Particle therapy – Physical, technical and clinical aspects

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Over recent years, high precision radiotherapy has been implemented widely into clinical routine. Modern techniques such as fractionated stereotactic radiotherapy (FSRT) and intensity modulated radiotherapy (IMRT) have enabled the Radiation Oncologist to apply high doses of radiation to defined target volumes while sparing normal tissues, especially organs at risk. This is especially important in regions where tumour volumes and sensitive normal tissue are in close proximity, such as in the skull base. Thus, it is possible to increase the total tumour dose and subsequently increase local control rates, while the risk for radiation induced side effects can be minimised.

However, in certain tumour entities, overall treatment results still remain unsatisfying. Therefore, particle therapy seems to be a promising alternative.

As early as 1946, Robert Wilson proposed the use of charged particles for tumour therapy [1]. The motor behind the idea to exploit the physical and biological characteristics of protons and heavier ions was the limitation of conventional photon radiotherapy in treating certain tumour entities. Especially for very radioresistant tumours, such as chordomas, chondrosarcomas or osteosarcomas, the use of particle beams offered a promising treatment alternative. For tumours localised in unfavourable anatomic sites such as the skull base, paranasal sinuses or paraspinal locations, the physical advantages of ion beams enable local dose escalation while adhering to normal tissue tolerance levels. Moreover, carbon or helium ions offer unique biological characteristics with an improved biological potential for the control of hypoxic or radioresistant tumours.

One benefit of particle therapy is the inverted dose profile, resulting in low RT doses in the entry channel and behind the defined target volume, while the required dose can be directed into the target area (Fig. 1).

The raster scanning technique for intensity-modulated, three-dimensional carbon ion RT was developed where highly focused pencil beams are deflected horizontally and laterally by magnetic dipoles. The depth of the Bragg peak can be varied by using different energies of the incoming beam. Thus, the required dose distribution can be adapted to any tumour shape, and highly conformal dose distributions can be achieved even to the tumour edge, without high doses within the entry channel (Fig. 2).

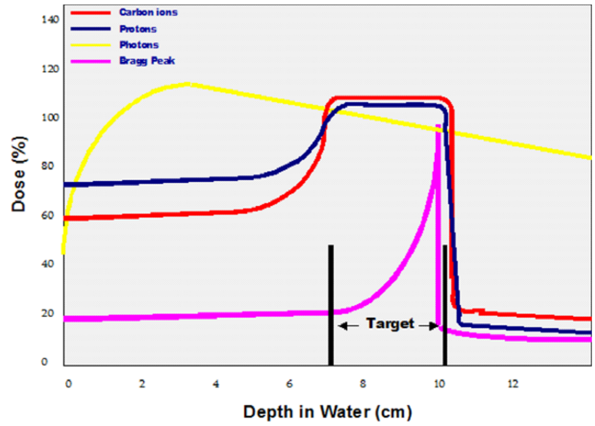

Fig. 1. Physical depth dose profiles of photons, protons and carbon ions.

With carbon ion radiotherapy, this physical privilege is accompanied by distinct radiobiological effects within the tissue, resulting in a higher relative biological effectiveness (RBE). Therefore, an increase in local tumour control and subsequent improvement of overall survival can be expected.

We have shown in a number of clinical studies that patients with radioresistant tumours such as chordomas, chondrosarcomas and adenoid cystic carcinomas may benefit from carbon ion RT. Other extracranial tumours including sacral chordomas, lung cancer and sarcomas have been treated with carbon ion RT effectively. Patients are treated using the intensity modulated raster scanning technique, and clinical study protocols for skull base chordomas and chondrosarcomas, as well as adenoid cystic carcinomas, have been completed successfully. Currently, a study on carbon ion RT in patients with intermediate risk prostate cancer is recruiting.

Carbon ion therapy is currently available in a few centres in Japan. At the University of Heidelberg we also perform treatment with carbon ions at

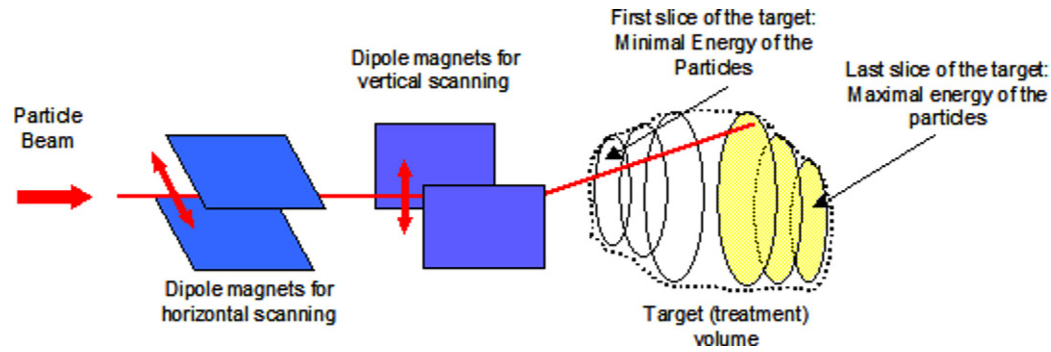

Fig. 2. Model of the intensity modulated raster scanning technique as developed at Gesellschaft für Schwerionenforschung (GSI) in Darmstadt, Germany.

the Gesellschaft für Schwerionenforschung (GSI) in Darmstadt.

Currently, we can offer treatment in three beam time blocks per year allowing the treatment of about 60 patients per year.

In Autumn 2009, a combined proton-carbon ion particle therapy centre at the University of Heidelberg (Department of Radiation Oncology), the “Heidelberg Ion Therapy Centre” (HIT), will take up clinical routine and allow the treatment of about 1300 patients per year.

In the near future, proton and carbon ion radiation therapy will be available in a number of new centres developing throughout the world. Clinical studies continuing to evaluate the role of particle therapy will have to be initiated to clearly define patients profiting most from this treatment. For paediatric oncology, particle therapy needs to be included in clinical trials, as children profit most from the reduction of the integral dose to the normal tissue over long-term follow-up; therefore, proton radiation therapy is considered a clear indication for paediatric patients. The role of carbon ion radiation therapy in paediatric oncology needs to be defined more clearly. Randomised trials comparing protons and carbon ions for tumours such as prostate cancer or chordomas and chondrosarcomas of the skull base will have to be performed to prove the superiority of one or the other modality or to show equal effectiveness. Studies are ongoing in patients with lung cancer and liver cancer as well as in patients with soft tissue sarcoma, which show promising first results.

Over the last decade, in more than 30 centres worldwide, valuable physical, biological and clinical expertise has been gained in the field of charged particle therapy. Ongoing technological advances may offer the clinical implementation of other ion species. Together with the development of newer technologies, mainly for beam application and treatment planning, a broader implementation of ions in the clinical setting will be possible. Among these technologies should be inverse treatment planning for particles, superior patient positioning possibilities and improved tumour tracking, such as gating or optimised raster scanning for moving targets, as well as improved biological planning optimisation.

Conflict of interest statement

None declared.

References

1 Wilson RR. Radiological use of fast protons. *Radiology* 1946;**47**: 491–8.