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Influence of SBRT fractionation on TCP and NTCP estimations for prostate cancer

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ABSTRACT

Introduction: Stereotactic body radiation therapy is widely used for the hypofractionated treatment of prostate cancer. The range of total doses used in different clinical trials varies from 33.5 to 50 Gy delivered in 4 or 5 fractions. The choice of an optimal total dose value and fractionation regimen for a particular patient can be carried out using the integral radiobiological criteria, namely tumour control probability (TCP) and normal tissue complication probability (NTCP). In this study, we have investigated the dependence of simulated TCP/NTCP values on total dose in the range of 30–40 Gy delivered in 4 or 5 fractions for patients with low-risk prostate cancer in order to find the optimal total dose value and fractionation regimen.

Methods: The anatomic data (DICOM CT images) of 12 patients with low-risk prostate cancer, who were treated at Tomsk Regional Oncology Centre, were used for the calculation. Dosimetric treatment plans for all patients were simulated using VMAT with 2 arcs in the Monaco treatment planning system v5.10 (Elekta Instrument AB, Stockholm) with a total dose equal to 36.25 Gy. The dosimetric plans were rescaled in the dose range of 30–40 Gy. The TCP and NTCP values were calculated based on differential dose volume histograms using the Niemierko model for both TCP and NTCP, and the Källman-s model for NTCP calculations. The TCP calculation was carried out using the uncertainty of well-known tumour radiobiological parameters values, including α/β value. NTCP was calculated for an anterior rectal wall, which was the most irradiated organ at risk due to its close contact with the planning target volume.

Results: The TCP and NTCP calculations for VMAT of the prostate cancer have shown that the optimal total dose ranges were equal to 32–34 Gy delivered in 4 fractions or 35–38 Gy delivered in 5 fractions. At doses lower than the optimal ones, the TCP values were lower than 95%, while TCP uncertainties were significant (as low as 80%). This fact might bring unexpectedly poor treatment results. At doses higher than optimal ones, the probability of toxicity to the anterior rectal wall became significant.

Conclusion: The optimization of radiation therapy regimen based on TCP/NTCP criteria could help to determine an optimal total dose and a number of fractions for a particular patient depending on patient-specific anatomic features and planned dose distribution.

1. Introduction

According to P.A. Herzen Moscow Research Institute, 40785 new cases of prostate cancer were diagnosed, and 12565 deaths caused by this disease were registered in Russia in 2017 [1]. Early stages of localized prostate cancer could be effectively treated using external beam radiotherapy. According to the Russian standards, a common treatment scheme prescribes the delivery of total doses in the range of 70–78 Gy with doses per fraction equal to 1.8–2 Gy. Prostate cancer is characterised by the low α/β ratio equal to 1.5 Gy as stated in Refs. [2,3]. Further, the α/β ratios of the nearest organs at risk (OARs) are equal to $\alpha/\beta = 3$ Gy for the bladder and $\alpha/\beta = 3.9$ Gy for the rectum. This fact has become the key point to start the worldwide development and implementation of hypofractionated treatment schemes.

For the last 15 years, the stereotactic body radiation therapy (SBRT) of prostate cancer has been thoroughly investigated because of the possibility to deliver a full treatment course in 4–6 fractions [4]. Several clinical trials have been conducted using different SBRT treatment schemes. In the case of prostate cancer, the schemes assumed the delivery of fractional doses in the range of 6.7–10 Gy in 4 or 5 fractions

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daily or on alternate days [4].

Because of the wide range of therapeutic total doses and fractional doses, it is necessary to find an additional optimization criterion based on tumour radiobiology, individual patient-specific anatomic features and performance potential of specific treatment equipment that includes linac, radiation treatment planning system, immobilization devices, etc. For this purpose, one could use the concept of Uncomplicated Tumour Control Probability (UTCP), which is described as a combination of tumour control probability (TCP) and Normal Tissue Complication Probability (NTCP) [5]:

$$UTCP = TCP \cdot (1 - NTCP). \quad (1)$$

The TCP/NTCP radiobiological criteria strongly depend on the dose distribution conformity and can be used for comparison of different treatment planning techniques, for example, 3D-CRT and IMRT [6,7] or single-arc and double-arc volumetric modulated arc therapy (VMAT) [8]. The comparison of different treatment regimens with respect to the total dose and fractional dose can be carried out using the well-known biologically effective dose (BED) concept based on the Linear-Quadratic model (LQM). However, TCP and NTCP naturally include LQM, and one can use them as optimization parameters that simultaneously depend on dose distribution conformity and total dose and fractional dose values. Thus, the use of TCP and NTCP criteria does not demand the exact prescription of the total dose value before treatment planning but allows choosing the optimal treatment regimen after simulation of dose distribution by the treatment planning system.

