Biological-Based and Physical-Based Optimization for Biological Evaluation of Prostate Patient's Plans

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Abstract. Modern modalities of radiation treatment therapy allow irradiation of the tumor to high dose values and irradiation of organs at risk (OARs) to low dose values at the same time. In this paper we study optimal radiation treatment plans made in Monaco system. The first aim of this study was to evaluate dosimetric features of Monaco treatment planning system using biological versus dose-based cost functions for the OARs and irradiation targets (namely tumors) when the full potential of built-in biological cost functions is utilized. The second aim was to develop criteria for the evaluation of radiation dosimetry plans for patients based on the macroscopic radiobiological criteria - TCP/NTCP. In the framework of the study four dosimetric plans were created utilizing the full extent of biological and physical cost functions using dose calculation-based treatment planning for IMRT Step-and-Shoot delivery of stereotactic body radiation therapy (SBRT) in prostate case (5 fractions per 7 Gy).

INTRODUCTION

The goal of radiation therapy is to maximize tumor response and minimize side effects in normal tissues. However, the optimization of treatment plans has traditionally been performed using surrogate approaches, such as the maximization of tumor dose and minimization of dose to organs at risk OARs. Currently, the biological effects of expected treatment efficiency are estimated mainly by the absorbed dose in the tumor and surrounding tissues, taking into account the total treatment time and fractionation. These principles have a statistical nature and are not based on clear biological principles. The progress in radiobiology led to the development of new models for assessing the cell death and complications in normal tissues, taking into account their biological characteristics. The currently used method for assessing dosimetric radiation plans for patients based on dose-volume limitations has a significant drawback: equally evaluate dosimetric plans while they meet the same dose-volume limitations. Therefore, there is a growing interest in the possibility of using biological target functions combining tissue architecture and dose sensitivity (an equivalent uniform dose concept, EUD), when evaluating irradiation plans as an alternative to dose-volume limitations [1]. An equivalent uniform dose concept has acquired significant popularity in the area of biologically based treatment planning as it involves the information about the organ functional architecture which is serial or parallel. It is in "dose-volume" region and is more familiar for clinicians. It also possesses desired mathematical properties. However, this function does not rely on too much necessary parameters to determine the effectiveness of radiotherapy, such as the case with tumor control probability (TCP) and normal tissue complication probability (NTCP). It was realized long ago that incorporating biological response functions, such as a TCP and NTCP, into the treatment planning process has the potential to produce more optimal plans resulting in improved treatment outcomes. Biological optimization became an even more attractive concept with the advent of the intensity-modulated radiation therapy IMRT and inverse treatment planning [2].

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The first aim of this study was to evaluate dosimetric features of Monaco treatment planning system using biological versus dose-based cost functions for the OARs and irradiation targets (namely tumors) when the full potential of built-in biological cost functions is utilized. The second aim was to evaluate the dosimetric plans for patients based on the macroscopic radiobiological criteria—TCP/NTCP.

METHODS AND MATERIALS

All radiation treatment plans have been simulated using Elekta Monaco planning system (v. 5.10) and have been delivered with an Elekta Synergy linear accelerator (40×40 cm maximum field size with 0.5 cm width of leaves) using kV cone-beam CT capability which was performed at Tomsk Regional Oncology Center (Tomsk, Russia). In the framework of this study four plans have been created utilizing the full extent of biological and physical cost functions [1, 2] using dose calculation-based treatment planning for IMRT Step-and-Shoot delivery of stereotactic body radiation therapy (SBRT) in prostate case (7 Gy for 5 fractions).

The biological plans named IMRTBio (hard condition for Target) and IMRTBio2 (priority for OAR) performed the following cost functions: Target EUD, Serial and Parallel. To create IMRTPh1 (priority for OAR) and IMRTPh2 (hard condition for Target) physical plans such functions as Target Penalty, Quadratic Overdose, Maximum Dose and Overdose DVH were used.

