Technological (r)evolutions will boost proton therapy as a treatment of choice

There is no doubt about the clinical advantages of proton therapy when it comes to dosimetry and normal tissue sparing, but there are still some aspects preventing it from being at the top of the 'therapy of choice' list. IBA's Chief Research Officer and Managing Director Yves Jongen discusses how rapidly evolving technology will help proton therapy take the lead as a treatment option of cancer tumors.

Size and costs are related: the compact Proteus®ONE solution makes it possible to offer proton therapy at half the prize today.

SIZE MATTERS

Smaller generally equals cheaper. The invention and integration of superconducting magnets allowed for the production of a compact, affordable proton therapy solution.

Traditionally, proton therapy centers have been large facilities, featuring three to five treatment rooms in order to optimize the return on investment. However, with the benefits of proton therapy not yet profoundly anchored in general medical practice, patient recruitment proved to be challenging in some cases. Requiring a considerable structure and investment, these multi-room centers were also unattainable for smaller hospitals that wanted to include proton therapy in their cancer treatment options. Manufacturers therefore sought and found a more compact solution in one-room systems.

Magnetize

The major obstacle is the amount of energy needed to accelerate protons, which are about 2,000 times heavier than electrons used to make photons, resulting in a much higher magnetic rigidity. Typically 6 MeV electrons from a linear accelerator, or linac, suffice to make photons which can go through the body. Such a linac is a relatively cheap piece of equipment, whereas reaching a 32-centimeter depth in the body with protons requires 230 MeV.
To obtain this amount of energy you need much bigger magnets to bend the beam. An important characteristic of a beam of particles is the magnetic rigidity – the product of the field times the radius of curvature of the magnet – which is a constant for a given energy. For 230 MeV protons the magnetic rigidity is 2.3 tesla-meter, which means that if you use a field of 1T – an average industrial field – you get a radius of curvature of 2.3 meters. However, superconducting magnets can push the magnetic field up to 4.6T, bringing the radius of curvature down to 50 centimeters. Yet you need extreme cryogenics to achieve the necessary 4 K temperature to cool these magnets down, which in turn increases materials costs.

Scale down

"Even if proton therapy may not become available at the same price as photon therapy in the near future, superconducting magnets – together with smaller, less revolutionary adaptations – already allow us to offer proton therapy at half the price today, as size and costs are related," states Yves Jongen. "Our original Cyclone®230 delivered 2T at extraction, the radius at which the beam came out of the machine being 1.1 meters and the radius of the cyclotron itself a little over 2 meters. This made the machine a total of 200 tons and 4.3 meters in diameter. Today we were able to reduce these measurements to 45 tons and 2.5 meters. This in turn makes transport and assemblage much simpler."

REDUCE THE INVESTMENT GAP WITH PHOTON THERAPY

Today, proton therapy reaches only a fraction of the patients it could benefit. IBA continues its research and development to find new approaches and breakthroughs with the purpose of making proton therapy available at a lower cost and thus broaden its' scope.

Expand the market

According to a Dutch study, 16% of cancer patients would benefit from proton therapy, while the percentage of patients being treated with proton therapy today is less than 0.8%. This makes it a technology in its infancy for which it is difficult to make any predictions when it comes to timing or the potential to increase the number of installations and lower the price.

