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DOZIMETRIJSKA VERIFIKACIJA KLINIČKOG SISTEMA ZA PLANIRANJE RADIOTERAPIJE

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Dosimetric verification of clinical radiotherapy treatment planning system

Dozimetrijska verifikacija kliničkog sistema za planiranje radioterapije

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Abstract

Background/Aim. The aim of the study was investigating the significant difference in: a) the dosimetric calculation of the radiotherapy treatment planning system (TPS) in relation to the values obtained by measuring on the linear accelerator (Linac), b) the accuracy of the dosimetric calculation between the calculating algorithms Analytical Anisotropic Algorithm (AAA) and AcurosXB in various tissues and photon beam energies. Methods. For End-to-End test we used the heterogeneous phantom CIRS Thorax002LFC, which anatomically represents the human torso with set of inserts known relative electron density (RED) for obtaining a CT calibration curve, comparable to the “reference” CIRS 062M phantom. For the AAA and AcurosXB algorithms and for 6 MV and 16 MV photon beams in the TPS Varian Eclipse 13.6, four 3D conformal (3DCRT), and one intensity modulated (IMRT) and volumetric modulated arc (VMAT) radiotherapy plans were made. Measurements of the absolute dose in the Thorax phantom, by PTW-Semiflex ionization chamber, were carried out on three Varian-DHX Linacs. Results. The difference between "reference" and measured CT conversion curves in the bone area is 3 %. For 476 phantom measurements, the difference between measured and TPS calculated dose of (3-6) %, we had in 30 (6.3 %) cases. According to regression analysis, the standardized Beta coefficient for relative errors, 6 MV vs 16 MV, was 0.337 (33.7 %, p < 0.001). Mean relative errors for AAA vs AcurosXB, using Mann-Whitney test, for bones were 1.56 % and 2.64 % (p = 0.004). Conclusion. The End-to-End test on Thorax002LFC phantom proved the accuracy of TPS dose calculation in relation to the one delivered to the patient by Linac. There is a significant difference for photon energies relative errors (higher values are obtained for 16 MV vs 6 MV). A statistically significant minor relative error in AAA vs. AcurosXB was found for the bone.

Key words: TPS, End-to-End test, heterogeneous phantom, calculating algorithms.
Apstrakt

Uvod. Cilj studije je bio istražiti da li postoji značajna razlika u: a) dozimetrijskoj kalkulaciji sistema za planiranje radioterapije (TPS) u odnosu na vrednosti dobijene merenjem u fantomu na linearnom akceleratoru (Linac), b) tačnosti dozimetrijskog proračuna između kalkulacionih algoritama Analytical Anisotropic Algorithm (AAA) i AcurosXB u različitim tkivima i energijama fotonskih snopova. Metode. Za End-to-End test koristili smo heterogeni fantom CIRS Thorax002LFC, koji anatomski predstavlja ljudski torzo sa setom umetaka poznate relativne elektronske gustine (RED) za dobijanje CT kalibracione krive koja se poredi sa referentnom dobijenom CIRS 062M fantomom. Za AAA i AcurosXB algoritme te za 6 MV i 16 MV fotonske snopove u TPS Varian Eclipse 13.6, napravljeno je četiri 3D konformalna (3DCRT), jedan intenzitetom modulisan (IMRT) i jedan zapreminski modulisan lučni (VMAT) radioterapijski plan. Merenja apsolutne doze u mernim pozicijama Thorax fantoma, jonizacionom komorom PTW-Semiflux, sprovedena su na tri Varian-DHX Linac-a. Rezultati. Razlika „referentne“ i merene CT konverzione krive u oblasti kostiju je 3 %. Od ukupno 476 mernih tačaka, razliku izmerene i TPS izračunate doze (3-6) %, imali smo u 30 tačaka (6.3 %). Regresionom analizom, standardizovani koeficijent Beta za relativne greške, 6 MV vs 16 MV je 0.337 (33.7 %, p < 0.001). Srednje vrednosti relativnih grešaka za AAA vs AcurosXB, koristeći Mann-Whitney test, za kosti su 1.56 % i 2.64 % (p = 0.004). Zaključak. End-to-End test na Thorax002LFC fantomu je dao potvrdu ispravnog računanja doze TPS-a u odnosu na pacijentu Linac-om isporučenu. Postoji značajna razlika relativnih grešaka između fotonskih energija (dobijene su veće vrednosti za 16 MV u odnosu na 6 MV). Utvrđena je statistički značajno manja relativna greška kod AAA vs AcurosXB, za kost. Ključne reči: TPS, End-to-End test, heterogeni fantom, kalkulacioni algoritmi.
Introduction

