Recent and future developments in proton therapy

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Historical introduction
Proton therapy offers a dosimetric advantage over photon radiotherapy, potentially delivering higher conformity of radiation doses to the tumour while sparing surrounding healthy tissue much better than even the most advanced photon techniques such as IMRT or tomotherapy. These advantages make proton therapy especially attractive for the treatment of children (see, for example, “Proton therapy for children” by Dr N Thorp, RAD Magazine 2010;36(418):17-18), as well as lesions in the brain and other critical areas of the body. However, mostly because of cost, the wide introduction of proton therapy has taken a long time.

The idea of using the peculiar depth dose characteristics of a proton beam (the deep Bragg peak) to treat tumours arose almost as soon as the particles were successfully accelerated. Robert R Wilson, Fermilab’s founding director, first proposed using protons for cancer therapy in a 1946 paper, “Radiological Use of Fast Protons” (Radiology 1946;47:487-491).

The first adaptation of a particle physics accelerator to use protons and other charged ions for medical purposes occurred in 1954 at the Lawrence Berkeley National Laboratory in California. Its example was followed in the 1960s, 1970s and 1980s by laboratories in Russia, Sweden, Japan, Canada and Switzerland, as well as more in the USA. Most of these earlier facilities were located in physics laboratories rather than medical institutions and have now mostly ceased operations or moved within hospital campuses.

The currently active proton facility with the longest track record is the MGH/Harvard Cyclotron Department in Boston, USA, which started in 1961 and has been in a new hospital-based facility since 2001. It has treated over 10,000 patients to date.

A proton beam of 62 MeV has been in operation at the Clatterbridge Centre for Oncology, in the Wirral, since 1989. Over 1,900 eye patients have been irradiated to date in its single treatment room.

The Loma Linda University Proton Treatment Centre in California, opened in 1990, was the first hospital-based high-energy proton treatment facility in the world. It can deliver beams of up to 250 MeV through three gantries and one fixed-beam room. It has treated well over 10,000 patients to date.

Current and upcoming facilities
There are 31 charged particle treatment facilities operating throughout the world as of June 2010. Of these, seven have energies around 60-72 MeV, only good for ocular tumours; the others have a minimum of 200 MeV up to 270 MeV. The USA leads with eight centres, followed by Japan with seven centres (of which two are C-12 heavy ions facilities).

Many more charged particle facilities are in the construction or design phase. Figure 1 shows the global distribution of proton therapy centres, excluding ocular-only beams and heavy ions facilities. Most remarkable is the expansion in Germany, where in a couple of years the current three facilities will expand to six centres, three of which will also be able to use C-12 beams.

Current status and future developments in equipment
The most common architecture for delivering charged particle therapy beams consists of a particle accelerator (cyclotron or synchrotron) linked to multiple treatment rooms by an evacuated beam line and guiding magnets. The rooms share the radiation beam (first come, first served); given that the majority of the time spent in the room for each patient consists of localisation and verification, this sharing can feed four or five rooms. Once the beam is diverted into one specific treatment room, it is directed and customised for the individual patient and field by means of a “nozzle” either at a fixed position or attached to a rotating gantry.

Of the currently operating facilities, 15 have at least one gantry, a fixed horizontal beam being still the most common installation. Most of the centres coming on line now, however, will have several gantries, tilting the balance. Figure 2 shows a typical beam line layout with gantries and fixed beams. As can be seen, the gantry structures are massive and, therefore, expensive.

For more information on current and proposed proton treatment centres, go to the PTCOG website: http://ptcog.web.psi.ch/index.html
Many of the proton therapy equipment manufacturers are introducing more compact gantry models, either by clever new design of the beam path or by turning to superconducting technologies. At least one manufacturer is already offering a radically different solution, a self-contained system consisting of a superconducting Synchrocyclotron mounted on a gantry that rotates around the patient.

Further in the future, exciting new technologies are being developed to find alternative ways of producing high energy particles. These include the use of high intensity lasers (see, for example, http://www.llnl.gov/str/MPerry.html, http://www.sciencemag.org/cgi/content/abstract/300/5622/1107 and http://www2.cnrs.fr/en/410.htm?&debut=16 ) and, more recently, dielectric wall accelerator technology (see http://www.llnl.gov/pao/news/sciencefeatures/2006/SF-06-04-02.html ). TomoTherapy Incorporated has proposed a bold design combining the DWA compact accelerator with its helical scanning delivery system (figure 3). If these developments succeed in producing compact accelerating systems that can fit in an existing treatment room and be serviced in a hospital setting, the prospects for widely available proton therapy will be greatly enhanced.

