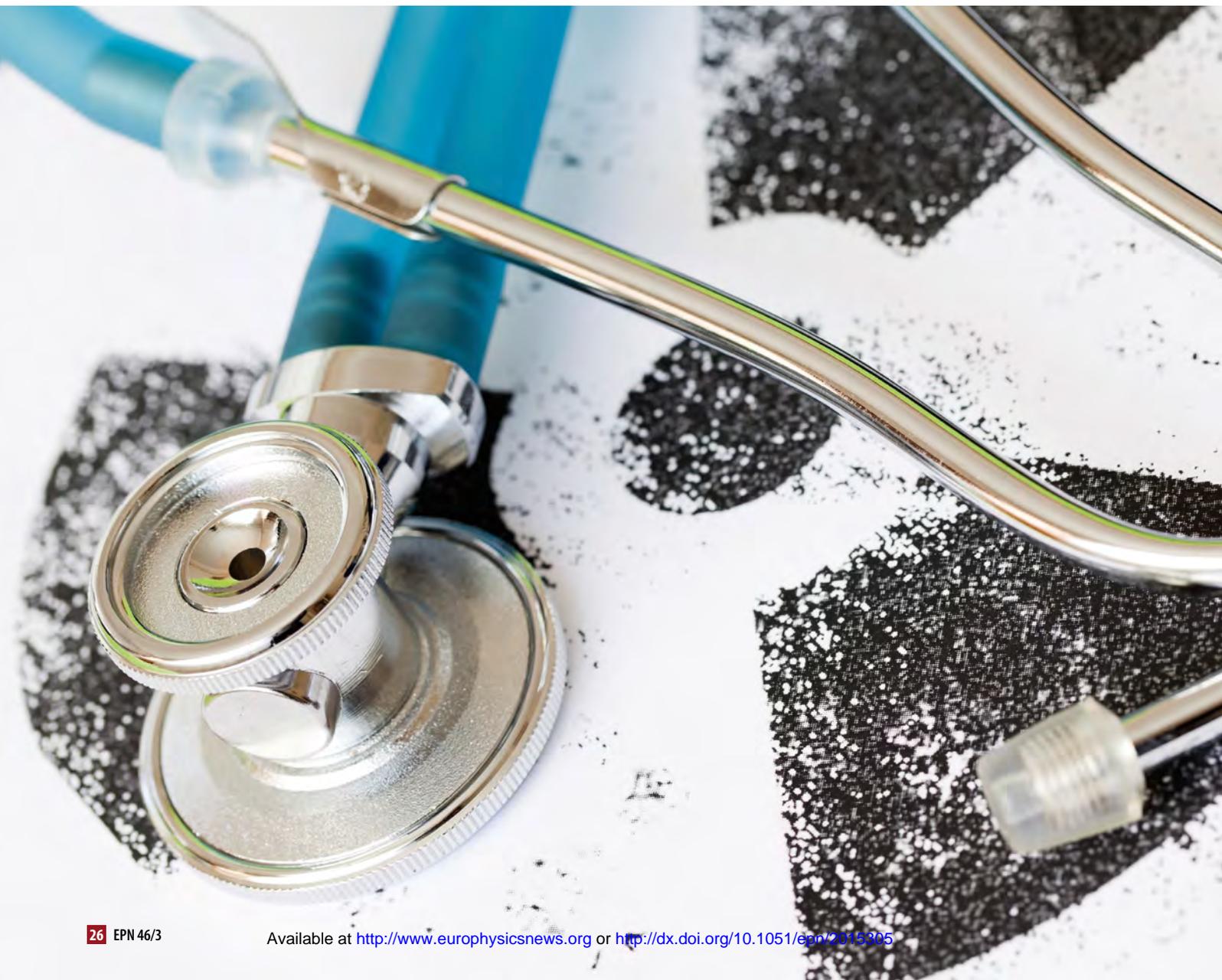


NUCLEAR PHYSICS FOR MEDICINE: HOW NUCLEAR RESEARCH IS IMPROVING HUMAN HEALTH

■ **Angela Bracco** – DOI: 10.1051/epr/2015305

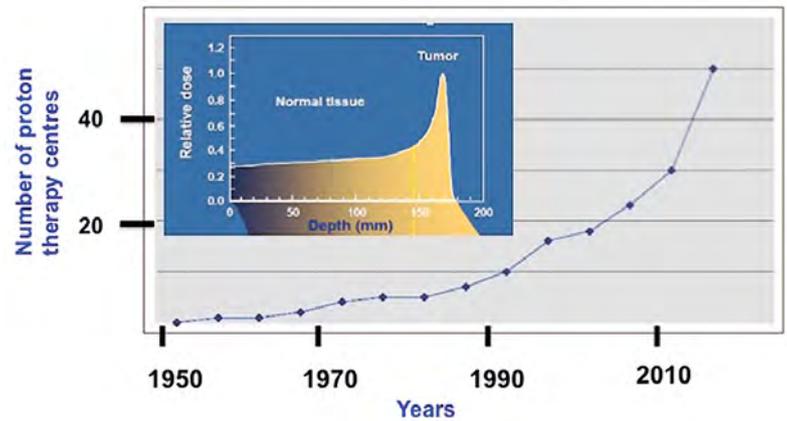
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The Nuclear Physics European Collaboration Committee (NuPECC) is an associated Committee of the European Science Foundation (ESF). Its mission is to strengthen European Collaboration in nuclear science through the promotion of nuclear physics, and its trans-disciplinary use and application in collaborative ventures between research groups.



NuPECC fulfils its mission with several activities, the most relevant being the preparation of Long Range Plans for Nuclear Physics. Other initiatives concern reports on specific topics. The latest NuPECC effort in this context is the report “Nuclear Physics for Medicine” issued in 2014. This volume was prepared by the best experts in the field under the NuPECC guidance and was presented in Brussels on 24 November 2014. This article aims to underline the motivations for this report and to briefly recall some exciting advances in nuclear technologies for medicine, developed at nuclear physics laboratories for basic science.

It is well known that techniques employing nuclear particles and radiation to understand, diagnose and cure diseases are continuously increasingly importance in healthcare. Much of the underpinning research and development is carried out in institutes devoted to nuclear physics studies. Indeed, nuclear physics has since the beginning been characterized