The goal of this paper was to study the UTCP dependence on the treatment scheme, which included total irradiation dose and the number of fractions. The investigation was based on the anatomic data of 12 patients with low-risk prostate cancer, who have been treated at Tomsk Regional Oncology Centre using SBRT. For the simulation of TCP values, the Niemierko model has been chosen [9,10]. The TCP values were simulated taking into account the uncertainty of well-known radiobiological parameters of the tumour, including the α/β ratio. The NTCP was calculated for the anterior rectal wall using both the Niemierko and Källman-s models [11–13].

2. Materials and methods

The 12 patients with localized prostate cancer ($T_2N_0M_0$ stage) were selected for this study (64–75 years old, PSA nadir of (4.8–8.7) ng/ml and Gleason score in the range from 4 to 7). The patients received the SBRT treatment at Tomsk Regional Oncology Centre with a total prescribed dose equal to 36.25 Gy in 5 fractions on alternate days. All the patients were treated by the same clinician.

The patients' tomographic data were obtained using a Toshiba Aquilion LB computer tomograph (CT) with 3 mm slice thickness. Before the CT scanning of an abdominal-pelvic region, the patients were immobilized in the treatment supine position using the Combifix frame [14]. The internal organs were fixed following the recommendations in Ref. [15]. A Foley catheter filled with 60 cc of physiological solution was used for the rectum. The bladder was filled by drinking a fixed amount of water.

For all patients, the clinical target volume (CTV) included just prostate without seminal vesicles. The planning target volume (PTV) included the CTV with a small margin (of 2–5 mm) in anterior/right/left directions and a reduced margin (of 0–3 mm) in a posterior direction due to the nearby anterior rectal wall. The total PTV varied from 33.59 to 110.23 cc for all patients. According to the dose prescription, the PTV coverage should not be less than 95% of the dose delivered to 95% of the volume.

Following the recommendations in Refs. [15–18], the OARs included the rectum wall divided into four regions (posterior/anterior/right/left), the bladder wall (divided into two parts) and the femoral heads. Table 1 presents the main restrictions of OAR irradiation that were used during treatment planning.

Table 1
Planning aims on OARs used during SBRT treatment planning.

Rectum	Bladder	Femoral heads
$V_{28\,Gy} \leqslant 40\%$ $V_{32\,Gy} \leqslant 33\%$ $V_{25\,Gy} \leqslant 20$ cm^3 $D_{max} \leqslant 105\%$ at an anterior wall $V_{90\%} < 3$ cm^3 at a side wall $D_{max} \leqslant 45\%$ at a posterior wall	$D_{max} \leqslant 105\%$ at a posterior wall	$V_{30\,Gy} \leqslant 10$ cm^3

2.1. Treatment planning and verification

All treatment plans were simulated using the Monaco treatment planning system v5.10 (Elekta Instrument AB, Stockholm) on the Elekta Synergy linac [19] with photon beam energy equal to 10 MV. A VMAT with two partially coplanar arcs was used. The first arc rotated from 220 to 160° clockwise with a collimator angle equal to 300°. The second arc rotated from 140 to 200° counter-clockwise with the collimator angle equal to 90°. The grid spacing was equal to 3 mm. The statistical uncertainty per calculation based on the 'Monte Carlo Photon' algorithm was equal to 0.5%. The minimal segment width was equal to 1 cm. The maximal number of control points per arc was equal to 100.

The quality of the plan delivery was evaluated by measuring the dose distribution using the SunNuclear rotational diode-array phantom ArcCHECK [20]. Each case study was analysed according to TG-244 recommendations for gamma passing rates with more sensitive metrics (2% dose difference at local normalization/2 mm distance-to-agreement/20% Threshold) [21,22]. The VMAT plan was acceptable for treatment if the QA passing rate was higher than 95%.

