PREFACE

Particle therapy

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Particle therapy is one of the cutting-edge areas of external beam radiotherapy worldwide, and was therefore chosen as the topic for my 2009 British Institute of Radiology President's conference. Since this meeting, the field has moved on and I am very pleased to now be able to introduce this special issue of the *British Journal of Radiology (BJR)* on the same subject. Some of the papers in this special issue grew from presentations at the 2009 meeting and others introduce new thoughts, theories and analysis on the subject.

Particle therapy represents a coming together of physics research applied to oncology. In some cases it offers the potential for a cure with reduced short- and long-term complications, and in others it offers the possibility for a very substantial dose escalation. Radiotherapy as practised in the UK has improved greatly over the last 8–10 years with the government-led investment programme and massive efforts from all quarters of the community. Although there is more to do, the foundations of high-quality imaging for diagnosis and treatment planning are well-established, making this the right time to make the step to particle therapy. The National Health Service's (NHS's) move to proton therapy, through organised patient referral abroad and planning for UK centres, is a welcome start.

At the time of writing the NHS continues to deliberate on the number and location of proton therapy facilities, while it is appropriate for a research journal to also focus on the future, especially the contribution that advanced imaging and carbon ions can play in future cancer treatments. There is a strong UK contribution to this special issue in terms of mathematical modelling both retrospectively, to gain maximum benefit from historical experience, and prospectively, to ensure that we embark on particle therapy with the tools at our disposal to predict all important aspects of the delivered dose distributions. Owing to my background, I am particularly pleased to be able to introduce the article from the

team at Tsukuba, which includes a discussion of boron neutron capture therapy (BNCT) in the context of dose escalation for invasive brain tumours.

This special issue begins with a review of the technology of the field from the Oxford team, Peach et al [1]. This is a rare article in that it is suitable for the non-specialist reader but includes all the important aspects of the current technology (cyclotrons and synchrotrons) and compares their capabilities with clinical needs. Potential future acceleration technologies are also introduced.

As the world embarks on clinical research with protons and carbon ions, it is important that we learn as much as possible for the existing clinical data with high linear energy transfer (LET) particles. The article from Jones et al [2] is an excellent example of the role of mathematical modelling in fully understanding previous experimental data sets, working through in detail some of the observations made during the Hammersmith and Clatterbridge neutron therapy programmes. The relative biological effectiveness (RBE) values of neutron therapy beams are similar to those of carbon ion beams, and all the issues of variability in response associated with tissue type and fraction size are common, so much can be learned from this kind of analysis.

This is followed by a wide-ranging and highly detailed review of the role of positron emission tomography (PET) imaging in radiotherapy (Price and Green [3]), with special emphasis on issues associated with high precision radiotherapy delivered by any technology. The role of PET for target volume definition is explored by tumour site in a readable and useful way.

The main clinical papers in this special issue concern therapies involving particles with high-LET, carbon ions and BNCT. Jensen et al [4] provide an authoritative review of the current clinical experience with proton and ion beam therapy by focusing on the developments in Heidelberg. The vision of the Heidelberg ion therapy centre is to place the very best radiotherapy within the context of a national specialist centre for cancer research (DKFZ) and this has much to be admired. The article itself reviews different cancer types and outlines the current world experience with X-rays, protons and ions, as appropriate. For each site considered, a summary

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table of published clinical results is provided, which makes this an extremely valuable article for the scientific community.

This is followed by an excellent article by Imai et al [5] reviewing the use of carbon ions for treatment of inoperable sacral chordoma at the National Institute of Radiological Sciences, Chiba, Japan. The results reported here are for a group of 95 patients between 1996 and 2007 and are extremely promising. The local control rates at 5 years are 88% and there is a low morbidity according to internationally recommended criteria. As well as the application of carbon ions, the treatment approach adopted also takes a fully detailed account of respiratory motion to enable the best application of the therapy beam.

The article from Matsuda et al [6] examines the importance of prognostic indicators in 67 patients with glioblastoma multiforme treated with conventional radiotherapy or high-dose particle therapy. The need for dose escalation to improve outcomes for glioblastoma patients is well-established, but this paper is unique in bringing together treatments delivered with two forms of particle therapy as mechanisms for dose escalation in these patients, protons and BNCT. It is a common criticism of institutional series that patient selection has influenced the findings. The careful analysis of prognostic factors performed by these authors indicates that their findings are robust, and dose escalation with particle therapy is showing a benefit for these patients.

