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Optimization of the theoretical dose distribution in the "Spread Out Bragg Peak" (SOBP) region in proton therapy by means of semi-analytical techniques

E. Nichelatti(1), C. Ronsivalle(2), L. Picardi(2) and R. M. Montereali(2)

(1) *ENEA C.R. Casaccia, Fusion and Technologies for Safety and Security Dept. Via Anguillarese 301, 00123 S. Maria di Galeria, Rome, Italy*
(2) *ENEA C.R. Frascati, Fusion and Technologies for Safety and Security Dept. Via E. Fermi 45, 00044 Frascati, Rome, Italy*

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Summary. — Proton therapy uses proton beams to destroy cancer cells. Since the energy deposition of protons peaks at the end of the trajectory (Bragg peak), healthy tissues close to the target are partially spared. In clinical practice, beams of different energies are composed to obtain a broadened peak (SOBP, Spread Out Bragg Peak) to treat the entire lesion region in a uniform manner. In the framework of the TOP-IMPLART project (linear accelerator for proton therapy under construction at ENEA-Frascati), we present a semi-analytical method that allows to optimize SOBP uniformity for two different energy-modulation techniques, passive and active.

1. – Introduction

Proton therapy consists of bombarding a tumor mass with accelerated protons. It is advantageous compared to other radiotherapy techniques, such as X-rays, because the amount of energy released by protons is concentrated at the end of their propagation, so that it is possible to confine the destructive action in the affected volume while preserving the adjacent healthy organs. The dose released by accelerated protons in matter *vs.* penetration depth ends with a well-defined peak (Bragg peak) where the highest values of dose are found. The depth of the Bragg peak depends on the energy of protons: it is 3 cm (ocular melanoma) at 60 MeV, 15 cm (head-neck tumors) at 150 MeV, 32 cm at 230 MeV (deep seated tumors). The accelerators typically used in proton therapy centers are cyclotrons and synchrotrons.

Generally, the size of a tumor is larger than the depth extension of a Bragg peak. Therefore, to uniformly release energy into the tumor volume, a combination of several distinct Bragg peaks having suitable intensities and energies is needed. The so-obtained dose distribution is known as Spread Out Bragg Peak (SOBP).

Effective delivery of the prescribed therapeutic dose to the planned target volume can be performed in two different ways: passive and active.

In passive-delivery systems, the particle beam extracted from the accelerator is modified by a degrader to get an appropriate energy, as occurs in cyclotrons (fixed-energy machines), and the superposition of Bragg peaks is generated by ridge filters or range modulation wheels (RMWs). A RMW that contains several absorbers of increasing thickness rotates and thus changes continuously the Bragg-peak range as a function of the rotation angle.

In active-delivery systems, the beam energy is varied directly by the accelerator: this is done on a time scale of 1 s in synchrotrons. In this context, an innovative 150 MeV radiofrequency (RF) pulsed linear accelerator named TOP-IMPLART (Terapia Oncologica con Protoni-Intensity Modulated Proton Linear Accelerator for RadioTherapy) for cancer therapy applications is under development and test at the ENEA-Frascati center. With respect to conventional circular machines usually employed for proton therapy, it gives the possibility of varying the energy and intensity of each pulse very quickly, on a scale of a few milliseconds.

In the framework of this project, funded by Lazio Region and led by ENEA in collaboration with the Italian Institute of Health (ISS) and the Oncological Hospital Regina Elena-IFO, fast and practical semi-analytical tools have been developed to achieve the desired dose distribution in targets with the accelerator operating in both modalities —passive and active energy modulation.

2. – The TOP-IMPLART accelerator

The TOP-IMPLART accelerator is a full linear machine consisting of a commercial low-frequency 7 MeV injector followed by a sequence of 3 GHz SCDTL (Side Coupled Drift Tube Linac) accelerating modules [1] driven by 10 MW 3 GHz klystrons through a proper RF power distribution network including splitters and phase shifters. The linac portion currently installed accelerates the proton beam up to 45 MeV. The following accelerating module, installed but not yet powered, will increase the energy up to 55.5 MeV. The temporal beam structure is a sequence of 2.7 μs pulses at a typical repetition frequency of 25 Hz. The output beam intensity can be continuously varied from zero to 30 μA by changing the pulse length or moving the injector parameters.

As the first energy of clinical interest —55.5 MeV (depth penetration in water 26 mm)—is near to be reached, preliminary tests of both passive and active energy modulation techniques are planned in the first months of 2021. Passive energy modulation will be obtained according to the usual methodology described in [2], while active energy modulation will be performed by switching off the modules and varying the RF power in the last active module. In principle, this can be done on a pulse-to-pulse basis.

3. – Semi-analytical tools for SOBP optimization

The purpose of the proposed semi-analytical tools is that of finding optimal energies and weights for a number of energy components whose Bragg peaks combine to form a desired SOBP, which should be as flat as possible. Although this task is performed numerically with suitable minimization algorithms, it takes great advantage —in terms of computational time and efficiency— of approximate analytical expressions used for Bragg-curve calculation [3]. The fluence-attrition and residual energy deposition effects induced by nonelastic nuclear interactions in the target material —water in the present paper— are also taken into account with a slightly different approach from Bortfeld's, as