▲ FIG. 1: Evolution of the number of proton therapy centres in the world between 1950 and 2015. Inset: the energy deposited (proportional to the dose) by a beam of charged particles at a given bombarding energy as a function of penetration distance. The high deposit of energy (where the tumor is located) is at the Bragg peak at the end of the particle trajectory.

by fast implementation of its discoveries to the benefit of society. Its medical applications constitute the fastest science transfer from basic research to social applications.

At accelerator-based nuclear physics laboratories the main aim of the research is the study of the core of the atom – the nucleus – in its many forms and complexities. For this purpose complex acceleration systems are employed to study a large variety of both stable and radioactive isotopes in order to understand how the fundamental forces of nature bind the nuclear components together, and generate the amazing structural and behavioural complexity seen in nuclei. Nuclear reactors dedicated to scientific research are also employed to make particular nuclear species, using the neutrons that are emitted in uranium fission.

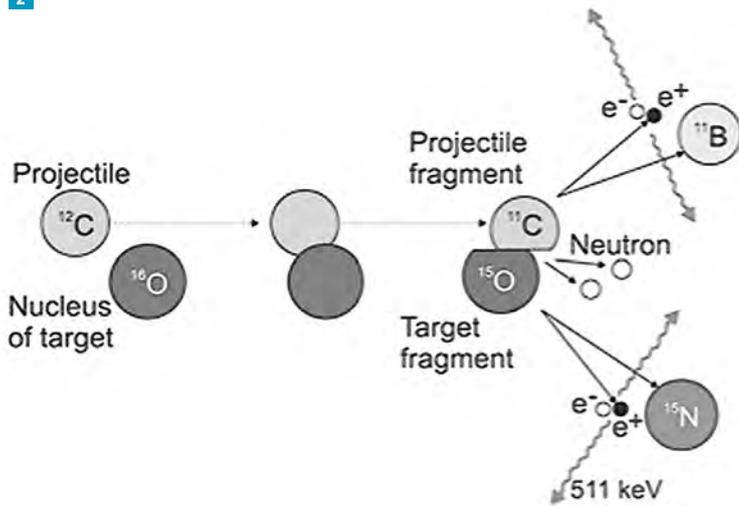
Nuclear medicine and radiation therapy encompass several aspects which are applications of basic research in nuclear physics:

- The emissions from radioactive isotopes can be employed as diagnostic tools by creating images of a patient’s tissues and organs to reveal details of both the structure and function. Radioisotopes are also used as tracers in pharmaceutical research to study the behaviour of drugs in the body.
- Beams of nuclei, as well as emissions from radioisotopes, can be targeted so as to kill cancer cells that are otherwise inaccessible or difficult to destroy by other means.

