PHOTONS AND HADRONS FOR HEALTH*

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Photons and hadrons are at the basis of one hundred years of research in fundamental particle physics and play nowadays a fundamental role in modern medicine. In diagnostics, computer tomography and positron emission tomography allow to explore the inner parts of the body and to determine with high precision the location of pathologies such as tumours. In the developed countries every 10 million inhabitants about 20000 oncological patients are irradiated every year with high-energy photons produced by electron linacs installed in hospital based radiotherapy centres. Hadrontherapy is a novel technique of radiotherapy which employs beams of charged hadrons, protons and carbon ions in particular. Due to their physical and radio-biological properties, they allow to obtain a more conformal treatment, sparing better the surrounding healthy tissues with a subsequent larger control rate and quality of life after treatment. By now about 40000 patients have been treated worldwide with protons and 15 hospital based centres are either running or under construction. Carbon ion beams are characterised by a larger biological effectiveness and are particularly indicated for the treatment of specific radio-resistant tumours. The fundamental role of photons and hadrons in modern medical applications is proof of the importance that fundamental research has for society.

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1. Photons and hadrons in medical diagnostics

Only one month after the discovery of X-rays in 1895, Wilhelm Conrad Roentgen used this new kind of penetrating radiation to explore the internal parts of human body, as shown Fig. 1(left). Since then X-ray imaging is one of the major tools in medical diagnostics that allowed to spare a large number of human lives, especially during wars. A modern evolution of this

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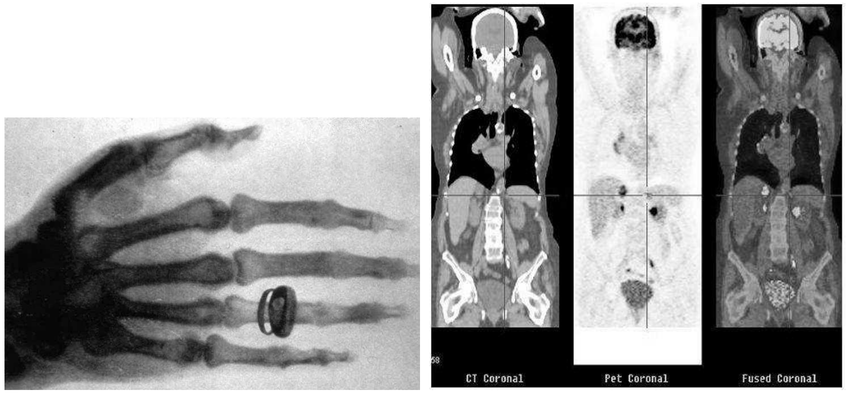

Fig. 1. One of the first radiographies by Roentgen (left) and a modern CT-PET image (right).

technique is the computer tomography (CT) which allows to obtain a three-dimensional representation of the body by measuring the electron density. To have information on the morphology of the body, another very important imaging technique is the Magnetic Resonance Imaging (MRI) which uses photons of much lower energies emitted by the transitions of protons in a magnetic field. In this way the density of protons in the body is measured allowing to obtain very precise images in which the different water content in tissues is mainly put in evidence. To have information about metabolism, nuclear medicine techniques are used by attaching a radionuclide to a specific molecule which is transported to the part of the body to be examined. At present about 85% of all examinations in nuclear medicine use $^{99\mathrm{m}}$Tc obtained through the decay of radioactive molybdenum produced by slow neutrons in nuclear reactors. This technique is called Single Photon Emission Tomography (SPET) and is based on the detection of the characteristic 140 keV photon emitted in the decay of $^{99\mathrm{m}}$Tc.

A more modern imaging technique is the Positron Emission Tomography (PET), based on the detection of the two back-to-back 511 keV electron–positron annihilation photons. The most common PET radioisotope is ^{18}F bound to a particular sugar — named FDG — that is rapidly metabolised by cancer and inflamed cells. ^{18}F is produced by bombarding ^{18}O targets with proton beams produced by small (about 15 MeV) cyclotrons. As shown in Fig. 1(right), the new frontier of medical imaging is the CT-PET, a device which is able to give precise information on morphology and metabolism combining CT and PET information into a single image. It is important to remark that in cancer radiation therapy no treatment plan would be possible without the precise information coming from the most modern imaging techniques.

2. Photons and hadrons in cancer radiation therapy

As sources of radiation radiotherapists use nowadays electron linacs and about 7500 of such accelerators are used to treat patients worldwide. They represent about 40% of all the accelerators running in the world and their number is continuously increasing [1]. The absorbed dose due to a beam of a few MeV photons (usually called X-rays by medical doctors) has a roughly exponential absorption in matter after an initial increase due to the build-up phenomenon, as shown in Fig. 2(left). For this reason the unavoidable dose given to the healthy tissues represents a serious limiting factor in conventional radiotherapy, especially if the tumour is located near organs at risk (OAR) the irradiation of which will results in unacceptable or even lethal secondary effects. To increase the dose to the tumour — and thus the tumour control rate — radiotherapists use multiple beams pointing to the geometrical centre of the target by means of a rotating mechanical structure on which the electron linac is mounted (isocentric gantry). The most recent development is the Intensity Modulated Radiation-Therapy (IMRT) in which the direction and the intensity of the photon beams are continuously varied by a computer controlled system.