Reduce the price tag

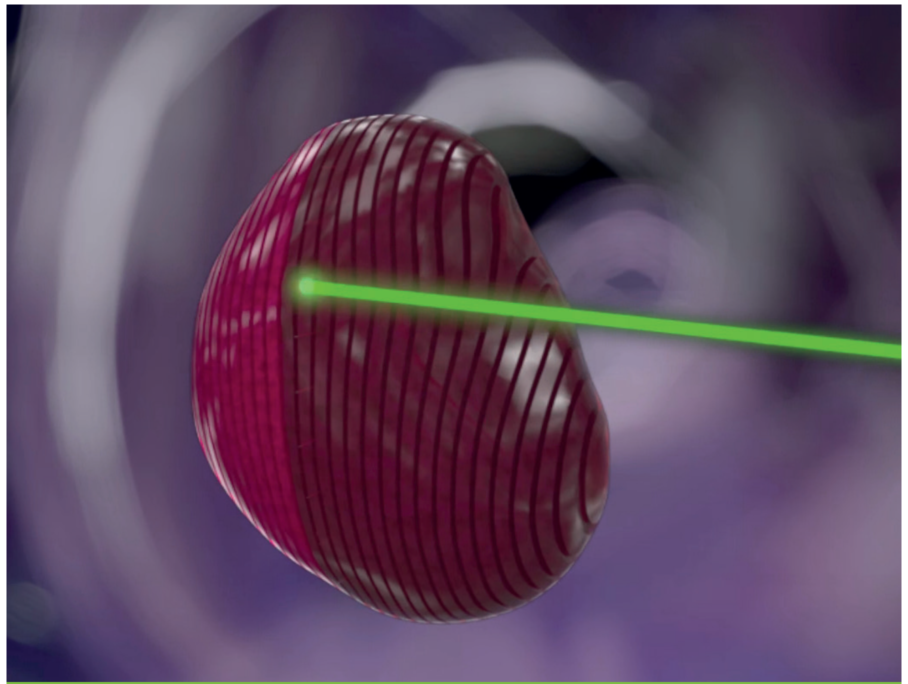
It's important to keep in mind that in conventional radiation therapy, the depreciation of the equipment represents only 5% of the total cost of treatment. In conventional radiation therapy, the largest part of the cost of the treatment is manpower: the large team of medical doctors, physicists, therapists and nurses needed to run a radiation therapy department.

This is why even if the cost of one proton therapy room is about ten times as expensive as a linac system, the total treatment cost is only twice as expensive. Even if there is no way found to offer proton therapy at the same price as photon therapy, the gap can be significantly reduced.

"I have good hopes we can eventually bring the cost per proton therapy room down to double the price of a photon linac installation based on our curve of experience and improved design, but it is as yet very difficult to put an exact timeframe on this. It will depend largely on the continuous support and rising demand we receive from the major players and pioneer institutions in the medical field," says Yves Jongen. "At

"In my opinion, everyone would be using proton therapy already if it were the same cost as conventional radiation therapy."

Yves Jongen, Chief Research Officer and Managing Director



The complex Pencil Beam Scanning (PBS) technology is more demanding for the equipment and the medical staff, yet nevertheless a cost-saving addition as it eliminates the need for patient-specific brass collimators.

"I have good hopes we can eventually bring the cost per proton therapy room down to double the price of a photon linac installation based on our curve of experience and improved design."

this point, not everyone fully realizes the potential of proton therapy, so any predictions regarding the market evolution are still very vague. Technological evolutions and clinical proof will bring more clarity."

THE ADVANTAGES OF PBS

Spot scanning or Pencil Beam Scanning (PBS) is one of the technological improvements that will alter the market. Although it requires dependable equipment, it eliminates the need for additional tools, increases the number of clinical indications for proton therapy and contributes to minimizing the overall radiation dose.

It is important to point out that 90 to 95% of the patients so far have not been treated with this feature but rather with passive scattering, which only allows for the irradiation of uniform fields. This means that all clinical data so far is mainly based on less optimal use of proton therapy.