Nuclear medical research is extremely interdisciplinary, and nuclear physicists have a lot of experience in working closely with other specialists in developing optimised instrumentation such as detectors, electronics and computer programs and in developing cost-effective treatment systems with commercial instrument companies.



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To emphasise the new developments on these issues the NuPECC report “Nuclear Physics for medicine” is organized in three chapters, one on hadron therapy, one on imaging and one on radioisotope production. In all chapters the contribution from basic research concerning accelerator, detector, and isotope production are emphasised.

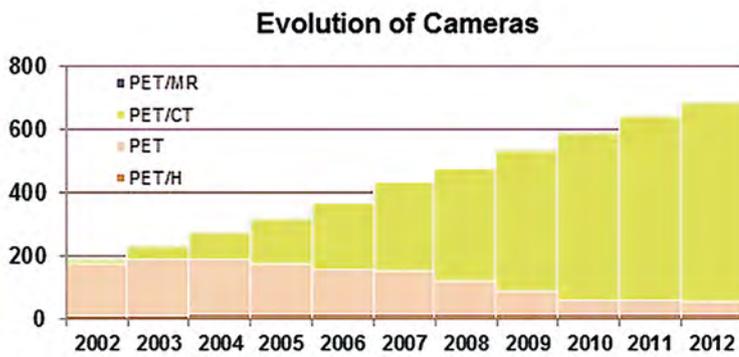
Hadron therapy

In 1946, accelerator pioneer Robert Wilson laid the foundation for hadron therapy with his article in *Radiology* about the therapeutic interest of protons for treating cancer.

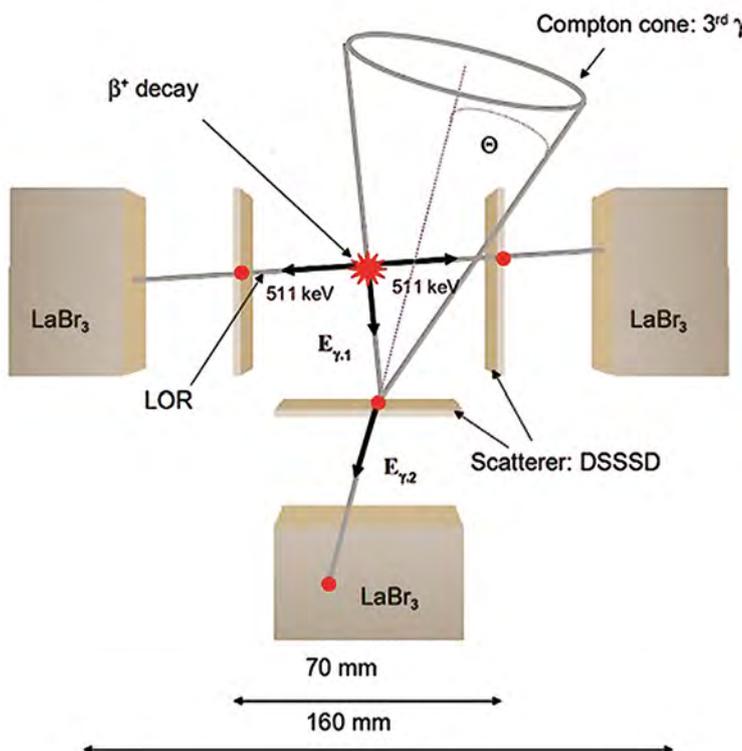
The rationale of using heavy charged particles in cancer is the exploitation of the high dose deposit (Bragg peak) at the end of the particle trajectory, and the absence of any dose beyond the particle range (see inset of Fig.1) thus sparing the surrounding healthy tissue. The physics behind this behaviour is that the ionisation probability (which determines the dose delivered) increases with decreasing velocity. This ability to discriminate between the volume to be treated and the surrounding healthy tissue, and the high dose uniformity in the volume treated are key characteristics of hadron therapy treatments.

