NCRI Clinical and Translational Radiotherapy Research Working Group (CTRad)
Proton Beam Therapy - information for a lay audience

Advances in radiotherapy

Radiotherapy is a key aspect of cancer care. It is delivered to around half of cancer patients and is a vital part of curative treatment in 40% of patients. Conventional radiotherapy uses high energy X-rays (photons) to destroy cancer cells by damaging their DNA. Radiotherapy seeks to put the maximum dose into the tumour (to kill it) while minimising the dose to the surrounding healthy tissue.

X-rays were discovered in 1895, and the first treatment of cancer with X-rays was performed in 1896. Since then the technology has changed considerably. Advances in radiotherapy technology now allow the high dose treatment to 'conform' closely to the shape of the tumour target. The most modern approach, known as intensity modulated radiotherapy (IMRT), can even achieve highly conformal treatment of tumour targets which have a complicated shape. IMRT works best when it is combined with image guidance to achieve the highest precision in the delivery of the radiotherapy. These developments have led to a reduction in side effects from radiotherapy, the possibility to give higher doses than before, and the treatment of some patients who would not have been treatable before.

However, some of the X-rays in any X-ray beam pass right through the patient. When taking an X-ray or CT scan for diagnosis, it is the X-rays that come through the patient which make the picture. For a treatment with X-rays we would prefer not to have any of the beam passing right through the patient - but that is impossible. Sometimes though it is particularly important not to have any of the beam passing through the patient towards critical areas like the spinal cord or sensitive parts of the brain. In these cases there is a way to avoid this 'exit dose', and that is to use charged particles, especially protons, to deliver the radiotherapy.

Proton Beam Therapy

The use of a proton beam to treat cancer is known as Proton Beam Therapy (PBT). Instead of using X-rays (photons), PBT uses charged particles called protons which are found in the centre (nucleus) of every atom.

The main advantage of using protons is that they deposit only a small dose of radiation during their journey to the target and then come to a halt, releasing a final sudden burst of energy. This is known as the Bragg peak. After the Bragg peak, the beam stops completely, so there is no exit dose.

In PBT, beams can be combined to produce the best plan for an individual patient. This allows higher doses to be given to tumours close to normal structures, such as the spinal cord or the eye, than can usually be achieved with X-rays.

Protons are accelerated by a special machine, either a cyclotron or a synchrotron, to produce a high energy beam. The amount of acceleration can be controlled, which means that the speed of the protons can be altered. The speed determines the range of the beam (that is, how far through the patient the beam passes before stopping), and the location of the Bragg peak. The accelerated beam is carried to the treatment room in a special beam line. There it passes through a treatment nozzle which enables precise delivery to the patient. For the best results, it is important to be able to point the PBT beams in any direction, so the treatment nozzle is mounted on a gantry which can move around the patient.

Patients who may benefit from Proton Beam Therapy

PBT is of particular relevance for highly selected groups of patients. Certain cancers of the spine (chondrosarcomas or chordomas) and childhood cancers have the strongest indication for PBT. Currently, the UK has one low energy Proton Beam facility at the Clatterbridge Cancer Centre in Liverpool that has treated rare eye cancers (mainly ocular melanoma) since 1989 with excellent outcomes (over 90% of patients have permanent disease control and preservation of eye sight).

However, patients with cancers that are deeper in the body require a high energy PBT clinical service. In 2008 the Department of Health started the Proton Overseas Programme, to allow patients (both adults and children) from England and the devolved nations to benefit from PBT, by funding treatment at proton centres abroad. This overseas programme has been successful and has paved the way for PBT centres to be established in this country.

Developing a national PBT programme

Recognising the need to improve patient access to advanced radiotherapy such as PBT, in 2013 the UK government pledged £250 million to build two NHS high energy proton beam centres located in major hubs of cancer research – one PBT centre at UCL Hospital in London and the other at The Christie in Manchester. These centres will have a capacity to treat up to 1500 patients annually with the service anticipated to open in 2018. This substantial investment from the Department of Health was required to support the building of the highly sophisticated facilities, the procurement of the complex equipment and to train the specialist workforce in time to treat the first patients in 2018. This programme is regarded as the most sustainable option for providing high quality integrated radiotherapy for the NHS and for future patients.