2.2. TCP calculation

TCP values were calculated using the Niemierko approach based on the equivalent uniform dose (*EUD*) [9,10]:

$$EUD = \left(\sum_i V_i \left(D_i \frac{\alpha/\beta + D_i/n_f}{\alpha/\beta + 2} \right)^a \right)^{-a}. \quad (2)$$

Here, V_i is the part of the target volume irradiated by a dose D_i ($\sum_i V_i = V$), a is the specific parameter equal to $a = -10$ for a tumour, n_f is the number of fractions. Differential DVHs (dDVHs) for the PTV obtained during the Monaco treatment planning were used for the TCP calculation. Because all dDVHs were calculated at the total dose value equal to $D = 36.25$ Gy, the dDVHs for different values of the total doses in the range of 30–40 Gy were obtained by rescaling:

$$D_i^k = D_i^{36.25} \frac{D_{tot}^k}{D_{tot}^{36.25}}. \quad (3)$$

Here, D_i^k is the total dose in the i-th part of the volume for the D_{tot}^k total dose; $D_i^{36.25}$ is the total dose in the i-th part of the volume for the $D_{tot}^{36.25} \equiv 36.25$ Gy total dose. Such rescaling is used in the Monaco treatment planning system, if one changes the total dose value without additional plan optimization. Fig. 1 shows an example of calculated dDVHs for one of the patients. In Fig. 1, one can see dDVHs both for the target (red curve) and the anterior rectal wall (blue curve) at the total dose of $D = 36.25$ Gy. The grey curves demonstrate the examples of the total dose rescaling used for the TCP values calculation.

The TCP can be calculated based on the EUD value as follows [9,10]:

$$TCP = \frac{1}{1 + \left(\frac{TCD_{50}}{EUD} \right)^{4\gamma_{50}}}, \quad (4)$$

where TCD_{50} is the 50% efficiency dose, i.e. $TCP(EUD \equiv TCD_{50}) = 50\%$, γ_{50} is a parameter that depends on the steepness of the TCP curve. Thus, the TCP value depends on α/β, TCD_{50} and γ_{50} parameters. These parameters were obtained from the published

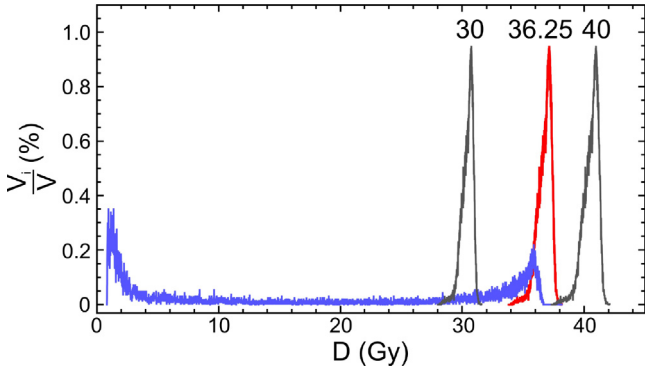

Fig. 1. An example of calculated dDVHs for the PTV (red curve) and the anterior rectal wall (blue curve) at the total dose of $D = 36.25$ Gy. The grey curves show rescaled dDVHs for the total doses of $D = 30$ Gy, and $D = 40$ Gy. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

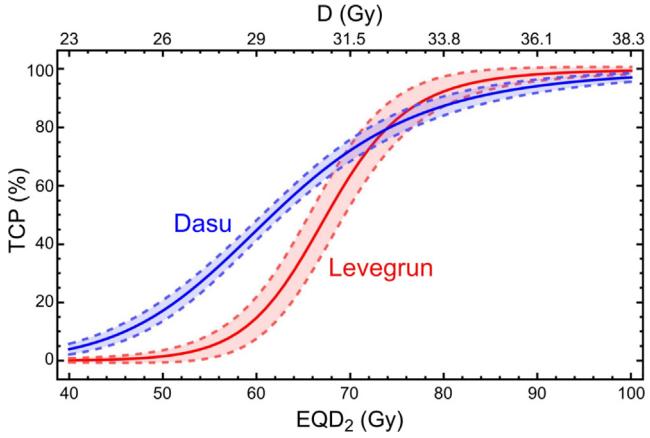

Fig. 2. Dependence of the TCP value on EQD_2 (lower scale) or on dose given in 5 fractions at $\alpha/\beta = 1.5$ Gy (upper scale) for TCD_{50} and γ_{50} values and their uncertainties given by S. Levegrün in Ref. [23] (red curve) and by A. Dasu in Ref. [24] (blue curve). Dashed curves show standard deviations of the calculated TCP values. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