According to statistics of the Proton Therapy Cooperative Group 39 proton and carbon ion therapy centres were operational at the end of 2012. In three centres only carbon ion treatment is applied (Lanzhou, Gunma, and Chiba), in another three centres both proton and carbon ion beams are used for treatment (Hyogo, Heidelberg and Pavia). Proton therapy is performed in 33 centres worldwide.

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Treatment verification

Nuclear reactions are used for treatment verification in hadron therapy. It is possible to exploit the production of unstable positron emitter nuclei, ^{10}C (with a half-life of 19.26 s); ^{11}C (20.39 min); ^{13}N (9.97 min); ^{14}O (1.18 min) and ^{15}O (2.04 min), in nuclear reactions induced by proton and carbon-ion beams, as schematically shown

◀ FIG. 2: Schematic of the nuclear reactions used for treatment verification in hadron therapy. A ^{12}C ion (projectile) colliding with an ^{16}O atom of the irradiated tissue may e.g. lose a neutron, resulting in the positron emitters ^{11}C and ^{15}O , respectively. They disintegrate under emission of a positron which annihilates with an electron in two photons with an energy of 511 keV. These two photons are used for imaging.

◀ FIG. 3: Evolution in the number of PET (Positron emission tomography) cameras. It can be seen how PET/CT (Computed Tomography) is now the preferred choice and that the number of PET scanners has sustained a constant growth over the last ten years.

◀ FIG. 4: Arrangement of three Compton camera modules to define the LOR (Line of Response) from β^+ annihilation in coincidence with the detection of the 3rd photon, a gamma-ray emitted by the daughter nucleus. Each module consists of a double-sided silicon strip detector (DSSSD), a scatterer and a LaBr_3 scintillator as absorber.

in Fig.2. Such nuclei emit low-energy positrons which travel a few millimetres in tissue before they annihilate with electrons.

The emission of characteristic pairs of annihilation photons can be detected with a PET (Positron Emission Tomography) scanner during the irradiation or 10–20 min afterwards. Since the momenta of photons from a single annihilation event are strongly correlated, a spatial distribution of positron-emitting nuclei can be reconstructed by tomographic methods and compared with calculations assuming specific distributions of the emitting nuclei in the body. Precise modelling (usually with the computer codes GEANT4 and FLUKA, developed for particle and nuclear physics) is thus one of the key issues of this method. The predictions from nuclear reaction models are key points and there is clear need to improve nuclear reaction models used in these codes, especially for a better description of (p,n) reactions on carbon and oxygen.



Radioisotopes are also used as tracers in pharmaceutical research to study the behaviour of drugs in the body

Imaging

Nuclear imaging techniques, SPECT (single photon emission Compton Tomography) and PET (Positron emission tomography), are invaluable tools both in the clinic and the pharmaceutical research laboratories. SPECT and PET are both capable of visualising the physical functioning of tissues and biomolecular changes by attaching the radioactive isotopes emitting gamma rays to a selected molecule.

Although SPECT is still better established than PET, interest in the latter is increasing because it offers twice as high a spatial resolution – at about 4 mm. Figure 3 shows the number of SPECT and PET used during the years and how the used PET method has increased in the last decade. It is well recognized that nuclear and particle-physics research is providing a range of developments that is benefiting medical imaging. Such developments in basic research include:

- New photodetectors based on miniaturised semiconductor chip designs enable compact, higher resolution instruments to be designed for small-animal PET (see e.g. J. Molnar *et al.*, *EPN* 46/2, p. 17 (2015)).
- Image quality can be improved by narrowing the location of the annihilation. This is achieved by measuring the time difference and this requires compact electronics and dedicated reconstruction algorithms, which are developed in nuclear physics laboratories.