The evaluation of treatments plans was performed based on conformity index CI and heterogeneity index HI [3, 4]. The quality of the plan delivery by accelerator was assessed by measuring the transverse dose distribution using IBA plate ion chamber-array phantom, MatriXX (IBA Dosimetry GmbH, Germany). The passing rates were determined according to the percent difference and distance-to-agreement (DTA) 3%–3 mm criterion [4].

The selection of the most effective radiotherapy plans was made by evaluating the UTCP (Uncomplicated Tumor Control Probability) criterion, the value of which is interpreted as the probability of controlling a tumor without radiation complications:

$$\mathrm{UTCP} = \mathrm{TCP}\,(1 - \mathrm{NTCP}), \tag{1}$$

where TCP—tumor control probability value, NTCP—normal tissue complication probability value.

For this purpose, automated import of cumulative dose-to-volume histograms—cDVH from the Monaco planning system was realized and then they were transformed into differential distributions—dDVH, necessary for the calculation of TCP/NTCP.

To calculate TCP and NTCP values in this paper Niemierko model [5–7] was used. In Niemierko model TCP value could be calculated as follows:

$$\mathrm{TCP} = \left(1 + \left[\frac{\mathrm{TCD}_{50}}{\mathrm{EUD}}\right]^{4\gamma_{50}}\right)^{-1}, \tag{2}$$

where $\mathrm{TCD}_{50} = 65$ Gy, $\gamma_{50} = 2.5$, $a = -10$ for prostate cancer according to [8],

$$\mathrm{EUD} = \left[\sum_i \left(v_i \left(D_\mathrm{i} \frac{\alpha/\beta + D_\mathrm{i}/n_\mathrm{f}}{\alpha/\beta + 2}\right)^a\right)\right]^{1/a}. \tag{3}$$

Here $\alpha/\beta = 1.5 \pm 0.5$ is a radiobiological constant for prostate cancer according to [8], v_i is the part of PTV that obtains the irradiation dose D_i, n_f is the number of fractions.

NTCP value could be calculated as follows [5–7]:

$$\mathrm{NTCP} = \left(1 + \left[\frac{\mathrm{TD}_{50}}{\mathrm{EUD}}\right]^{4\gamma_{50}}\right)^{-1}, \tag{4}$$

where $\mathrm{TD}_{50} = 80$ Gy, $\gamma_{50} = 2.7$, $a = 8$ for rectum and $\mathrm{TD}_{50} = 80$ Gy, $\gamma_{50} = 3.6$, $a = 7$ for bladder [8]. EUD in Eq. (4) is calculated using Eq. (3), but α/β ratio is taken for OARs. We used values $\alpha/\beta = 3$ both for rectum and bladder [8].

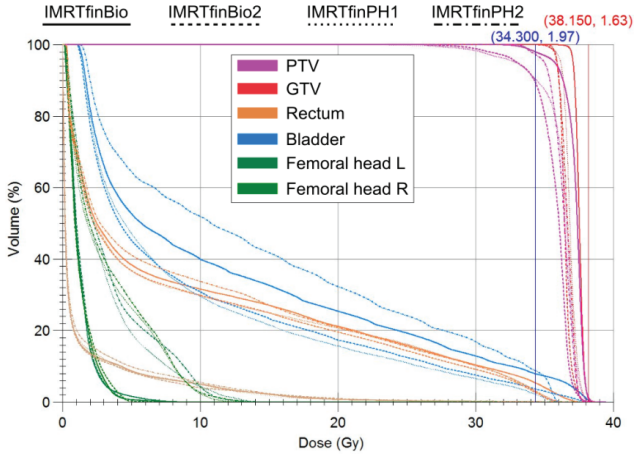

FIGURE 1. The comparison of biological-based and physical plans for prostate patient

RESULTS

The delivery parameters such as the number of segments (*S*) and number of MU (MU) for SBRT prostate plans were as follows: for IMRTBio plans $S = 66$ and MU = 1406, for IMRTBio2 plan $S = 75$ and MU = 1304, for IMRTPh plans $S = 77$ and MU = 1896.

