The relationships between the total volumes of OARs and the doses they received in the case of EBRT treatment of the prostate cancer

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Abstract. In the case of the external beam radiotherapy (EBRT) treatment of the prostate cancer there exist two categories of toxicity effects: genito-urinary and gastro-intestinal. The main objective of this work is to investigate the relationships between the total volumes of organs at risk (OARs) and the doses they received in the case of the EBRT treatment of prostate cancer. Knowing these relationships it could be possible to reduce the dose contributions to the OARs by increasing or decreasing their volumes by the intake of an amount of a fluid or applying a special diet during the EBRT treatment and, consequently, in such a way to decrease the possibility of appearing of toxicity effects. Through this work the results obtained by analysis of the data collected from dose volume histograms of 30 patients have been presented. The correlations between the doses received by bladder and rectum and theirs volumes have been investigated. We found the strong significant Pearson’s negative correlations, obtained in the case of bladder between \(D_{\text{mean}}\) and the volume ratios \(V/V_{\text{PTV}}\) \((r = -0.729\) and \(r = -0.707, p < 0.01)\) as well as between \(V_{65}\) and \(V/V_{\text{PTV}}\) \((r = -0.627\) and \(r = -0.605, p < 0.05)\). In the case of rectum only significant positive Spearman’s correlation was found between \(D_{\text{max}}\) and \(V\) \((r = 0.524, p < 0.05)\). The obtained results impose the necessity for monitoring and applying a special and planned diet, as a part of the whole EBRT treatment of prostate cancer in order to ensure the reproducible conditions for OARs.

1. Introduction

Viewing from a position of an external beam radiotherapy (EBRT) treatment success and prevention of disease recurrence, an adequate coverage of the target volume by a prescribed dose is of extreme importance. The dose received by organs at risk (OARs), during this treatment, is related to the toxic effects that accompany a radiotherapy treatment. The likelihood of these effects is mostly related to the dose on the OARs and can significantly affect the quality of life of patients after the treatment.

During an EBRT treatment of the prostate cancer, two categories of toxic effects can occur [1]:

- Genital-urinary (GU), related to the radiation dose received by bladder and
- Gastro-intestinal (GI), related to the radiation dose received by rectum.

It is very complex to make some predictions about the probability of the occurrence and toxicity grade level of the GU effects. This is due to the impacts of numerous factors on the occurrence of the
toxic effects as well as the fact that some of these effects are related to the radiation doses on the different bladder’s substructures [2]. The lack of knowledge about the mechanisms of radiation action on OARs is the additional problem in prediction of the probability of the toxicity effect occurrences and their toxicity grade levels. GU toxic effects are manifested as: incontinence, hematuria, frequent voiding, voiding obstruction and pain when voiding [3].

In order to reduce the possibility of toxicity effect appearances, the various constrains of radiation doses received by OARs have been established to be applied during the treatment planning process. A special diet for patients undergoing EBRT treatment of prostate cancer is the possible to affect bladder and rectum volume changes and thus the dose-volume contribution as well as an occurrence of toxicity effects. Through this work, the correlations between the doses received by bladder and rectum and their total volumes as well as the target volumes have been analyzed.

2. Materials and methods

In the presented analysis we use the data from dose volume histograms (DVHs) for 30 patients undergoing 3D conformal radiotherapy (3DCRT) treatment of prostate cancer. All patients were treated in two or three phases with the total prescribed dose of 72 Gy. The standard fractionation of 2 Gy per fraction was used. The target volume included the prostate and the base of the seminal vesicles. Simulation of the patient in the standard, supine position was performed on a CT simulator Philips Brilliance 6. The standard CT protocol for pelvis imaging was used during the simulation: slice thickness 5 mm, pitch factor 1, FOV 500, tube voltage 120 kV and tube current 200 mA.

After the process of CT simulation has been completed, the delineation of the planning treatment volumes (PTVs) was performed on the FOCAL system for planning radiotherapy treatment, for all three phases of the treatment, as well as OARs: rectum, bladder and femoral bones.

The treatment preparation was performed on the Elekta’s XiO treatment planning system (TPS) using the six radiation therapy treatment fields technique [4]. The requirement for a minimum of 95% coverage of treatment volumes with prescribed dose, in each of treatment phases, was applied for each treatment plan as well as dose constrains to the OARs according to recommendations [5, 6, 7].