reports [23,24], based on approximation of the clinical data. In our research, we assumed that the parameter values are random ones, and that they follow a Gaussian distribution with the mean values and root-mean-squares equal to $\alpha/\beta = (1.5 \pm 0.31)$ Gy [24], $TCD_{50} = (67.5 \pm 1.9)$ Gy and $\gamma_{50} = (4 \pm 0.9)$ [23]. The TCD_{50} and γ_{50} parameter values presented by S. Levegrün et al. in Ref. [23] were divided into 'high' and 'low' subgroups with respect to T-stage, Gleason score and PSA value. For the patients in our investigation, all T-stages, Gleason scores and PSA values were 'low' according to Levegrün's classification. For this reason, we averaged the corresponding TCD_{50} and γ_{50} values from these 3 subgroups described in Ref. [23]. A. Dasu and I. Dasu in Ref. [24] also presented TCD_{50} and γ_{50} for 'low-risk' patients according to their approximation of clinical data. According to Ref. [24], $TCD_{50}^{Dasu} = (61.7 \pm 1.1)$ Gy and $\gamma_{50}^{Dasu} = (1.9 \pm 0.26)$. Fig. 2 shows the dependence of TCP values and their standard deviations on total dose at the TCD_{50} and γ_{50} values given by S. Levegrün and A. Dasu. From Fig. 2, it is obvious that the parameter values presented by A. Dasu lead to overestimation of the TCP values for the low-dose values. That is why the parameter values proposed by S. Levegrün et al. in Ref. [23] were used.

For the simulation of TCP values, 5000 histories were calculated using random normally distributed α/β, TCD_{50} and γ_{50} values. The simulated TCP value distributions were analysed by the distributions mean value, and 5%-quantile and 95%-quantile were taken as lower and upper uncertainty limits. The TCP and NTCP values numerical simulation and statistical analysis were carried out using the 'Wolfram Mathematica' software [25].

2.3. NTCP calculation

During the SBRT of prostate cancer, the anterior rectal wall is irradiated to the highest doses if one does not take into account urethra that is naturally included in PTV. The NTCP was calculated using both Niemierko and Källman-s approaches [9,10,12,13]. The Niemierko model for NTCP calculation is the same as for the TCP one (see Eqs. (2), (4)). The following parameter values were used for it: $\alpha/\beta = 3.9$ Gy, $TCD_{50} = 80$ Gy, $\gamma_{50} = 4$ and $a = 8.33$ [26,27].

According to the Källman-s model, the NTCP value can be calculated as follows [12,13]:

$$NTCP_K = [1 - \prod_i (1 - F(D_i)^s)^{V_i}]^{-s}, \tag{5}$$

where

$$F(D_i) = 2^{-\exp\left[e\gamma_{50}\left(\frac{D_i\frac{\alpha/\beta + D_i/nf}{\alpha/\beta + 2}}{TCD_{50}}\right)\right]}. \tag{6}$$

Here, s is the OAR relative 'seriality'. In our calculation, we assumed that s is equal to $s = 1.5$.

3. Results

Table 2 shows the average dose coverage of the PTV in the form of a mean value and confidence interval at confidence level of $P = 95\%$. Irradiation of OARs was within the limits as shown in Table 1 for all patients. The average QA passing rate of the dosimetric plans for all patients was equal to 96.8% ([96.0%, 97.7%]) at criterion 2%loc/2 mm/20%.

The dosimetric treatment planning results presented in Fig. 1 and in Table 2 along with the results of treatment plan QA demonstrate that the VMAT plans based on two arcs were very effective. All dosimetric plans delivered more than 97% of the prescription dose to more than 98% of the PTV. At the same time, an overdose of the PTV was not significant and did not exceed 105% for most of the patients and 110% for all patients. The irradiation of the OARs was within the restrictions shown in Table 1. For the bladder and femoral heads, the NTCP values were close to zero. Despite the fact that the anterior rectal wall was partly irradiated with high doses due to its close contact with the PTV, the average dose delivered to the rectum was within the prescribed limits.