Modern radiotherapy (RT) undoubtedly represents the technologically most complex branch of medicine today. In the treatment of malignant diseases, as a cure we use ionizing radiation directed towards the volume in which the tumor cells are located, in order to permanently destroy them with the maximum possible protection of the surrounding healthy tissue.

In the past two decades, with the development of information technology, we have witnessed the emergence of new ones: radiation therapy techniques, radiotherapy treatment planning systems (TPS) with calculating algorithms for the dosage calculation in a patient, units for multisliced computed tomography (CT) and image-guided treatment delivery, which enables better and more precise treatment for patients.

Based on the data set previously measured on the Linac and CT simulator, TPS calculates three-dimensional (3D) dose distribution in the patient. Unfortunately, many cases of incorrect data imports and usage of TPS were published, which also led to accidents with lethal outcome 1,2.

Namely, 28% of accidents in RT are due to the wrong TPS dose calculations, caused by: poor knowledge of TPS, incorrect data entered in TPS, and lack of TPS calculation quality assurance (QA TPS) 3. International recommendations are that the delivered dose of radiation in the patient is no more than 5% different than prescribed, and the incidence of TPS calculation errors is less than (3-4)% depending on the complexity of the RT treatment and anatomy. On the other hand, sub-dosage of the tumor of 5% affects the reduction of the treatment curability by around 20%, which points to the importance of the accuracy and precision of each procedure performed during the implementation of the RT treatment 4.

Therefore, the implementation of the QA-TPS procedure (such as the "End-to-End" test) for TPS in RT is crucial for reducing the number of accidents. There are several studies that helped develop guidelines and protocols for linear accelerators (Linac) based QA TPS for
3D Conformal Radiotherapy (3DCRT) \(^5\text{-}^8\) and Intensity Modulated Radiotherapy (IMRT) \(^9\text{-}^{10}\) depending on the calculation algorithm used in TPS \(^{11}\text{-}^{12}\). Nowadays, in addition to 3DCRT and IMRT radiation techniques, volumetric modulated arc therapy (VMAT) is also used in routine practice.

It is clear that preparation and implementation of an “End-to-End” test is of great importance, which is used to control the overall precision of the entire RT chain. It is made up of a set of practical tests conducted on a heterogeneous phantom. In general, an “End-to-End” test consists of: a) recording a calibration curve on a CT simulator and comparing it with a reference (entered into TPS), b) creating characteristic RT plans of all RT techniques, energies of photon beams and calculating algorithms, c) irradiation prepared plans on Linac and measuring doses in defined phantom positions (type of tissue).

Based on the “End-to-End” test, we have launched a dosimetric study to investigate: a) whether there is a significant difference in the dosimetric calculation of TPS (for: 3DCRT, IMRT and VMAT radiation techniques) in relation to the value obtained by Linac measuring in the phantom, b) whether there is a significant difference in the accuracy of the dosimetric calculation between the calculation algorithms Analytical Anisotropic Algorithm (AAA) and AcurosXB, depending on the type of tissue in which the dose is applied and photon beam energies.