The treatment plan evaluations were done on the basis of DVHs. Data collected for PTVs have implied their total volumes $V_{PTV1}$ and $V_{PTV2}$. Data collected for bladder and rectum have implied: their total volumes $V$, $V_{65}$, $D_{\text{max}}$ and $D_{\text{mean}}$. The analysis included the determination of the values of Pearson’s and, in the case when the assumption of normality was violated, Spearman’s correlation coefficients between $V_{65}$, $D_{\text{max}}$ and $D_{\text{mean}}$ values for OARs in relation to their total volumes as well as in relation to the volumes of the PTVs, e.g. $V_{PTV1}$ and $V_{PTV2}$ and their corresponding $D_{\text{max}}$ values. The statistical analysis was done using IBM SPSS Statistics Software Version 23.

3. Results

Table 1. Descriptive statistics for bladder and rectum.

|        | Bladder | Rectum |
|--------|---------|--------|
| $D_{\text{max}}$ (Gy) | $N$ | Mean | Std. Deviation | $N$ | Mean | Std. Deviation |
|        | 26 | 72.05 | 1.33 | 16 | 66.61 | 18.98 |
| $D_{\text{mean}}$ (Gy) | 26 | 49.81 | 11.13 | 16 | 35.59 | 10.32 |
| $V_{65}$ (cc) | 26 | 33.12 | 19.84 | 16 | 26.54 | 15.29 |
| $V$ (cc) | 26 | 112.43 | 52.28 | 16 | 72.27 | 16.61 |

Prior to the statistical analysis of Pearson’s or Spearman’s correlation, in the case when the normal distribution assumption was violated, the collected data were tested to normal distribution by using the Shapiro-Wilk test of normal distribution. Then, the descriptive statistic data were obtained. In the case of bladder, due to the outliers, data for four patients were excluded from the analysis, so the analysis...
was performed on the sample of 26 patients in total. In the case of rectum, data of 16 patients were used in the analysis. The assumption of normal distribution was violated in the case of \(D_{\text{max}}\) and \(D_{\text{mean}}\) samples for rectum. The results of a descriptive statistic for OARs are shown in table 1. The results of the correlations analysis for bladder and rectum are shown in table 2 and 3, respectively.

### Table 2. Pearson’s correlations for bladder.

| \(D_{\text{max}}\) (Gy) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|-------------------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Pearson Correlation     | 0.143      | 0.664                 | 0.563                 | -0.373                 | -0.402                 |
| Sig. (2-tailed)         | 0.485      | 0.000                 | 0.003                 | 0.061                  | 0.042                  |
| \(N\)                  | 26         | 26                    | 26                    | 26                     | 26                     |

| \(D_{\text{mean}}\) (Gy) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|--------------------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Pearson Correlation      | -0.490     | 0.677                 | 0.620                 | -0.729                 | -0.707                 |
| Sig. (2-tailed)          | 0.011      | 0.000                 | 0.001                 | 0.000                  | 0.000                  |
| \(N\)                   | 26         | 26                    | 26                    | 26                     | 26                     |

| \(V_{65}\) (cc) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|-----------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Pearson Correlation | -0.440     | 0.712                 | 0.641                 | -0.627                 | -0.605                 |
| Sig. (2-tailed)  | 0.025      | 0.000                 | 0.000                 | 0.001                  | 0.001                  |
| \(N\)           | 26         | 26                    | 26                    | 26                     | 26                     |

### Table 3. Spearman’s and Pearson’s correlations for rectum.

| \(D_{\text{max}}\) (Gy) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|--------------------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Spearman’s \(\rho\) Correlation Coefficient | 0.524      | 0.394                 | 0.541                 | -0.247                 | -0.347                 |
| Sig. (2-tailed)          | 0.037      | 0.131                 | 0.030                 | 0.356                  | 0.188                  |
| \(N\)                   | 16         | 16                    | 16                    | 16                     | 16                     |

| \(D_{\text{mean}}\) (Gy) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|--------------------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Spearman’s \(\rho\) Correlation Coefficient | 0.132      | 0.368                 | 0.453                 | -0.350                 | -0.488                 |
| Sig. (2-tailed)          | 0.625      | 0.161                 | 0.078                 | 0.184                  | 0.055                  |
| \(N\)                   | 16         | 16                    | 16                    | 16                     | 16                     |

| \(V_{65}\) (cc) | \(V\)     | \(V_{\text{PTV1}}\) | \(V_{\text{PTV2}}\) | \(V/V_{\text{PTV1}}\) | \(V/V_{\text{PTV2}}\) |
|-----------------|------------|-----------------------|-----------------------|------------------------|------------------------|
| Pearson Correlation | 0.321      | 0.501                 | 0.482                 | -0.423                 | -0.420                 |
| Sig. (2-tailed)  | 0.225      | 0.048                 | 0.058                 | 0.103                  | 0.105                  |
| \(N\)           | 16         | 16                    | 16                    | 16                     | 16                     |