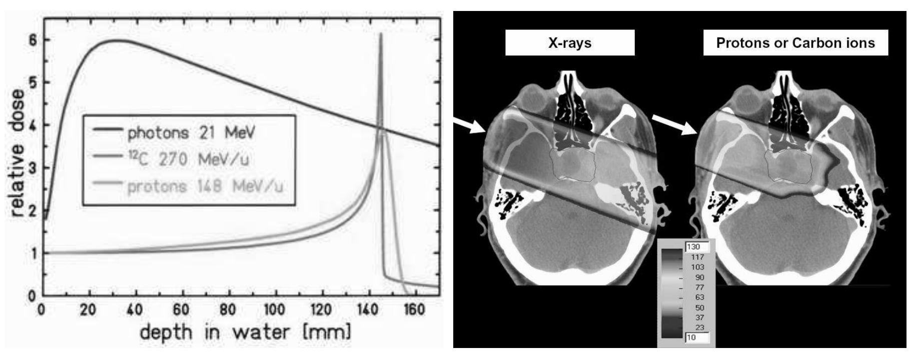

Fig. 2. Depth-dose distributions for a photon beam produced by 21 MeV electrons, by a 148 MeV proton and 270 MeV/u carbon ion beam (left). Representation of the dose distribution for a single beam of photons and a single beam of protons or carbon ions (right).

Hadrontherapy is a collective word and describes the many different techniques of oncological radiotherapy which make use of fast non-elementary particles made of quarks. Protons and carbon ions are at present the most used hadrons to locally control many types of tumours. Neutrons are also used, in particular in the Boron Neutron Capture Therapy (BNCT). Hadrontherapy with beams of π^- has also been performed in the past at PSI, TRIUMF and Los Alamos [2] while the first measurements of the biological effectiveness of antiprotons have been recently performed at CERN [3]. As presented in Fig. 2(left), the depth–dose curves of proton and light ion beams are completely different from those of photons. These charged particles have little scattering when penetrating the body and give the highest dose near the end of their range, in the so called 'Bragg peak', just before coming to rest. The proposal of using protons and ions in radiotherapy was advanced in 1946 by Wilson [4] but at that time neither precise imaging techniques nor enough powerful accelerators were available. It must be noted that to penetrate 25 cm deep in the body 200 MeV protons and 400 MeV/u carbon ion beams are needed. On the top of that, hadrontherapy is a multi-disciplinary field which requires competences from many different fields, often difficult to put together. For these reasons hadrontherapy is becoming a clinical reality only in the last decade.

Protons and light ions are not only advantageous because they deposit their maximum energy density in the Bragg peak at the end of their range, where they can produce severe damages to the cells while sparing both traversed and deeper located healthy tissues. They penetrate the patient practically without diffusion and, being charged, they can easily be formed as narrow focused pencil beams of variable penetration depth so that any part of a tumour can be accurately and rapidly irradiated. Moreover, carbon ions have the added advantage of a larger biological effectiveness, fundamental for the treatment of particular forms of solid tumours which are resistant both to photons and protons. The advantage of hadron therapy with respect to the most advanced IMRT is shown in Fig. 3 where the healthy tissues surrounding the tumour are definitely better spared when the irradiation is performed with protons. It is straightforward to remark that, sparing much better the surrounding healthy tissues, proton therapy is very important in the treatment of pediatric tumours. Due to the complexity and cost of the

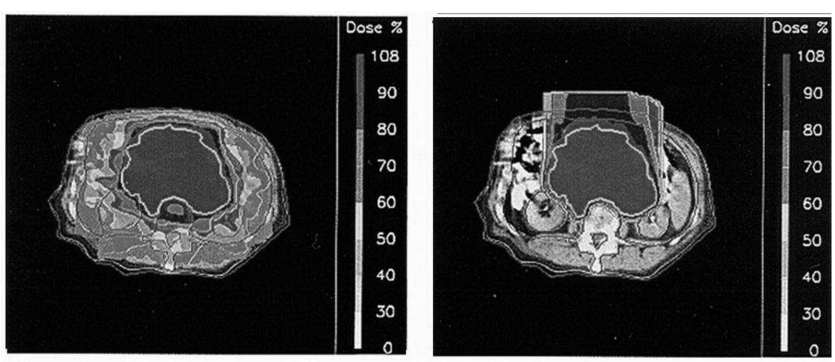

Fig. 3. Comparison between a treatment plan obtained with nine different X-ray beams (left) and a single proton beam (right) [5].