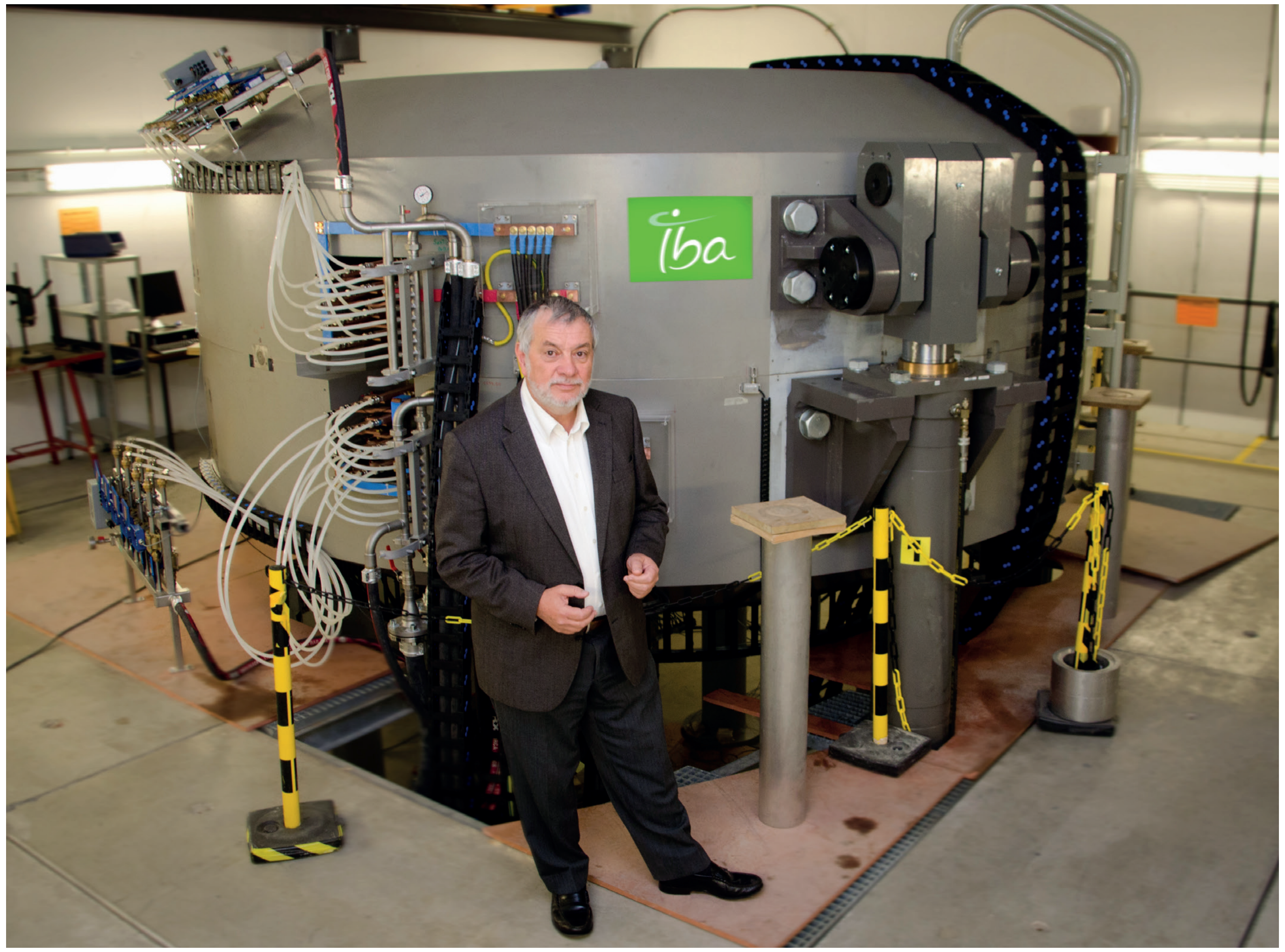
Increase number of clinical indications

PBS offers much more robust field characteristics, increasing the number of patients for whom proton therapy becomes the preferred treatment. Of course, this is an even more complex technology, making it more demanding for the equipment as well as the medical staff. Real-time human supervision becomes virtually impossible with PBS, because things move so fast during the treatment.