Since the Department of Health's announcement, the University of Oxford has announced the development of a new Precision Cancer Medicine Institute which will include proton beam research facilities. Three private healthcare companies have also stated plans to build their own proton therapy centres in the UK.

Clinical and ethical considerations

The introduction of a PBT service poses important research questions relating to the development and availability of this new technology. When evaluating new cancer treatments, it is important that decision making is based on high quality evidence. The collection of clinical evidence to support the use of PBT, and to refine its indications, is one of the cornerstones of the PBT programme in this country.

One of the most pressing issues about PBT is whether randomised controlled trials should be undertaken before this treatment is made widely available. Due to the small number of patients treated to date, evaluation of PBT is problematic and currently lacks robust data from clinical trials. There are still uncertainties about the safety and relative effectiveness of PBT, and clinical trials will provide powerful evidence to support its use; however, there are concerns that it might not be feasible to undertake randomised controlled trials, and collaborative working with other PBT centres has been suggested as a way to address some of the issues. Recent evaluation of PBT data from patients with chordoma indicates that PBT cannot be reviewed in isolation and should be evaluated alongside high quality partnering treatments like surgery. A recent position paper from the Chordoma Global Consensus Group on the integrated treatment approach to chordoma highlights this.

Developing strategies for selecting which patients should receive PBT is also of great importance. A model-based approach developed by the Dutch government proposes that patients should be offered PBT if their personal radiotherapy plans show that their side effects would be significantly reduced if PBT was used instead of conventional radiotherapy. However, challenges remain in using such methodologies to select patients, so prioritising indications and obtaining robust data will be the priority over the next few years.

The NHS is well placed to evaluate and improve PBT and to help establish its most appropriate application in the clinic. Considering the current phase of the service development, there is great motivation in the radiotherapy research community to progress the research agenda and provide an evidence base of the best possible treatment approaches.

Useful resources

Reference about advances in radiotherapy

Ahmad SS, Duke S, Jena R, Williams MV, Burnet NG. Advances in radiotherapy. *BMJ*. 2012;345:e7765.
http://www.bmj.com/content/345/bmj.e7765.long
This article explains the role of newer radiotherapy techniques and the future of radiotherapy treatment.

UK references about PBT

NHS choices: Proton Beam Therapy – "What is proton beam therapy?"
http://www.nhs.uk/news/2014/09september/Pages/what-is-proton-beam-therapy.aspx
This article provides a good starting point describing what PBT is and how it works.

Health Education England: National Proton Beam Therapy Programme
https://www.youtube.com/watch?v=2MadsdvYOis
This short film developed by Health Education England sets out how PBT can benefit patients and includes footage of what the new sites may look like.

Cancer Research UK: PBT science blog July 2015 – "Proton beam therapy: where are we now?"
http://scienceblog.cancerresearchuk.org/2015/07/16/proton-beam-therapy-where-are-we-now/
This article provides an excellent overview of the current situation of the development of the national PBT programme.

Reviews on PBT

Crellin AM and Burnet NG. Proton Beam Therapy: The Context, Future Direction and Challenges Become Clearer. Editorial. *Clin Oncol (R Coll Radiol)*. 2014; 26: 736-738.
http://www.sciencedirect.com/science/article/pii/S0936655514003835
This review highlights the challenges of developing a national PBT facility and strategies to help the UK to contribute to PBT research.

Jones B and Burnet N. Radiotherapy for the future. Protons and ions hold much promise. *BMJ* 2005; 330(7498): 979-80. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC557134/
This editorial highlights the potential impact of a proton service to patients with hard to treat tumours.

De Ruysscher D, Mark Lodge M, Jones B, Brada M, Munro A, Jefferson T, Pijls-Johannesma M. Charged particles in radiotherapy: a 5-year update of a systematic review. *Radiother Oncol*. 2012 Apr; 103(1): 5-7. http://www.sciencedirect.com/science/article/pii/S0167814012000060
This review highlights the importance of a coordinated research effort through clinical trials to investigate the role of protons and to provide robust clinical data.

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