**Material and Methods**

Under the same, standardized, methodological principles, this study investigated the influence of various RT factors: radiation techniques, photon beam energy, calculation algorithm and tissue types, in regards to the TPS calculated dose. Dosimetric tests cover all techniques of external beam radiotherapy (EBRT) and anatomical structures are similar to those encountered when working with patients. All-round testing was carried out at the same facility in a relatively short period of time by engaging a same professional team, which generally implies repeatability and accuracy of the measurement.
Phantom
In all segments of this study, was used the heterogeneous phantom CIRS Thorax002LFC (Computerized Imaging Reference Systems Inc., Norfolk, Virginia), which anatomically represents the average human torso (30 cm long, 30 cm wide and 20 cm thick). It is made of plastic water, lungs (density 0.21 g/cm³) and bone-spinal cord (1.6 g/cm³), with 10 cylindrical inserts where the ionization chamber can be placed (Figure 1) and the dose measured at the particular place. The phantom also has a set of inserts (muscle, bone, lung and adipose equivalent tissue) of known relative electron densities (RED)\textsuperscript{13}.

![Figure 1. CIRS Thorax002LFC phantom with inserts for soft tissue (1-5), lungs (6-9) and bone (10).](image)

Scanning the Phantom on a CT simulator
The Thorax002LFC phantom was scanned on a sixteen slice CT simulator LightSpeed (GE, Boston, Massachusetts) gantry wide bore 80 cm diameter, at a voltage in the X ray tube of 120 kV (thorax protocol). First it was scanned with inserts of known electron density, in order to obtain the CT calibration curve that is the ratio between RED and Hounsfield units (HU). The materials used are in the range of -1000 for air, 0 for water and 1000 HU for materials that simulate the bone. The obtained curve is compared with the “reference” curve in TPS, which was created by scanning the CIRS 062M phantom (25 cm long, 33 cm wide and 27 cm thick) that possesses 16 inserts with a known RED under the same conditions of the CT simulator. Acceptable difference RED for the same HU value, between curves, is \(\pm 0.02\) (i.e. \(\pm 20\) HU for the same RED value, except for water \(\pm 5\) HU)\textsuperscript{4}. The second time, the Thorax002LFC phantom is scanned (thorax protocol) with the corresponding cylindrical tissue inserts (Figure 1), for the making of a set of RT plans in the TPS.
The creation of clinical RT plans for dosimetric measurements

For study purposes, in the EBRT radiotherapy planning system Varian Eclipse 13.6 (Varian, Medical Systems, Palo Alto, California), six RT plans were made, four 3DCRT, one IMRT and VMAT. All plans were made for two photon energies 6 MV and 16 MV, as well as for two calculating algorithms: AAA and AcurosXB. This way, the isodose distribution in the phantom was obtained, i.e. we got the absolute dose in different tissues (measuring points).

The beams geometry and the isodose distribution as well as the position of the measuring points of the 3DCRT plans are shown in Figure 2, while the detailed parameters of the plans are given in Table 1.

Figure 2. CIRS Thorax002LFC phantom with measuring points (1-10), beam geometry and isodose distribution for four 3DCRT RT plans, clinical tests 1-4.
| Clinical test 1 | Clinical test 2 | Clinical test 3 | Clinical test 4 |
|----------------|----------------|----------------|----------------|
| SSD 100 cm     | SAD, isocentre at point 1 | SAD, isocentre at point 5 | SAD, isocentre at point 5 |
| 1 direct field | 1 tangential field | 4 fields-box | 3 non-coplanar fields |
| field size (FS) 20x10 cm² | FS 15x10 cm² | FS AP and PA 15x10 cm² | FS 4x4 cm², G 30°, C 0°, Table 90° |
| gantry (G) and collimator (C) angle 0° | G and C 90°, wedge 60° | FS LatLeft and Right 15x8 cm² | FS LatLeft 4x16 cm², G 90°, C 60°, LatRight 4x16 cm², G 270°, C 300° |
| deliver 2 Gy to point 3 | deliver 2 Gy to point 1 | deliver 2 Gy to point 5 | deliver 2 Gy to point 5 |
| measurement points: 1 - 10 | measurement points: 1 - 4 | measurement points: 1 - 6, 8, 10 | measurement point: 5 |

For the purposes of making IMRT and VMAT RT plans, at the transverse CT slices of the CIRS Thorax002LFC phantom, planning target volume (PTV) and the heart are contoured at the length of 8 cm, while the lung and spinal cord are contoured to the entire length of the phantom. (Figure 3)¹⁰. Detailed geometric-dosimetric parameters of these plans with dose limits for organs at risk (OAR), are given in Table 2.