Passive scattering still makes it possible to oversee treatment prescription on a sheet of paper, allowing for verification on the spot. With PBS, up to ten thousand points are delivered to the tumor, each having its own specifications assembled in the treatment computer prescription file. There is no way to humanly verify if the system is doing as asked as these thousands of points are delivered at a tremendous speed for the purpose of limiting the time of treatment. The only way to do simultaneous verification is by having a second computer checking the computer that is feeding treatment specifications to the beaming equipment, so it requires very trustworthy equipment. As it nevertheless eliminates the need for patient-specific brass collimators to block the radiation shower from going beyond the treatment field, it saves on work hours to measure and produce these. This makes PBS a cost-saving addition to any proton therapy installation.

Restrict the dose

Minimizing the overall exposure and radiation to healthy tissue has always been an important aspect of radiation therapy. This is where proton therapy offers a real advantage and has a huge clinical potential. A nuclear reaction making neutrons disperse through the body when sending proton beams inside is unavoidable, but the method of deliverance can make a big difference in volume and radius. Although the amount of neutrons is near-negligible compared to the protons delivered to the tumor, growing evidence that unnecessary radiation induces secondary cancer requires improved methods to avoid irradiation outside the field. These secondary cancers develop with a delay of decades, making them inconsequential in treatment of elderly people, but a major issue when it comes to treatment of youngsters. These findings are relatively recent, but make it essential to continue research regarding delivery methods, PBS being the most appropriate at the moment.



"The accompanying treatment image manipulation software will play an important role, becoming increasingly powerful and indispensable."

True 3D imaging, like CBCT, is used for tumor localization and patient alignment, but might also be used for proton range accuracy and daily plan correction.

"PBS significantly increases the number of patients for whom PT becomes the preferred treatment."

DEFINING LIMITS

Our body is not perfectly stable and the same goes for tumors. Measurement tools contribute in large part to the efficiency of radiation therapy and refining these tools would significantly multiply the power and precision of proton therapy. Cone beam CT (CBCT) and CT-on-rails are candidate technologies to enable imaging directly in the treatment room whereas prompt gamma cameras should allow to verify the beam range.

Improve imagery

Rigorously and regularly measuring the size and shape of the tumor and correctly positioning the patient underneath the beam are paramount. True 3D imaging is used today for tumor localization and patient alignment as in conventional radiation therapy. In proton therapy, we anticipate that it might also be used for proton range accuracy and daily plan correction.

Cone beam CT (CBCT) and CT-on-rails are candidate technologies that have recently emerged in this field, to enable imaging directly in the treatment room. Both have merits and disadvantages. CT imaging gives a better contrast and high spatial resolution: it gives better soft tissue appearance with low imaging doses, in particular due to the option to limit the field of view. In addition, the quick collection of data reduces the possibility of motion artifact.

On the other hand, CBCT offers the possibility of imaging directly in the treatment position, but still faces some challenges arising from the X-ray diffusion, resulting in images with reduced quality and containing some artifacts. CT-on-rails can be seen as a compromise: CT imagery is located within the treatment room. The patient lies on a stationary patient couch that can be brought into the scanner. It provides excellent image quality, opening possibilities for managing changes in inter-fraction patient setup and organ motion, but it requires that the patient be moved from the treatment position to the imaging position. Experience will show the specific benefits of these two approaches when it comes to proton therapy. The accompanying treatment image manipulation software will play an equally important role, becoming increasingly powerful and indispensable.

Verify beam range

Measuring beam depth is another issue. Because 90% of the body is made up of water, water phantoms are usually used for testing. You can adjust up to one-quarter of a millimeter in water, allowing for an exquisitely accurate definition of the beam range. However, in an actual patient, there is always the remaining 10% to take into account.

Take for example a brain tumor, generally inoperable and irradiated through the nasal cavities. If these are healthy and clear on the day of treatment planning, but the patient develops a cold by the day the radiation is performed, density in the nasal cavities will have changed. Mucus having a density of 1 whereas air has a density of 10^{-3}, these changed conditions will change the range of the beam. Not reaching the distal part of the tumor will cause treatment failure.