accelerator, beam transport lines and dose distribution systems, hadrontherapy has been mostly performed using accelerators dedicated to fundamental nuclear and particle physics and inside research laboratories. In 1993 the first hospital-based centre became operational at the Loma Linda University Medical Centre in California. This centre is shown in Fig. 4 and is nowadays able to treat about 1000 patients per year. Following the example of Loma Linda, in the year 2004 there are three dedicated hospital-based centres for deep proton-therapy in the United States and four in Japan. Many other are under construction or financed (in USA, Germany, Switzerland, Italy, Japan, Korea and China) and commercial companies offer turn-key centres for proton-therapy based on synchrotrons or cyclotrons and 2–4 gantries for a price of about 50–60 million Euros. This justifies the statement that since the beginning of the new century proton-therapy is booming [2]. Carbon ion

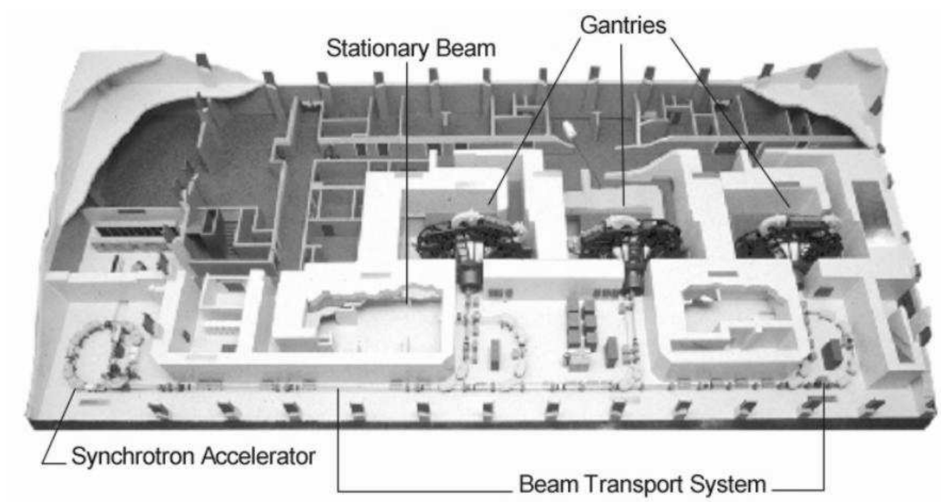

Fig. 4. The proton-therapy facility of the Loma Linda University Medical Centre based on a 7 m diameter synchrotron, three gantry rooms and one room with horizontal beams.

therapy is still at the frontier between research and clinical practice [6]. Up to present, the only two places where patients have been treated with beams of carbon ions are the GSI Laboratory at Darmstadt (250 patients) and the Heavy Ion Medical Accelerator Centre (HIMAC) in Japan (2000 patients). Together with HIMAC, a second hospital based carbon ion centre has been recently constructed in Hyogo (Japan). To accelerate carbon ions up to 400 MeV/u about 30 metre diameter synchrotrons are needed. The distribution of the dose is performed with fixed beam lines due to the difficulty and cost of rotating gantries equipped with very large magnets. The pilot project at GSI has been a great clinical success and the construction of the hospital based Heidelberg Ion Therapy (HIT) facility started in November 2003 and is scheduled to be completed in 2007. This is an ambitious project that features the first carbon ion gantry, which weights about 600 tons. Another European centre is being built in Pave, a University town located 30 km Southwest of Milan. CNAO (the Centro Nazionale di Adroterapia Oncologica) has been designed by TERA, a non-profit Foundation created in 1992 and recognised by the Italian Ministry of Health in 1994, in collaboration with CERN and INFN. Two more centres for proton and carbon ion therapy will be built in Europe in the near future one in Lyon (France) and one in Austria.

Hadrontherapy is nowadays in an evolutionary phase in which many proton and ion therapy centres will be put in operation in the next five years and the number of treated patients will largely increase [2]. This process will surely be pushed by the continuously increasing interest of industrial companies. According to a recent study of the Italian Association for Oncological Radiotherapy (AIRO) [7], one centre for carbon ion therapy and five centres for proton-therapy will be needed for a population of 50 million inhabitants. It has to be remarked that nowadays hadrotherapy centres have necessarily to be based on large and costly particle accelerators and dose distribution systems. The cost of these installations is of the order of 50 million Euros for proton-therapy centres and 100 million Euros for carbon ion facilities. The cost and the complexity of these installations are clearly the limiting factors for the diffusion of hadrontherapy. Some innovative solutions have appeared in the last years, still based on standard particle accelerators like proton and carbon ion dual super-conducting cyclotrons or combinations of cyclotrons and linear accelerators [8], allowing the construction of a multi-disciplinary centres for diagnostics and therapy. Anyway none of these technologies appear at long term to be revolutionary and capable to lead to a diffusion of hadrontherapy comparable to the one of X-ray therapy with electron linear accelerators. At a very long term, the acceleration of hadrons based on laser plasma techniques represents a very interesting and challenging possibility [9].

After one hundred years from the fundamental work by Einstein on the nature of the photon, the many applications of particle physics to medicine have lead to a remarkable progress capable to spare a large number of human lives and to increase the quality of life of many patients after medical treatment. This contributions proof the importance of fundamental research for society.

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