Adaptive cell killing for ion beam treatment planning of hypoxic tumors *

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Introduction

Recent *in vivo* molecular imaging techniques allow to provide informations on intra-tumor biological heterogeneity [1], i.e., to map qualitatively and quantitatively regions of different functional activity within a tumor tissue. Among these features, hypoxia, i.e., the condition of unsufficient cell oxygenation, has a great importance, since the increased radioresistance of the not fully oxygenated tissues, quantified by the oxygen enhancement ratio (OER) has a crucial impact on treatment prognosis.

Materials and methods

Several approaches for adapting a radiotherapeutical treatment of such heterogeneous tumors have been proposed, mainly based on a differential scaling of the dose (dose painting [1]) or redistribution of the linear energy transfer (LET painting [2]) across the target. Alternatively to these methods we suggested a "killing painting" approach, where the optimization drives the survival level to be uniform in the overall target. The GSI leading treatment planning system for particles TRiP98 [3] has been updated for this purpose. Beyond the multiple field optimization [4], the optimization task has been modified in order to adapt for an intratumour heterogeneity due to hypoxia, and then for a different oxygen content, varying from one voxel to another [5].

The gradients formulation which drives the optimization has been updated so that the oxygen distribution can be coupled with the dose averaged LET in each voxel, in each iteration step. Thus we achieve an optimal distribution of the latter, also adjusting the dose required to restore the prescribed cell killing effect.

Results

In figure 1 it is shown an example of a simulated water phantom where a tumor target has a smoothly varying oxygen distribution, logarithmically increasing with the distance from the target center. The optimization automatically drives the convergence of the irradiation parameters (fluences of the raster spots of each field) in order to produce the optimal plan, and one can clearly see how the LET is automatically adjusted, without any prescription, to match the hypoxic distribution. After evaluating the possible advantages of using different ions[6], we are going to extend this approach to the combination of different beam modalities in the optimization task.

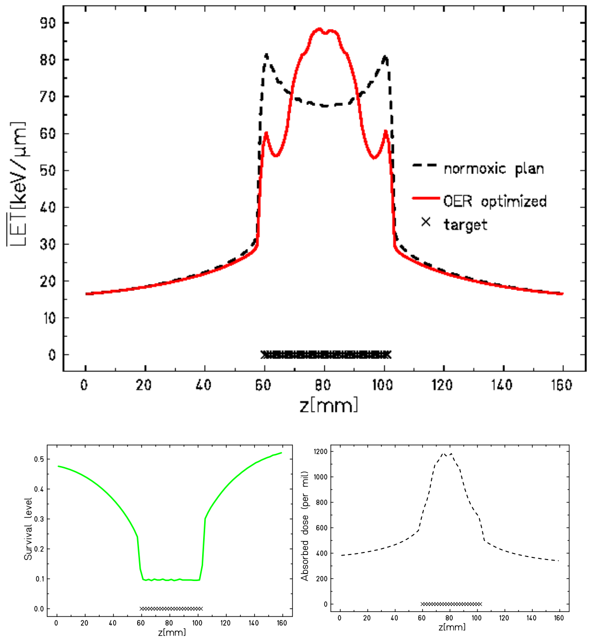

Figure 1: Upper panel: LET distribution in a conventional plan with two opposing ^{12}C ion fields compared with an OER-optimized plan for a tumor with an oxygenation smoothly decreasing towards its center. Lower panel: corresponding survival level (left hand side) and overall absorbed dose distribution (right hand side, in per mil of prescribed dose).

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