The same goes for irradiation of the prostate or ovaries, going through the intestines, which are generally filled with water, but prone to containing bubbles or gases. As treating some unneeded healthy tissue is still better than potentially missing part of the tumor, clinicians today are still opting for a large safety margin, whereas using the sharpest gradient at the distal edge of the tumor, totally sparing e.g. an organ at risk right behind would therefore lead to superior treatment. A tool allowing us to precisely measure radiation depth would as a result multiply the power of proton therapy.

To this purpose, IBA came up with the idea to capture and measure prompt gamma rays emitted from proton-induced nuclear reactions. "We are confident that the prototypes of our prompt gamma cameras will be ready for testing in 2015, after which they can be fine-tuned based on test results. Implementing these will again represent a major asset to our proton therapy installations and cancer treatment in general," concludes Yves Jongen.

KEY REFERENCES

- Compact system: J. Hérault, Head Medical Physicist - Centre Antoine Lacassagne, Nice, France
- PBS: J. Metz, Radiation Oncologist – U. Pennsylvania, Philadelphia, PA
- Imaging (CBCT) : L. Rosen, Radiation Oncologist – Willis Knighton Hospital, Shreveport, LA

BIOGRAPHY
YVES JONGEN

Chief Research Officer and Managing Director, based in Louvain-la-Neuve, Belgium

Yves Jongen is Chief Research Officer for Ion Beam Applications. After founding IBA in 1986, he served as general manager and co-general manager of the company until March 2000, when he assumed his current role. Founded in Louvain-la-Neuve, Belgium, IBA has become a world leader in particle accelerator technology and its applications, particularly in medical imaging, cancer therapy and sterilization. Prior to founding IBA, Mr. Jongen served for 16 years as manager of the UCL Cyclotron Research Center, a multidisciplinary organization established by the Catholic University of Louvain-la-Neuve (UCL), with several cyclotrons for fundamental and applied research. He holds a dozen patents and is the author of approximately 200 publications in the particle accelerator field and their applications. Mr. Jongen graduated cum laude from UCL in 1970 as a civil engineer in electronics and earned an additional certificate in nuclear sciences. He has received the Georges Vanderlinden prize for science, awarded by the Belgium Royal Academy, for his work in physics and electricity, and shared the magazine Trends-Tendances "1997 Entrepreneur of the Year" honors for the French-speaking part of Belgium with the former CEO of IBA, Pierre Mottet. In 2013, Yves Jongen was also nominated to the European Inventor Awards by the European Patent Office for making Proton Therapy more accessible to patients worldwide.

IBA, THE HIGH WAY TO PROTON THERAPY

In proton therapy, the development of practical and patient-centered solutions is only possible through constant collaboration, open engagement and shared research objectives. With more than 25 years of experience designing and developing proton therapy systems across the globe, IBA has grown a strong and vital community of proton therapy professionals. Together, this unprecedented community – of clinical leaders and distinguished technological experts – is advancing proton beam technology and clinical innovations. By entering the IBA Proteus community:

- *Your clinicians and researchers will leverage the latest outcome-driven practices being advanced by a clinical proton beam users using a common technological platform and the capacity of your team to be trained with the utmost care and the highest standards of quality.*

- *Your project management team will be able to collaborate with the world's most experienced team of proton therapy experts (600+), cutting-edge technology and robust processes in system installation and operation.*

- *Your executive team will leverage the know-how and clinical understanding built on 25+ projects and 25,000+ patients treated to secure the institutions' investment.*

Together with our people, by sharing our passion for innovation and patient care, you can take comfortably the highway to the future of cancer care. The IBA Proteus Community includes among others Massachusetts General Hospital Burr Proton Therapy Center, ProCure Proton Therapy Centers, University of Florida Proton Therapy Institute, University of Pennsylvania Health System Roberts Proton Therapy Center… in North America; or Centre de Protonthérapie Orsay de l'Institut Curie, Universitätsklinikum Carl Gustav Carus …in Europe; and Korean National Cancer Center, Appolo Health Group… in Asia.

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