The comparison of biology-based (IMRTBio, IMRTBio2) and physical (IMRTPh1, IMRTPh2) SBRT prostate plans on based dose-volume histogram for GTV, PTV, bladder, rectum, femoral heads (L,R) is presented in Fig. 1. To evaluate tolerance doses on OAR for SBRT with fivefold fraction in all plans TG-101 protocols were used, i.e. for bladder Dose of 18.3 Gy no more 15cc of Volume and MaxDose < 38 Gy, for rectum Dose of 25 Gy no more 20cc of Volume and MaxDose < 38 Gy, femoral heads Dose of 30 Gy no more 10cc of Volume.

The evaluation parameters of Monaco plans quality with respect to target coverage, conformity and heterogeneity indices, and passing rates are listed in Table 1.

In Table 2 TCP and NTCP values calculated for all treatment plans are presented.

TABLE 1. The evaluation parameters of IMRT SBRT Monaco plans quality

Plans	Structure	% of volume	% of dose	Max dose	CI	HI	Passing
IMRTBio	GTV PTV	100 98	100 98	38.6 39	0.86 0.77	1.02 1.06	99.6%
IMRTBio2	GTV PTV	100 95	99 94	37.5 37.5	0.7 0.62	1.03 1.08	98.1%
IMRTPh1	GTV PTV	100 95	99 95	38.6 37.8	0.69 0.7	1.04 1.07	96.5%
IMRTPh2	GTV PTV	100 98	99 97	38.2 38.5	0.6 0.6	1.09 1.10	96.2%

TABLE 2. TCP and NTCP values calculated for all treatment plans

Plans	TCP	NTCP rectum	NTCP bladder
IMRTBio	99%	1.1%	0
IMRTBio2	96%	0.6%	0
IMRTPh1	97%	0.7%	0
IMRTPh2	97%	0.6%	0

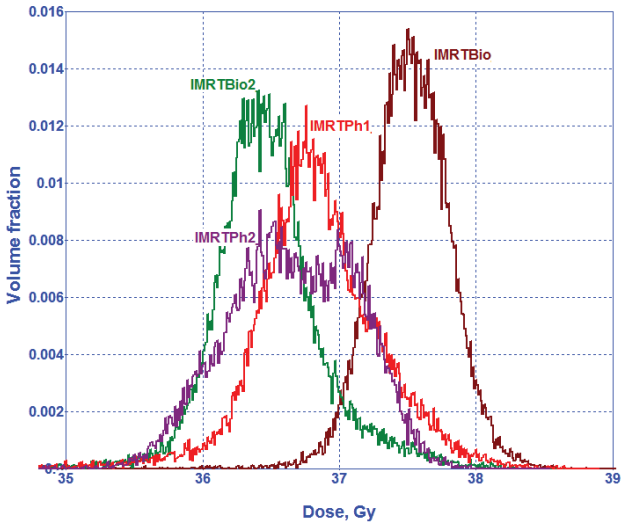

FIGURE 2. Differential dose-volume distributions for PTV of the patient irradiation plans under consideration

The calculation using Eqs. (2)–(4) is carried out by differential dose-volume distributions $\{v_i, D_i\}$ for PTV and OARs, obtained from the data shown in Fig. 1. Figure 2 shows the differential dose-volume distributions for PTV calculated for the patient dosimetric plans discussed above.

DISCUSSION

Thus, the best result for control of target irradiation shows plan IMRTBio, but the probabilities of critical organ exposures have shown good results both in terms of physical and biological functions. Nevertheless biological cost functions offer more control over the dose distribution than physical functions, and a smaller number of them is required to fully shape the dose distribution.

CONCLUSION

Modern radiotherapy can delivery highly conformal dose distribution and can create different dose level within the treated volume.

The evaluation of dosimetric plans obtained using macroscopic radiobiological criteria showed that SBRT plans optimized using biological-motivated cost-functions result in highly conformal dose distributions. The plans offer shorter treatment-time benefits and provide efficient dose delivery without compromising the plan conformity for tumors in the prostate, thereby improving patient comfort and clinical throughput. The short delivery times minimize the risk of patient setup and intrafraction motion errors often associated with long SBRT treatment delivery times.

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