Mathematical analysis of approximate biological effective dose (BED) calculation for multi-phase radiotherapy treatment plans

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Abstract

Purpose: There is growing interest about biological effective dose (BED) and its application in treatment plan evaluation due to its stronger correlation with treatment outcome. An approximate biological effective dose (BED_A) equation was introduced in order to simplify BED calculations by treatment planning systems in multi-phase treatments. The purpose of this work is to reveal its mathematical properties relative to the true, multi-phase BED (BED_T) equation.

Methods: The BED_T equation was derived and used to reveal the mathematical properties of BED_A. MATLAB (MathWorks, Natick, MA) was used to simulate and analyze common and extreme clinical multi-phase cases. In those cases, percent error and Bland-Altman analysis were used to study the significance of the inaccuracies of BED_A for different combinations of total doses, numbers of fractions, doses per fractions and α/β values. All the calculations were performed on a voxel-basis in order to study how dose distributions would affect the accuracy of BED_A.

Results: When the voxel dose-per-fractions (DPF) delivered by both phases are equal, BED_A and BED_T are equal (0% error). In heterogeneous dose distributions, which significantly vary between the phases, there are fewer occurrences of equal DPFs and hence the imprecision of BED_A is greater. It was shown that as the α/β ratio increased the accuracy of BED_A would improve. Examining twenty-four cases, it was shown that the range of DPF ratios for 3% P_{error} varied from 0.32 to 7.50Gy, whereas for P_{error} of 1% the range varied from 0.50 to 2.96Gy.

Conclusion: The DPF between the different phases should be equal in order to render BED_A accurate. OARs typically receive heterogeneous dose distributions hence the probability of equal DPFs is low. Consequently, the BED_A equation should only be used for targets or OARs that receive uniform or very similar dose distributions by the different treatment phases.

Impact: To our knowledge, it is a usual practice to use BED_A instead of BED_T due to its convenience with current treatment planning systems (TPS). This was shown to be a potential problem with our mathematical analysis of BED_A. The goal of this work was to quantitatively measure the accuracy of BED_A under many different circumstances, and also reveal its potential imprecision in clinical circumstances regarding healthy organs. This work puts emphasis on the importance of creating future TPS with the capability of calculating the BED_T.

Key Results: Using the multi-phase equations of BED_T and BED_A, specifically two-phases (e.g., primary and boost), the percent error (P_{error}) equation was derived. Five variables within this equation are the α/β ratio, which is a tissue-dependent constant of the linear-quadratic (LQ) cell- survival curve model,

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the dose-per-fractions (DPF) for both phases, and the number of fractions for both phases. The P_{error} equation reveals the many varying factors in the accuracy of BED_A. **Figure 1** displays the change of P_{error} with respect to four of the variables, except α/β, which is instead shown in **Figure 2**. As seen, the main determining factor in the accuracy of BED_A is the DPF-ratio, which, when it gets equal to 1, P_{error} becomes equal to 0% (see **Figure 1**). Since DPF- ratio is the most important factor in the accuracy of BED_A,

and due to its dependence upon the dose distribution, we have shown that using BED_A on OARs could potentially lead to significant errors. On the other hand, its application to target volumes would instead produce less error due to fact that target volumes typically receive more homogeneous dose distributions.
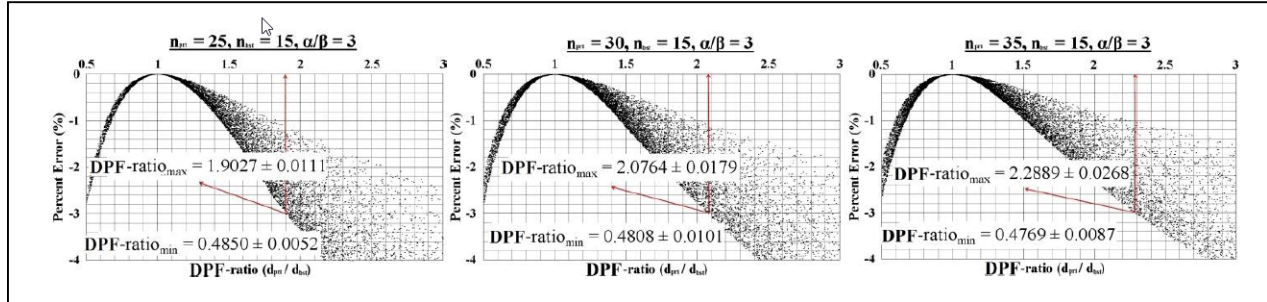
FIG. 1: As seen in all three plots, as the DPF-ratio steers from 1, P_{error} increases. Also, as n_{pri}/n_{bst} increases, P_{error} decreases. The DPF-ratio$_{max}$ and DPF-ratio$_{min}$ reveal the ratios that lead to a 3% error of BED_A.
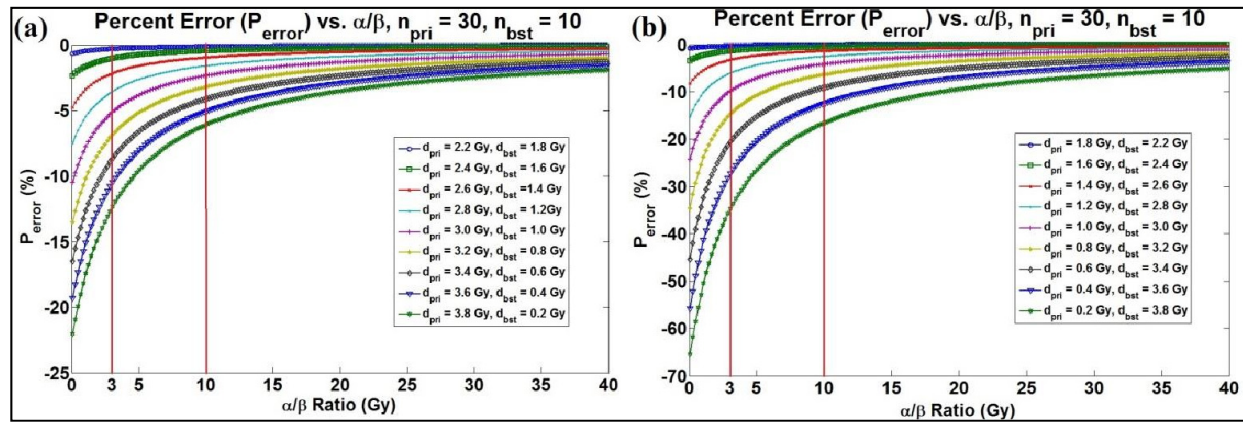
FIG. 2: (a) This is a plot with DPF-ratios > 1, while (b) is with DPF-ratios < 1. When d_{pri}/d_{bst} is less than one, notice the steeper drop in P_{error} with a change in DPF.