### 4. Discussion

#### 4.1. Descriptive statistics

From table 1 it is obvious that the mean value of \(D_{\text{max}} = 72.05\) Gy for bladder corresponds to the total prescribed dose (72 Gy) to the target volume, which can be explained by the fact that one part of the bladder volume is covered by the radiation fields or it is delineated as a part of the target volume. The same can be concluded for rectum for which \(D_{\text{max}} = 66.61\) Gy. The slightly lower mean \(D_{\text{max}}\) value for rectum could be a consequence of the more pronounced tendency to spread it more during the treatment plan preparation. On the other hand, the mean value of \(D_{\text{mean}}\) for both OARs, is far below the prescribed dose to the target volume due to the fact that the most of bladder and rectum volume is outside the radiation field. The percentage of the total volumes received the dose of 65 Gy \((V_{65} = 33.12\% \text{ for bladder and } V_{65} = 26.54\% \text{ for rectum})\) are far below constrain.
4.2. Correlations - bladder

According to the results presented in table 2, a significant Pearson’s positive correlation was found between \( D_{\text{max}} \) and the total volumes of PTVs, e.g. \( V_{\text{PTV1}} \) and \( V_{\text{PTV2}} \) (\( r = 0.664 \) and \( r = 0.563 \), respectively, \( p < 0.01 \)). This is mainly caused by the fact that a part of bladder’s volume is located in the treatment area and, as such, it received more than 95% of the prescribed dose. For the same reasons significant correlation was not found between \( D_{\text{max}} \) and the total bladder’s volume.

A significant negative Pearson’s correlation was found between \( D_{\text{mean}} \) and bladder’s volume \( V \) (\( r = -0.490, p < 0.05 \)). This can be explained in a way that, when bladder’s volume increases a percentage of this volume, placed outside a radiation field area, also increases reducing the mean dose received by bladder. Even more, an increase in bladder’s volume leads also to an increase of the \( V/V_{\text{PTV}} \) ratios and, as a consequence, the significant Pearson’s negative correlations were obtained between \( D_{\text{mean}} \) and the ratios \( V/V_{\text{PTV1}} \) (\( r = -0.729, p < 0.01 \)) and between \( D_{\text{mean}} \) and \( V/V_{\text{PTV2}} \) (\( r = -0.707, p < 0.01 \)). The significant Pearson’s positive correlations were found between \( D_{\text{mean}} \) and volumes \( V_{\text{PTV1}} \) and \( V_{\text{PTV2}} \) (\( r = 0.677 \) and \( r = 0.620 \), respectively, \( p < 0.01 \)). An increase in the PTV volumes causes also an increase of bladder’s volume located in the treated area.

For the same reasons as in the case of \( D_{\text{mean}} \) a significant Pearson’s negative correlation between \( V_{65} \) and \( V \) (\( r = -0.440, p < 0.05 \)), between \( V_{65} \) and the ratios \( V/V_{\text{PTV1}} \) and \( V/V_{\text{PTV2}} \) (\( r = -0.627 \) and \( r = -0.605 \), respectively, \( p < 0.05 \)) as well as between \( V_{65} \) and volumes \( V_{\text{PTV1}} \) and \( V_{\text{PTV2}} \) (\( r = 0.712 \) and \( r = 0.641 \), respectively, \( p < 0.01 \)) were found.

4.3. Correlations – rectum

In the case of rectum only significant positive Spearman’s correlations were found between \( D_{\text{max}} \) and \( V \) (\( r = 0.524, p < 0.05 \)) and between \( D_{\text{max}} \) and \( V_{\text{PTV2}} \) (\( r = 0.541, p < 0.05 \)). As in the case of bladder, this is mainly caused by the fact that a part of bladder’s volume is incorporated in a treatment area and as such it received more than 95% of a prescribed dose.

A significant Pearson’s positive correlation between \( V_{65} \) and \( V_{\text{PTV1}} \) (\( r = 0.501, p < 0.05 \)) was found. This is due to the fact that an increase in the target volume \( V_{\text{PTV1}} \) will increase a percentage of the total rectum’s volume, directly exposed to the radiation field, which received the radiation dose of 65 Gy.

5. Conclusion

The strong significant negative correlations obtained in the case of bladder between \( D_{\text{mean}} \) and ratios \( V/V_{\text{PTV}} \), as well as between \( V_{65} \) and ratios \( V/V_{\text{PTV}} \) impose the necessity for monitoring and applying a special and planned diet during EBRT treatment of prostate cancer. Even more, this should be done to ensure the reproducible conditions for bladder during the treatment time. In such a way, the predictions about the doses received by bladder during the treatment, made on the basis of DVHs data, becomes more reliable.

Although a less strong correlations between \( D_{\text{max}} \) and \( V \) for rectum, for the same reasons as in the case of bladder, the abovementioned diet approach needs to be included as a part of the whole treatment.

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