Figure 3. IMRT and VMAT RT plans with beam geometry and isodose distributions, as well as the locations of measuring points (1 - 10).
Table 2 Geometric parameters of IMRT and VMAT RT plans with dose limits for OAR.

| Clinical test 5 | IMRT | Clinical test 6 | VMAT |
|-----------------|------|-----------------|------|
| SAD- 9 IMRT fields | K 0°, G: 0, 40, 80, 120, 160, 200, 240, 260, 280, 320° | SAD-1 full arc | K 30°, G: 181 - 179°, clockwise |
| Deliver 2 Gy to PTV (100 % at target mean) | | | |
| Dose constraints for OAR: | | | |
| Spinal cord: $D_{\text{max}} < 75 \%$ of the prescribed dose | | | |
| Total lung: $D_{20\%} < 35 \%$ | | | |
| Heart: $D_{\text{max}} < 55 \%$ of the prescribed dose | | | |
| measurement points: 1 - 10 | | | |

Measurements on Linacs

The measurements were carried out on three Varian DHX Linacs (Varian Medical Systems, Palo Alto, California), with multi leaf collimator (MLC) Millennium120 and nominal photon energies of 6 MV and 16 MV. One of the Linac has no option of VMAT delivering. To measure the absolute dose in the defined measuring positions of the Thorax002LFC phantom, we used the PTW-Semiflex 0.125 cm$^3$ ionization chamber (Freiburg, Germany) with the SuperMax electrometer (Standard Imaging Inc., Middleton, Wisconsin). The ionization chamber and the electrometer were previously calibrated in the secondary standard dosimetry laboratory. Measurement uncertainty (for measuring chain) is expressed as combined and expanded measurement uncertainty with expansion factor $k = 2$ (95 %).

The absorbed dose at all the measuring points was determined based on the IAEA TRS 398 protocol $^{14}$. In the lungs and materials equivalent to bone, doses are measured in small water volumes (volume of ionization chamber) within these materials. Therefore, the measured doses in these points may have a larger error than the spots in plastic water. The influence of these small water volumes can be increasing the calculated dose up to 2 % for a material equivalent to the lungs and 0.3 % for a material equivalent to the bone $^{15}$.

The total number of measuring points on three Linacs was 476, that is, 132 on Linac 1 (92 for 3DCRT and 40 IMRT), 172 on Linac 2 (92 3DCRT and 40 IMRT/VMAT) and 172 on Linac 3 (92 3DCRT and 40 IMRT/VMAT). Divided by tissues, 280 measurements were done on soft tissue, 152 in the lungs, and 44 in the bone. Two hundred and thirty-eight measurements were done on photon beams 6 MV and 16 MV, as well as with calculating algorithms AAA and AcurosXB.

Statistical Analysis

Evaluation of the absolute dose values measured at each measuring position on Linac ($D_{\text{meas}}$) and calculated on TPS ($D_{\text{cal}}$), due to a limited number of measuring positions in the
Thorax002LFC phantom, was normalized with the dose measured at the reference point $(D_{\text{meas,ref}})$ for each test. Therefore, the equation for calculating the relative error is:

$$X(\%) = 100\% \left( \frac{D_{\text{cal}} - D_{\text{meas}}}{D_{\text{meas,ref}}} \right)$$

(1)

Allowed deviations for 3DCRT plans were $(2-4)\%$, while for IMRT/VMAT $(3-4)\%$ (Figure 5-6).

Data are presented as arithmetic mean value with standard deviation (SD) or confidence interval (CI). The Kolmogorov-Smirnov test was applied to assess the normality of the studied continuous data.