Fig. 3 shows an example of TCP, NTCP and UTCP values dependence on the total dose. The distributions were calculated for both 4 and 5 fractions. Error bars show the TCP uncertainty values obtained due to the uncertainties of radiobiological parameters used for the simulation. The NTCP values are shown for both models used. The UTCP values presented were calculated using the results of the Niemierko NTCP model.

Table 2
Percentage of PTV covered by the percentage of prescribed dose averaged over all patients.

D %	V_{PTV}, %	D %	V_{PTV}, %
95	99.8 [99.5, 100.1]	102	48.4 [39.3, 57.5]
96	99.3 [98.7, 100]	103	22.7 [12.5, 32.9]
97	98.5 [97.3, 99.7]	105	2.9 [−0.5, 6.4]
98	96.9 [94.6, 99.1]	107	0.1 [0, 0.15]
99	93.1 [88.8, 97.4]	110	0
100	85.1 [78.6, 91.6]		

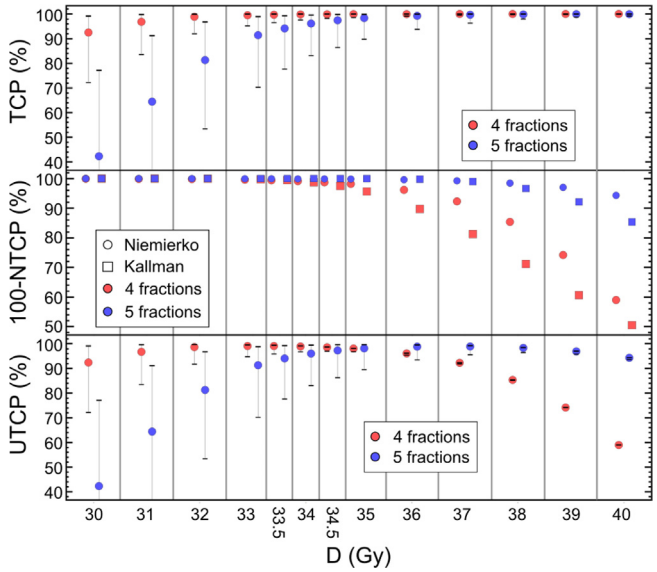

Fig. 3. An example of calculated TCP (upper plot), NTCP (central plot) and UTCP (lower plot) values dependence on total dose. Red points stand for 4 fractions, blue ones stand for 5 fractions. Circles show the Niemierko model and rectangles show the Källman-s model. Error bars show the TCP values' uncertainties obtained due to the uncertainties of radiobiological parameters. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

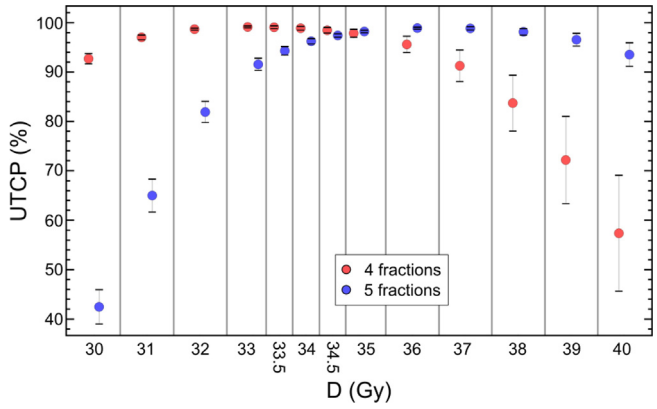

Fig. 4. The UTCP value dependence on total course dose averaged over all 12 patients. Red points stand for 4 fractions, blue ones stand for 5 fractions. The error bars show the confidence interval at confidence level 95%. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 4 shows the dependence of UTCP value on total course dose averaged over all 12 patients. Error bars, in this case, show the confidence interval at confidence level 95%.

4. Discussion

The example in Fig. 3 makes it possible to understand the general dependencies of the TCP, NTCP and UTCP values and the range of their uncertainties on total course dose and the number of fractions.

The TCP values for both 4 and 5 fractions increase with an increase in total dose tending to 100%, as expected. The influence of radiobiological parameters' uncertainties become negligible with the dose increase. In the case of the 4-fraction irradiation scheme for doses higher than 33 Gy, the lower uncertainty limit of a TCP value is higher than 95%. In the case of the 5-fraction irradiation scheme, the same is true for dose values higher than 37 Gy. For these irradiation regimens, one could expect high radiotherapy efficiency for most of the patients.