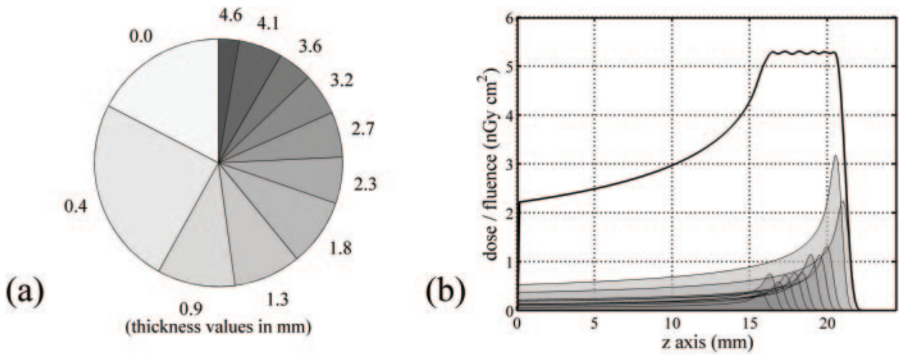

Fig. 1. – Passive-SOBP optimization result for the example described in the text: (a) angular apertures and thicknesses of the 11 sectors of a PMMA RMW; (b) corresponding dose distribution in the water target —the shaded-area curves are single components due to each sector.

thoroughly explained in [4], due to the alternative best fitting we adopted of nonelastic-nuclear-interaction probability data.

In the passive-modulation case, the task of finding optimal energies and weights of the energy components translates into identifying optimal thicknesses and angular apertures of the RMW sectors. To this purpose, the energy spreads of the entering and transmitted protons are properly taken into account during the optimization process.

As an example application of the passive-modulation case, we considered a 50 MeV proton beam entering a water target after crossing 40 cm of air from the accelerator exit, with a PMMA (density $\rho = 1.18\,\mathrm{g/cm^3}$) RMW placed halfway. The optimization program, coded in Matlab, was instructed to find the angular apertures and thicknesses of the RMW to obtain a SOBP in the 25% ending depth inside the target, corresponding to a depth range from 15.9 mm to 21.3 mm in water. The results for an 11-sector RMW are shown in fig. 1; the obtained dose per unit fluence within the flat part of the SOBP amounts to an average of 5.27 nGy cm^2, with r.m.s. deviation from it of 0.34%.

As far as active modulation is concerned, because the typical energy distributions of a linac operating in such a modality can be strongly irregular, we developed an approach to optimization of the energy components that consists of two distinct stages [4]. In the first stage, called *preliminary stage*, the energy components that give rise to the SOBP are temporarily replaced with Gaussians, whose widths are dynamically updated during optimization by interpolating the data of a look-up-table (LUT) previously prepared by means of LINAC beam-dynamics code [5]; this LUT contains a list of (peak energy, standard deviation) couples of Gaussians whose spectral areas are equal to those of the actual energy components corresponding to the same peak energies. In the second optimization stage, called *refining stage*, the (peak energy, weight) couples resulting from the preliminary stage are read and, after a new definitive LINAC computation is performed to find the actual energy distributions corresponding to the peak energies, these are used in place of the Gaussian ones for a new optimization run, during which only the weights are let change, while keeping the peak energies fixed. In-depth details about this approach to active modulation are reported in [4], together with a few example applications for SOBP targets involving proton energies up to $\sim$50 MeV.

As an example of active modulation, we report here the results obtained for SOBP optimization in the energy range 46.6–54.6 MeV with 8 energy components. Figure 2 shows the dose plots corresponding to the refining stage, whose peak energies and weights

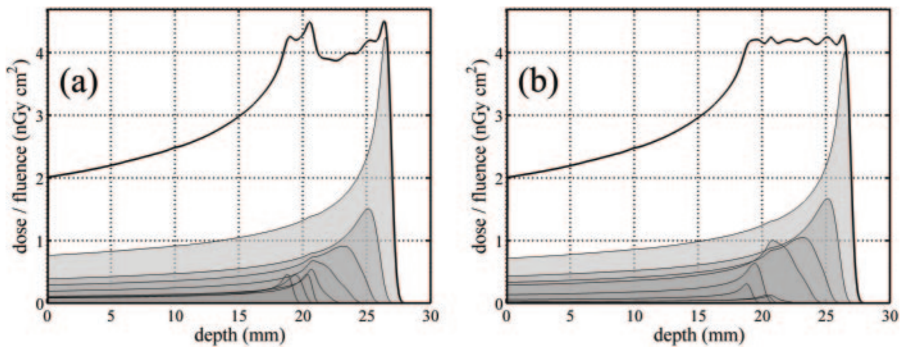

Fig. 2. – Refining stage of the active-SOBP example described in the text: (a) SOBP curve right after substitution of Gaussian energy components with LINAC-generated actual ones, before optimization is applied; (b) final SOBP curve after optimization. The shaded-area curves are single energy components.

were optimized in the preliminary stage, after substitution of the Gaussian components with the actual ones (a) before and (b) after optimization. The final dose per unit fluence in the flat part of the SOBP amounts to an average of 4.19 nGy cm^2, with r.m.s. deviation from it of 0.67%.

4. – Conclusions

Summarizing, in our approach to both passive- and active-modulation SOBP, the weights and energies of analytically computed Bragg curves are numerically optimized, with a double-stage process for the active case. The approximate analytical evaluation of Bragg curves is the key to dramatically shorten computational times with respect to all-numerical approaches, such as Monte Carlo codes. Due to the involved approximations, our tools are not meant to be used in a therapy planning system —however they are reliable enough for LINAC commissioning. With respect to other published analytical approaches to SOBP, besides the differences already listed in [4], we underline that irregular energy distributions in an active-energy-modulation LINAC have been taken into account for the first time. Another point worth stressing is that our inclusion of inelastic nuclear interactions differs from what reported elsewhere [3,6] in a more accurate fit of nuclear-interaction *vs.* energy probability [4].

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