Strength of the association between independent factors (accelerators, algorithms, tissues, photon energies, tests) and relative error data (dependent factor), was determined by using univariate and multiple linear regression analysis. Further detailed assessment was carried out using GLM univariate ANOVA (post hoc Bonferroni test) and Mann-Whitney U tests.

All the analyses were estimated at minimal $p < 0.05$ level of statistical significance.

Complete statistical analysis of data was done with the statistical software package, SPSS Statistics 18 (USA).

**Results**

**CT to RED conversion**

By measuring HU values for known RED values, we obtained the CT conversion curve for the CIRS Thorax002LFC phantom. The obtained curve was compared with the "reference" (TPS) curve, where the difference in the area of large electronic densities is seen (Figure 4), while in the lower density region, the match is within the allowed values. The RED values for bones (829 HU) differ by 3 % while the difference in HU (RED 1.51) is 10 % (Figure 4).

![Figure 4](image.png)

Figure 4. Shows CT calibration curves obtained by CIRS Thorax002LFC and CIRS 062M phantom ("reference" curve located in TPS).
**Results of clinical test cases**

The differences between measured and TPS calculated doses at different measuring points (tissues) and RT plans (case 1 - 6), with values of tolerances (agreement criteria) measured on three Linacs are presented in Figures 5 and 6. The results are grouped by calculating algorithms and photon beam energies.

Figure 5. Difference between measured and TPS calculated doses in each of the tests (cases) and measuring points for the AAA calculation algorithm and (a) 6 MV photon beam, (b) 16 MV photon beam.
Figure 6. Difference between measured and TPS calculated doses in each of the tests (cases) and measuring points for the AcurosXB calculation algorithm and (a) 6 MV photon beam, (b) 16 MV photon beam.

Of the total of 476 measuring points, the difference between measured and the TPS calculated doses greater than 4 %, we had in 11 points (2.3 %), (4-5) % in 10 points (2.1 %) and (5-6) % in one position (0.2 %). A (3-4) % deviation was recorded at 19 measuring points (4 %). The calculated (TPS) dose was in 353 cases (74.2 %) lower than measured and in 123 measurements (25.8 %) higher.

As Kolmogorov-Smirnov test revealed non normal distribution of relative errors, some data transformation was necessary.
Firstly, negative sign marks obtained in any point, were corrected by adding corresponding fix value to all data. This way, all relative errors have become positive. In the second part, these data were further transformed by applying $\log_{10}(X)$ transformation and used in all presented analysis.

Using the univariate and multivariate regression analysis, the effect of independent (explanatory) variables on the relative errors X (%), was examined (Table 3).
Table 3. Univariate and multiple linear regression analysis of independent factors potentially associated with inaccurate dose calculation (measured vs calculated).

| Independent variables          | Univariate |          |          | Multiple |          |
|-------------------------------|------------|----------|----------|----------|----------|
|                               | Beta¹ (95% CI²) | p-value | Beta (95% CI) | p-value |
| Linac (1-3)                   | -0.013 (-0.018-0.013) | 0.769 | 0.009 (-0.012-0.015) | 0.825 |
| Algorithm (AAA vs AcurosXB)   | 0.112 (-0.006-0.054) | 0.015 | 0.112 (0.009-0.052) | 0.006 |
| Tissue (soft vs lung vs bone) | 0.259 (0.035-0.071) | <0.001 | 0.272 (0.039-0.072) | <0.001 |
| Energy (6 MV vs 16 MV)        | 0.337 (-0.068-0.114) | <0.001 | 0.337 (0.069-0.113) | <0.001 |
| Case (1-6)                    | -0.163 (0.005-0.018) | <0.001 | -0.183 (-0.007-0.019) | <0.001 |

¹Standardised regression coefficient  
²Confidence interval (unstandardized coefficient B)

Using the univariate analysis of variance (GLM model, ANOVA), we examined the main effects of independent predictors on the relative error $X$ (%) (Table 4). Because of the large number of potential interactions of independent variables (total of 26), their effects on the measured results were not shown.