The NTCP values shown in Fig. 3 in the form of $(100 - NTCP(\%))$ decrease with an increase in total dose, representing higher radiation damage to the anterior rectal wall. The damage is higher when applying 4-fraction irradiation due to the higher dose per fraction. Both NTCP models show the same dependence of NTCP values on the total dose. However, the absolute values of NTCP are different. In general, the Källman-s model predicts higher damage than Niemierko's model. Pearson's correlation coefficient was calculated for pairs of NTCP values given by the Källman-s and Niemierko's models. The resulting correlation coefficients were equal to 0.956 and 0.962, respectively. Such high correlation coefficients show that both models predict negative effects in a similar way, being just different only in absolute values.

The general dependence of UTCP on the total dose includes UTCP value increase to the maximum and then its decrease tending to zero. Such dependence is obviously due to the dependences of TCP and NTCP values on the dose. At low-dose values, even a small dose increase causes an increase in TCP value with a negligible change of NTCP value. At high dose values, the TCP approaches 100%, while $1 - NTCP$ value decreases due to higher damage to OARs. The fractionation regimen shifts the general UTCP dependence along the abscissa axis to higher or lower total dose values. In Fig. 3, the optimal irradiation regimen was chosen to be of 33–34 Gy in 4 fractions or 36–37 Gy in 5 fractions.

The average UTCP dependence shown in Fig. 4 has a similar behaviour to the one discussed before. For each fractionation regimen, there is an optimal total dose that maximizes the UTCP value. For this optimal dose, the confidence interval also appears minimal. In the case of 4 fractions, an optimal total dose value is equal to 33 Gy, and in the case of 5 fractions, it is in the range of 36–37 Gy. The UTCP value change for doses close to optimal is not significant. The dose ranges of 32–34 Gy in 4 fractions and of 35–38 Gy in 5 fractions could be considered for the treatment of patients. For lower and higher doses, the UTCP value decreases and the confidence interval increases due to different TCP and NTCP values for various patients. Doses higher than 35 Gy in 4 fractions are not recommended to be used for the treatment due to significant radiation damage to the anterior rectal wall, as follows from the NTCP calculation results. Doses lower than 35 Gy in 5 fractions result in a low TCP value and should not be considered for the treatment. An additional risk of using low doses is TCP value uncertainty, which might be very high. For example, in the case of 33 Gy given in 5 fractions, the simulated lower TCP uncertainty value shown in Fig. 3 for one of the patients is equal to 70%, while mean TCP value is equal to 90%. It may result in unexpectedly poor control of a tumour.

There have been several clinical trials devoted to SBRT of prostate cancer carried out. In the trials, the total doses were in the range from 33.5 to 50 Gy given in 5 fractions that allowed qualitative comparison of the clinical results and the results obtained on the basis of the TCP/NTCP concept.

B.L. Madsen et al. in Ref. [28] have reported the findings of localized prostate cancer treatment of 40 patients using 33.5 Gy delivered in 5 fractions. The median follow-up period was equal to 41 months. The authors in Ref. [28] have reported that biochemical freedom from relapse was equal to 70% according to ASTRO definition, and 90% if an alternative failure definition 'nadir +2 ng/ml' was used. The acute gastrointestinal (GI) toxicity was equal to 39% (GI). Late Grade 1–2 toxicity was equal to 37% (GI). No late Grade 3 or higher toxicity has been reported. The authors in Ref. [28] have concluded that '…biochemical response seems appropriate; however, it may be possible to achieve a lower PSA nadir and lower rates of biochemical relapse with dose escalation'.

Several other clinical trials have been carried out delivering in 5 fractions the total dose values of 36.25 Gy [29], 35–36.25 Gy [30] and 35–37 Gy [31]. D.E. Freeman and C.R. King in Ref. [29] have claimed a 5-year biochemical progression-free survival rate equal to 92.7% for 41 patients. In the work, 6 cases (13%) of rectal toxicity Grade 1 and 1 case (2.5%) of toxicity Grade 2 were mentioned.

A.J Katz and J. Kang in Ref. [30] have presented the data on 95.6% rate of biochemical recurrence-free survival for a 7-year follow-up period with 3.2% of GI late toxicity Grade 2 for 35 Gy and 4.5% for 36.25 Gy.

