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Treatment planning with heavy ions

Abstract  The use of heavy charged particles in radiotherapy potentially represents an advance towards better local tumour control and a decrease in morbidity related to radiation injury of healthy tissues surrounding the target volume. This assertion only holds, however, if treatment planning systems give a real representation of the three-dimensional dose distribution, including physical and biological aspects, especially for heavier ions. The influence of linear energy transfer on the biological effects, its variations related to depth, particle, target tissue, position in the Bragg peak, etc. make the possible models for treatment planning extremely complex. A brief review of the problems to be addressed and some solutions is presented from the radiation oncologist’s point of view.

Introduction

“Advance in radiotherapy can be achieved by obtaining a greater tumor control and by reducing the morbidity of treatment, both early and late” (S. Dische). The use of charged particles in radiotherapy represents an indisputable advance in localization of the dose delivered to tumour masses, thereby allowing reduction of the dose received by adjacent healthy tissues. For example, protons improve the physical selectivity of the irradiation, i.e. the dose distribution, while high linear energy transfer (LET) radiations produce different biological effects, decreasing the differences in radiosensitivity and allowing radiation therapy to control radioresistant tumours. Fast neutrons represent the best known of these high LET particles, but they suffer from a relatively poor physical selectivity.

The two approaches of physical selectivity and biological advantages are combined by heavy ions such as carbon, oxygen, neon (we will acknowledge that physicians call protons and heavier charged particles heavy ions even if for physicists all charged particles from protons to neon are light ions). Using these particles, a highly selective, high LET radiation therapy can be carried out for radioresistant tumours without damage to healthy tissues, greatly enhancing the therapeutic ratio for a tumour lying in or close to critical structures such as the brain and the spinal cord. Preliminary results obtained at the Lawrence Berkeley Laboratory (LBL), Berkeley, demonstrate an improved local control of unresectable, slowly growing tumours, confirming extrapolated data from proton and neutron therapy. Furthermore, radioactive light ion beams or spontaneous positron emission in a particle beam can be used to verify the accuracy of treatment planning by checking the range of the particle with a PET camera: this allows a feedback control of the depth dose deposition [1]. One of the main practical problems in using these ions remains the difficulty of taking into account all their characteristics and their variations in a reliable treatment planning system. Such a system would have to include not only the physical dose distribution but also the dose corrected for the biological effects of these particles. For heavy charged particle therapy more than for classical radiotherapy, cure depends on an accurate delivery of the treatment, which implies being able to perform accurate treatment planning [2, 3].

The purpose of this paper is neither to make an exhaustive review of the physical and biological problems of charged particle treatment planning nor to describe the methods expected to give the best results but to consider from the point of view of the radiation oncologist the questions addressed.

Basis for treatment planning with low LET charged particles (proton or helium)

It is certainly useful to analyse the methodology employed in the simplest case (one proton port for an entire treatment) and therefore to investigate the increasingly com-
The position of the tantalum rings surgically inserted defines the aperture of the collimator. The depth of penetration of the beam and the width of the spread-out Bragg peak are also specified using the programme. These parameters can be adjusted in order to optimize the dose distribution, which may be represented in any plane orientation aligned or not on the beam axis. Dose volume histograms (DVH) [6, 7] are calculated for the main structures of the eye. They contribute to a better understanding of the dose distribution in a whole organ or in some of its parts. DVHs represent the first step towards a more accurate analysis of the tumour control rates and moreover of the normal tissue complication probability (NTCP) [8, 9].

As a short summary, this programme gives the main topics of the parameters used in a heavy particle treatment planning system: 3D representation of normal structures, 3D reconstruction of the tumour, 3D representation of these structures in a beam-eye view, visualisation from any angle, contouring of the target volume and aperture of the beam in this view, 3D calculation of those distribution, elaboration of DVH, calculation of range and modulation, edition of files for a milling machine (collimator, modulating wheel, range shifter).

High-energy, multiple ports proton therapy

While the use of a single port is relevant for eye treatments, for deep-seated tumours this technique is rather unusual. The combination of multiple ports is necessary to ensure a homogeneous dose distribution in the target volume and an optimal protection of the surrounding healthy tissues. A perfect definition of the different structures related to the tumour, normal or critical tissues has to be elaborated from multimodality imaging documents (x-ray CT, MRI, positron emission tomography, PET) including corrections for geometric discrepancies between the sets of images [10—12]. The calculation of tissue densities along the particles path and their influence on the dose distribution are much more critical than for neutral beams. While 3-cm-thick bone reduces the intensity of a cobalt-60 beam by some 11% at all depths beyond it, the effect on a charged particle beam is to reduce the range by around 2 cm [13]. In that case, a part of the target volume will remain untreated. In the same way if some hollow cavity is included in the beam, its real contour has to be taken into account very accurately. If it is underestimated, the range will be longer than calculated, and if a critical structure lies at the end of the calculated range, some of it will receive a full dose. On the other hand, if this cavity is partially filled by an exudate such as the maxillary antrum during radiotherapy or influenza), the range will be diminished. The status of these cavities often has to be verified along the radiation course in order to avoid over or underdosage, a simple cold being able to nullify a sophisticated treatment planning! This example explains the interest in beam-monitoring systems based on PET. The first measurements made in the LBL stressed the relevance of this method [14]. All inhomogeneities must not only be known but also compensated for to shape the target volume [15]. One has therefore to define the number of ports, their orientation (coplanar or non-coplanar) and their weight to try to optimize the dose distribution in the tumour and surrounding tissues. Very often, critical structures are located at the end of the path to benefit from the fall-off of the Bragg peak. It is of real interest to spare these healthy tissues by shaping the beam to the distal contour of the target volume. This compensation has to be added to the compensation for inhomogeneities in the calculations of the milling files. Currently, this is accomplished for each port by using a compensator milled in wax or lucite from the data of the treatment planning (Fig. 1 a). Lateral protection is provided by adapting the collimation to the beam aperture, including a safety margin all around the envelope of the target volume. The collimator is also milled for each port.

Up to now, heavy charged particle beams have been spread out using ridge filters or modulating wheels in order to cover the whole length of the target volume in the beam direction conveniently [16]. These devices achieve a fixed passive modulation of the beam. They produce extra irradiation of healthy tissues located upstream of the target volume (Fig. 1 a). Moreover, the introduction of these elements in the beam increases the scattering and the lateral penumbra. Several methods have been proposed to reduce these effects. The treatment volume may be divided into many layers and the size of each layer adapted to the target volume using a variable collimator, thus avoiding unnecessary irradiation of normal tissues by reducing the