Table 4. GLM univariate ANOVA (main effects of independent variables)

| Parameters                          | F   | Significance |
|-------------------------------------|-----|--------------|
| Linac (1-3)                         | 1.546 | p=0.215 |
| Algorithm (AAA vs AcurosXB)         | 15.591 | p<0.001 |
| Tissue (soft tissue vs lung vs bone)| 30.309 | p<0.001 |
| Energy (6 MV vs 16 MV)              | 51.432 | p<0.001 |
| Case (1-6)                          | 14.230 | p<0.001 |

For independent predictors, in which a statistically significant effect was found for the relative errors (deviations), the significance of the differences between the mean values of the relative errors of certain categories was investigated, using the Bonferroni test (steam comparisons). The overview of this analysis is given in Table 5.
Table 5. Significance of differences in: calculating algorithms, type of tissue, photon beam energy and radiation techniques (cases), using the Bonferroni test.

| Parameters          | Deviation (%), absolute values | Significance\(^1\) |
|---------------------|--------------------------------|-------------------|
|                     | N     | X ± SD                  |                   |
| Algorithm:          |       |                         |                   |
| AAA (1)             | 238   | 1.36 ± 1.10             | 1 : 2 – p < 0.001 |
| AcurosXB (2)        | 238   | 1.46 ± 1.06             |                   |
| Tissue              |       |                         |                   |
| Soft tissue (1)     | 280   | 1.26 ± 0.99             | 1 : 2 – p = 1.000 |
| Lung (2)            | 152   | 1.48 ± 1.10             | 1 : 3 – p < 0.001 |
| Bone (3)            | 44    | 2.10 ± 1.27             | 2 : 3 – p < 0.001 |
| Photon beam energy  |       |                         |                   |
| 6 MV (1)            | 238   | 1.12 ± 0.94             | 1 : 2 – p < 0.001 |
| 16 MV (2)           | 238   | 1.69 ± 1.13             |                   |
| Case                |       |                         |                   |
| Case 1              | 120   | 1.59 ± 1.15             | 1 : 2 – p < 0.001 |
| Case 2              | 48    | 1.51 ± 1.31             | 1 : 3 – p < 0.001 |
| Case 3              | 96    | 1.00 ± 0.87             | 1 : 5 – p < 0.001 |
| Case 4              | 12    | 1.80 ± 1.09             | 1 : 6 – p = 0.003 |
| Case 5              | 120   | 1.41 ± 1.07             | 4 : 5 – p = 0.033 |
| Case 6              | 80    | 1.50 ± 0.95             | 5 : 6 – p > 0.044 |

\(^1^\) post hoc Bonferroni test

In addition, we investigated the magnitude of the mean value of the relative errors, depending on the calculation algorithms and tissue types (Table 6) with the Mann-Whitney U test.

Table 6. Algorithm and tissue depending differences.

| Tissue | AAA     | AcurosXB | Probability\(^2\) |
|--------|---------|----------|-------------------|
|        | Mean (%)| 95 % CI \(^1\) | Mean (%)| 95 % CI | (p) |
| Soft   | 1.15    | 0.99 - 1.31 | 1.37     | 1.20 - 1.54 | 0.072 (n.s.) |
| Lung   | 1.68    | 1.40 - 1.97 | 1.27     | 1.07 - 1.47 | 0.085 (n.s.) |
| Bone   | 1.56    | 1.01 - 2.10 | 2.64     | 2.16 - 3.13 | 0.004 |

\(^1\)Confidence intervals; \(^2\)Mann-Whitney U test
Discussion

Based on the comparison of the „reference“ and measured conversion curves, we established a difference in the area of higher electronic densities (RED values for bones vary by 3 %), while in lower density areas, the match is within the allowed values (Figure 4). However, it is estimated that difference of 8 % in bone relative electron density affects dose TPS calculation accuracy less than 1 % 16.

Out of a total of 476 measuring points, the deviation between TPS calculated and measured doses of (3-6) % was obtained in 30 measuring points (6.3 %) (Figures 5, 6).

