detector and simulated imaging of in-beam Compton+PET signals, in this case for proton beam irradiation, to be further optimised for application to RIB in BARB. Images adapted from ref. 11.

BARB will therefore represent the definitive test of the true advantages of RIB in CPT, and will assess whether, through use of RIB, CPT can exploit fully the precision enabled by the charged particle physics.

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