J. Davis et al. in Ref. [31] have described the findings of a multicentre SBRT investigation into localized prostate cancer of 437 patients. The total dose values were in the range of 35–37 Gy delivered in 5 fractions. For 78% of the patients, the dose was equal to 36.25 Gy. The two-year biochemical disease-free survival of the patients with low-risk prostate cancer was equal to 99%. The proctitis of late Grade 1 and Grade 2 have been reported as 3% and 2% of cases, respectively.

R. Hannan et al. in Ref. [32] have presented a clinical trial in which total doses of 45–50 Gy were delivered in 5 fractions. In that case, the freedom from biochemical failure was reported to be equal to 100% in 3 years and 98.6% in 5 years. In the case of 50 Gy dose, 6.6% of GI toxicity Grade 3 and 3.3% of GI toxicity Grade 4 were reported [32].

The analysis of clinical trial findings [28,29,31,32] shows that the biochemical progression-free survival increases significantly with an increase in total dose delivered. This fact coincides absolutely with the TCP dose dependence simulated. According to our calculations, a dose change from 33.4 Gy to 40 Gy allows increasing the TCP value from 90% to 100%. The reported results of 92.7–99% biochemical progression-free survivals at 35–37 Gy delivered in 5 fractions reasonably coincides with the simulation models taking into account TCP uncertainties. It is hard to analyse in more detail because the TCP value depends heavily on the PTV coverage level, which is individual for each patient. The dose increase up to 40 Gy delivered in 5 fractions results in 100% TCP value in our simulations, which coincides with the results by R. Hannan et al. [32].

The calculated dependence of TCP on total dose does not contradict the existing clinical results. An interesting point to mention is a calculated second optimal dose value equal to 33 Gy delivered in 4 fractions. To our knowledge, such a treatment scheme has not been tested yet.

The use of TCP/NTCP criteria allows changing the scheme of dose prescription for a particular patient. As a rule, the total dose value and the number of fractions are prescribed before the dosimetric treatment planning using, for example, the BED approach. During the treatment planning procedure, one should optimize the dose distribution within a specific volume according to the prescription. Homogeneity and conformity are the criteria of the plan quality. Thus, one has two independent classes of criteria: dosimetric ones and radiobiological ones. TCP/NTCP criteria allow to 'convert' dosimetric criteria to radiobiological ones and, thus, to combine them. As was mentioned before, TCP/NTCP criteria are used for comparison of different dose distributions and for their optimization [6–8]. However, TCP/NTCP criteria are not used for total dose and fractionation optimization, despite the fact that LQM is naturally included in the TCP/NTCP concept. This fact potentially allows for changing the dose prescription scheme. In the new scheme, the treatment planning starts with some standard prescription. After optimization of the dose distribution, the total dose values and the number of fractions are defined based on the TCP/NTCP value, naturally depending on dose distribution quality for the particular patient. Based on TCP/NTCP criteria, the clinician could decide that, for example, for a particular patient 35 Gy delivered in 5 fractions is optimal, but for another one, 37 Gy delivered in 5 fractions is optimal. The use of TCP/NTCP criteria allows increasing the variety of treatment schemes for the particular clinician treating the particular patient using the particular equipment.

5. Conclusion

As expected, the VMAT dose delivery technique leads to good coverage of the PTV and low irradiation of OARs. We can conclude that the approach used based on 2-arc irradiation has resulted in high-conformality dose field distribution planned with a dosimetric treatment planning system and verified by a 3D dosimeter. This approach has been used in the Tomsk Regional Oncology Centre as a starting template for all new patients with localized prostate cancer.

TCP/NTCP optimization of SBRT of low-risk prostate cancer for 12 patients has shown that there were two optimal fractionation regimens, namely 32–34 Gy in 4 fractions and 35–38 Gy in 5 fractions. At doses lower than the optimal ones, the TCP values were lower than 95%, and TCP uncertainties were significant (80% and lower), which may result in unexpectedly poor treatment results. At doses higher than the optimal ones, the probability of toxicity to the anterior rectal wall became significant. The results obtained on the basis of the radiobiological simulation were in good agreement with the results of the clinical trials on prostate cancer SBRT.

The 5-fractions regimen has been chosen to be the standard one with a total dose equal to 36.25 Gy for all new patients in Tomsk Regional Oncology Centre with low-risk prostate cancer and without contraindications to hypofractionated SBRT.

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