The measured dose is in 188 cases (79 %) higher than TPS calculated for AcurosXB, while in the case of AAA the same is noticed in 165 (69.3 %) cases. Depending on the tissue type, the measured dose in bone is in the 88.6% of the cases higher than the calculated, for the lungs in 76.3 % and soft tissue in 70.7 %.

When the bone tissue is analyzed independently, the AcurosXB leads in 95.5 % of points to the increased measured dose in relation to the calculated (81.8 % in the case of the application of the AAA algorithm).

Based on the univariate and multivariate regression analysis, we can notice a significant influence of calculating algorithms, tissue type, photon beam energy and test type (Case 1-6) on the relative error (deviation) in both models (Table 3). This data indicate that these variables are significant independent predictors with an influence on the size of the relative error. Depending on the Linacs, there is no significant effect on the size of the relative error. Based on the value of the standardized Beta coefficient (Table 3), the greatest influence on the relative error is the photon beam energy (Beta = 0.337; 33.7 %), then on the tissue type (Beta = 0.272; 27.2 %), test types (Beta = -0.183; 18.3 %) and the applied calculation algorithm (Beta = 0.112; 11.2 %). The direction of the sign (+ or -) indicates that greater relative errors can be expected when using 16 MV in comparison to 6 MV (which is in accordance with the results of the studies Gershkevitsh et al.17, Rutonjski et al.15 and Knoos et al.18), in bone tissue compared to soft tissue and lungs, in tests-cases 1 and 2 (compared to others cases) and in the application of the calculation algorithm AcurosXB vs. AAA.
Using the univariant analysis of variance (GLM model, ANOVA), this study confirmed significant effects on the relative error (previously obtained by univariant and multivariate regression analysis), depending on the applied calculation algorithm, type of tissue, photon beam energy and type of test (Table 4).

If we focus on the specific research objectives of this study, the supplementary (post hoc) analysis (Bonferoni test, Table 5) shows that the AcurosXB calculating algorithm leads to a statistically significant increase in the relative error compared to the AAA. The highest values of the relative error are registered for bone tissue (2.10 ± 1.27).

By comparing the AAA and AcurosXB calculating algorithms, a statistically significant difference in registered relative errors in bone is shown (Table 6). The corresponding mean values and 95% of the confidence limit are 1.56% for the AAA algorithm and 2.64% for AcurosXB. The fact that with the applied calculation algorithms there is no overlap of the 95% of confidence limits, it indicates a statistically significant difference for bone. Applied calculating algorithms lead to approximately the same (statistically non-significant) relative errors in soft tissue and lungs (which is opposite to the Schiefer et al. 10 study, which established the same degree of accuracy of the two algorithms except for the lungs, where AcurosXB has a smaller relative error).

The design of the study also caused the appearance of certain weaknesses primarily in the statistical part of the examination. In the case of simultaneous examination of multiple independent variables (multiple regression analysis, GLM univariate ANOVA with multiple independent variables), ideally the highest reliability is obtained when the number of samples in each group is approximately the same. Phantom characteristics (the unequal number of measuring points relative to the type of tissue) significantly contributed to this problem.

The selected statistical methods due to their robustness and reliability, but also the fact that different statistical techniques confirm the results of the test, indicate to a large extent the correctness of our conclusions.
Conclusion
The performed End-to-End test on the heterogeneous phantom CIRS Thorax002LFC gives us a confirmation of the correct TPS dose calculation (for all EBRT techniques, photon beam energy, calculating algorithms and different types of tissue) and delivery to the patient on Linac, in our RT center daily clinical practice. The mentioned phantom in practice can be used for control, but not for obtaining a reference calibration curve. The analysis of the results showed that there is no statistically significant difference between the Linac, but there is between photon energies (greater relative errors can be expected when using 16 MV compared to 6 MV). In addition to the calculation algorithms (AAA vs AcurosXB), there were no significant differences in soft tissue and lung relative errors, but for the bone there is difference in favor of AAA.
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