The special issue concludes with two further papers from the UK that involve mathematical modelling. While large numbers of patients have already been treated with proton therapy, uncertainties remain in the RBE values used for both protons and carbon ion radiotherapy. The impact of these uncertainties are considered in detail by Jones et al [7]. The discussion is facilitated by the introduction of a new factor that combines physical dose sparing and RBE. This is used with uncertainties in RBE applied to investigate the overall clinical impact and the effect on imposition of normal tissue dose constraints and a better understanding of the interplay between these uncertainties and changes in fractionation—a topic of very great importance in particle therapy.

We conclude with an article that points the way to a future for all radiotherapy modalities. It discusses the models and mechanisms by which we understand the long-term consequences of treatments for patients. Induction of further cancers through treatment is an issue of great concern to patients, and is one that applies to cytotoxic chemotherapy and radiotherapy alike. If the radiotherapy community is to play a full part in delivering the best quality of life for patients post-treatment, better prediction of the likely incidence of second cancers together with rational field placement might influence treatment strategies. Timlin et al [8] describe a possible methodology, and perform example comparison of simple X-ray and proton treatments for either superficial or deep-seated target volumes. It is clear from these indicative examples that proton therapy does not always necessarily result in a reduced long-term risk of second malignancy compared with X-ray treatment. Careful consideration of the number of fields and the total normal tissue volume traversed is essential. This again points to the need for

advanced delivery technologies using scanned beams and fully rotating gantries to reduce the number of fields necessary to achieve the required treatment dose distribution.

The discerning reader will notice that this issue does not focus mainly on proton therapy and efficacy comparisons with X-ray radiotherapy. The evolution of proton therapy facilities from passively scattered to actively scanned beam approaches, and the consequent improvement in dose distributions and reduced numbers of applied fields, is comparatively new in proton therapy. Very few publications on the clinical efficacy of scanned beam technologies are available, but this is the area which will produce the required clinical evidence (in one way or another) over the next 10 years or so. Comparisons of the best available X-ray radiotherapy with passively scattered proton therapy approaches are unlikely to produce dramatic across the board clinical differences as the achievable dose distributions are quite similar. It is therefore essential that new delivery technologies are available to countries with health systems that lend themselves to the performance of good quality clinical trials. The UK health system provides such an environment. Our development of facilities to treat large populations with actively scanned beam technology in the next 5 years could mark the start of a very significant contribution to the evidence-base for proton therapy.

Taking a global perspective, the UK does need to develop a position on research into carbon and other heavier ions for therapy. As an interim measure, the current assessment and referral system for patients to go abroad for proton therapy could be used as a model through which the UK could refer willing patients for inclusion in clinical trials of carbon ion therapy at the growing number of European centres (Heidelberg and soon Pavia and Caen). However, as is the case for protons now, this could be only a temporary measure to pave the way for a UK research facility exploring the use of heavy ions. This issue's number and strength of submissions from the team at the Gray Institute shows that the UK research community is ready to support such a development.

The *BJR* serves the international research community by publishing up-to-date developments in this and other fields by acting as a forum for discussion and a stimulus for further work. Scientists everywhere will want their research output to be at the leading edge of worldwide activity and therefore engagement and involvement in particle therapy is essential. I very much hope that this *BJR* special issue will play a valuable role in this exciting and important field.

References

1. Peach K, Wilson P, Jones B. Accelerator science in medical physics. *Br J Radiol* 2011;84(Spec No 1):S4–10.
2. Jones B, Underwood TSA, Carabe-Fernandez A, Timlin C, Dale RG. Fast neutron relative biological effects and implications for charged particle therapy. *Br J Radiol* 2011; 84(Spec No 1):S11–18.
3. Price PM and Green MM. Positron emission tomography imaging approaches for external beam radiation therapies:

- current status and future developments. *Br J Radiol* 2011;84(Spec No 1):S19–34.
4. Jensen AD, Mütter MW, Debus J. Review of clinical experience with ion beam radiotherapy. *Br J Radiol* 2011;84(Spec No 1):S35–47.
 5. Imai R, Kamada T, Sugahara S, Tsuji H, Tsujii H. Carbon ion radiotherapy for sacral chordoma. *Br J Radiol* 2011;84(Spec No 1):S48–54.
 6. Matsuda M, Yamamoto T, Ishikawa E, Nakai K, Zaboronok A, Takano S, et al. Prognostic factors in glioblastoma multiforme patients receiving high-dose particle radiotherapy or conventional radiotherapy. *Br J Radiol* 2011;84(Spec No 1):S55–60.
 7. Jones B, Underwood TSA, Dale RG. The potential impact of relative biological effectiveness uncertainty on charged particle treatment prescriptions. *Br J Radiol* 2011;84(Spec No 1):S61–9.
 8. Timlin C, Houston M, Jones B. Malignant induction probability maps for radiotherapy using X-ray and proton beams. *Br J Radiol* 2011;84(Spec No 1):S70–8.