“Statistical models in optimization of radiotherapy treatments”

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Introduction: In Radiotherapy (RT) the Treatment Planning Systems (TPS) are medical device. Some of them are biologically based TPS treatment planning system (BBTPS), and use radiobiological (RB) indices: TCP (Tumor control probability) and NTCP (Normal Tissues Complication Probability) for evaluating and/or optimizing treatment in cancer patients.

Additional to the phenomenological/mechanistic TCP/NTCP models, Statistical models project (SMp) has formulated new cell kill and sub-lethal damage (K and SL respectively) formalisms, which involve all possible factors affecting the biological radiation effects (BRE). These formalisms have allowed development of RT-computational simulators aimed to evaluate the TCP/NTCP for RT treatments without using formulas of these indexes, but their own probabilistic definitions [1]

Nowadays Poisson statistics, effective dose (Deff), sigmoid curves, equivalent uniform dose (EUD),TCP Poisson-LQ, NTCP Poisson-LQ and NTCP Lyman are used in three commercially available and most commonly used BBTPS: Monaco® V1.0 (CMS/Elekta, Maryland Heights, MO), Pinnacle® V8.0h (Philips Medical Systems, Andover, MA), and Eclipse V10.0 (Varian Medical Systems, Palo Alto, CA). Many of the RB and probabilistic concepts employed by these BBTPSs described in [2]and RB software [3] represent serious errors and deficiencies in the RT.

The optimization process is based on iterative evaluations, where we find the best treatment aimed to obtain high TCP without violating pre-established complications for the normal tissues (NT) or OARs. The optimization can be done varying the values of imparted dose, number of the fractions or inter-fraction times, which is the methodology used by the software in [3] ; or varying the dose-volume histogram (DVH) such as it is used by the BBTPSs in their IMRT planning inverse modules[2]. Given the NT complication depends on BRE, organ type (serial and parallel) and the regional damage distribution (RDD), a new cost function is proposed for being used in the IMRT module together the values of BRE that represent the mean organ damage, as well as the RDD characterized by BREz and BREl, the mean organ superficial and perimeter damage respectively.

Materials and Methods: The three quoted BBTPS were investigated. Macro-probabilistic and RB studies were done for all models and formalisms used by these BBTPS and the recent RT computational simulator evaluating TCP and NTCP.

Results and Discussion: A new cost function is proposed for the IMRT planning inverse modules of the BBTPSs that only uses values related to TCP and NTCP:

\[ F(TCP, TCP_0, NTCP_i, NTCP_0) = \sum \frac{(TCP - TCP_0)}{NTCP_i} * H(TCP - TCP_0) * H(NTCP_0 - NTCP) \]  (1)

where TCP0 is the desired TCP specified by the user. Function H is the Heaviside step function. The NTCP0 is limit for the NTCP in each i\(^{th}\) associated end-point.

Translational Impact: (a) Development of the methodology for implementing optimization modules into of BBTPS and RT computational simulator; and (b) Determination of errors and deficiencies related to RB and probabilistic concepts in the current RB software and BBTPS.

Disclosure Statement: Conflict of interest: none.