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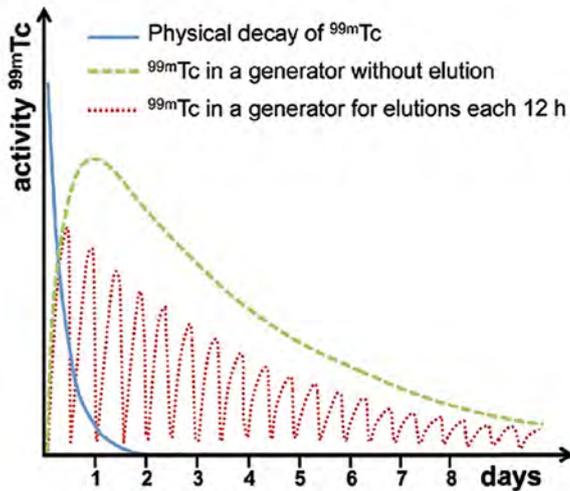


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► FIG. 5: ^{99m}Tc activity (blue) available from a ⁹⁹Mo/^{99m}Tc generator as function of time in comparison to the decay of ^{99m}Tc produced directly (green). The red curve gives the activity if one applies the elution process (namely the process of extracting one material from another) every 12 hours.



The latest development for imaging (still in R&D phase) is based on the simultaneous detection of three gamma-rays, as schematically illustrated in Fig. 4.

Radioisotopes

Identifying and producing new economically and medically useful radioisotopes is an important research area in nuclear physics. Radionuclides are the essential fuel that drives all nuclear medicine applications, and all radioisotopes have to be produced by the artificial transmutation of stable elements via nuclear reactions first investigated at nuclear physics facilities.

During recent decades, more than 3000 radioactive isotopes have been discovered in this way. These radioisotopes are the precursor of the stable isotopes on earth and are studied to understand the complex nuclear astrophysics problem of nucleosynthesis.

While many of these 3000 radioactive isotopes are very short-lived or extremely difficult to produce, several dozens have properties that make them potentially useful for medical applications. Therefore radioisotope production keeps profiting from tight synergies with other nuclear physics activities.

A medical isotope must:

- have a half-life long-enough to be delivered, but short enough not to cause unnecessary radiation exposure for the patient or present waste-disposal problems;

- have appropriate chemical properties so that it can be coupled to molecules that preferentially bind to specific tissues;
- for imaging purposes: emit long-range, medium-energy radiation so that it can be detected outside the patient's body;
- for therapy: emit short-range radiation that deposits the maximum amount of energy in a defined target tissue volume.

Concerning radioisotope production one relevant recent success from nuclear physics is the development of the “generator technique”. Thanks to this technique very short-lived isotopes are accessible in the clinic from the decay of longer-lived ‘generator’ isotopes (see Fig. 5).

For the production of radioisotopes the number of dedicated proton accelerators has increased during the years. The present situation is summarized in Fig. 6.

It is really very difficult to mention here all issues discussed in the NuPECC report. I hope, with these personally selected issues, to have made the point that this field is very broad in topics and very productive.

Before concluding it is important to underline two points. The first is that the new facilities for nuclear physics presently under construction have in their scientific programs, in addition to basic research, research for applications. In particular, applications in the field of medicine exploit well new technologies in nuclear physics. The second is that accelerator facilities used for nuclear medicine have evolved in recent decades, going from fundamental research laboratories, conceived and built mostly by academic research teams, to turn-key industrial ensembles. In Europe an example of spin-off company for accelerator from Nuclear physics laboratories is the IBA company.

As a final remark I like to thank the conveners and members of the working groups for their essential contribution, and in particular I convey my special thanks to Marco Durante, David Brasse and Ulli Köster who also have presented the report in Brussels.

I like to invite the reader to download the report from www.nupecc.org/pub/npmed2014. ■

About the Author



Angela Bracco is a full professor in experimental physics at the Università degli Studi di Milano. Her research interest is in nuclear structure as addressed via gamma spectroscopy and using nuclear reactions including those with radioactive beams. She is presently chair of the NuPECC expert board and member of the steering committee of the AGATA collaboration. AGATA is the last generation of detection systems for gamma-ray detection with position sensitivity and thus with useful applications in various fields.

► Fig. 6: Number of cyclotrons operational worldwide in 2013 against their maximum proton beam energy.