Current status in delivery techniques
The vast majority of the currently active proton therapy centres produce clinical beams by means of passive spreading techniques. Only two of the existing centres utilise a dynamic spot scanning delivery on a routine basis.

In passive spreading techniques, the proton beam is spread by placing scattering material into the path of the protons. A single scatterer broadens the beam sufficiently for treatments requiring small fields.

For larger fields, a second scatterer is needed to ensure a uniform dose profile. A combination of custom-made collimators and compensators conform the dose to the target volume. The spread out Bragg peak used for treatment is obtained via a set of range modulator wheels or ridge filters inside the nozzle of the delivery system (figure 4).

Future developments in delivery techniques
While the pursuit of pencil beam scanning is amply justified by the advantages outlined above, there is an added incentive, the possibility of combining the properties of proton beams with the sophistication of inverse planning and intensity modulation. Several theoretical studies have indicated that intensity-modulated proton therapy (IMPT) results in lower integral dose than intensity-modulated x-ray therapy (IMRT) for the same tumour coverage and conformity. Scanning can be used to deliver true IMPT, as dose distributions can be varied on a point-by-point basis. By varying the proton beam intensity and/or the speed of the scan, dose can be painted non-uniformly on a field-by-field basis to yield an overall uniform target dose.

IGRT
Accurate pre-treatment alignment of the patient is just as imperative for proton therapy as for high-precision photon treatments such as IMRT, a task that is generally achieved by patient imaging. Although there are many image-guidance techniques available in the photon world, the technology is lagging somewhat behind in proton therapy facilities.

While on-board kilovoltage imaging is now common on conventional linacs, allowing the acquisition of cone beam CT (CBCT), the massive size and slow speed of proton gantries (when present) are impediments to easily reproducing such an arrangement for proton centres. A more promising solution could be an in-room robotic CBCT coupled with robotic patient positioning. Such a set-up should ideally offer fast 3D/4D imaging and easy integration with alignment capabilities, as well as the ability to image patients in various positions, with the same position used for pre-treatment imaging and treatment delivery. Challenges in establishing such systems include registration of the CBCT origin with beam position, ensuring accurate correlation of the in-room CBCT with the planning CT, and accurately converting Hounsfield numbers to proton stopping power for CBCT to facilitate adaptive therapy. The set-up must also offer reproducibility and speed, and the positioning device must not interfere with the proton beam.

Proton radiotherapy
One exciting possible avenue for improving the mapping of proton stopping power within the patient is to acquire...
images using the proton themselves. A low intensity/low dose proton beam, with a range larger than the patient separation, could be imaged at the exit side. The residual range as a function of position will accurately indicate the sum of stopping power values for all voxels along a ray line. Multiple projections could be acquired by rotating the beam around the patient and a CBCT-like reconstruction of the stopping power values for each voxel could be obtained. This imaging technique will eventually reduce the current uncertainty in proton treatment planning calculations and lead to more accurate treatments.

Motion management
Proton therapy poses at least the same requirements for accurate, repeatable patient positioning and set-up as does IMRT. In addition, low- and high-density structures moving in and out of the beam – due to patient motion or tumour shrinkage, for example – will alter the range of the Bragg peaks. Therefore, it is essential that both the target volume and surrounding structures are in their planned positions.

While this requirement holds for all proton therapy techniques, scattering techniques are more forgiving of tumour and organ motion because of the smearing effect of the broadened beam. The enhanced ability of proton scanning to paint dose conformally, on the other hand, increases the risk of target misses due to organ motion. This risk can be mitigated by image-guidance techniques such as gating or by using fast multiple re-paintings that compensate for organ motion by effectively smearing out the dose deposition over time.

PET treatment verification
Tissues that are irradiated with protons will become slightly radioactive and produce various isotopes, including some positron emitters with short half-lives. If the distribution of these isotopes can be imaged with a PET camera or 3D PETCT soon after the end of a treatment fraction, the activation map relative to the patient anatomy could confirm the accuracy of the proton treatment planning calculations and highlight any deviations from the expected dose distribution. Repeated PET imaging over the length of treatment could give valuable information on organ motion and changes in patient anatomy over time, facilitating the introduction of adaptive therapy. The availability of on-board PET imaging (already offered by at least one manufacturer) offers the prospect of real-time monitoring of the dose deposition during the delivery of a treatment fraction, allowing in-vivo verification of the progress of scanning beam delivery.