IMPACT OF STRINGENT TOLERANCE CRITERIA ON VERIFICATION OF ABSORBED DOSE DISTRIBUTIONS AND EVALUATION THROUGH INHOMOGENEOUS MEDIA

by

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Advances of radiation delivery devices have increased the complexity of the radiation oncology treatments. Herewith, outcome of the treatment, as well as patient safety, strongly depend on the consistency of absorbed dose delivery. Both can be ensured by comprehensive system of verification of calculated absorbed dose distributions. Standard method is evaluation of calculated absorbed dose distribution according to gamma method, using a 2-D detector and a homogeneous phantom, to obtain measured dose distribution. Purpose of this research was to investigate the influence of tolerance criteria on gamma passing rate. Additionally, the agreement in heterogeneous phantom was analysed. Absorbed dose calculations were performed using systems Monaco and XiO. Detector with 1020 ionization chambers in homogeneous phantom and semi-anthropomorphic phantom was used for measurements. Absorbed dose distributions of around 3500 patients were analysed using gamma method. In homogeneous phantom, average gamma passing rates were within tolerance for 3 %/2 mm. For measurements in heterogeneous media, the highest average gamma passing rate was obtained for small volumes of medium treatment complexity ($\bar{\gamma}$ = 93.84 %), while large volumes of treatment with low complexity yielded the lowest gamma passing rates ($\bar{\gamma}$ = 83.22 %).

Key words: pre-treatment absorbed dose verification, tolerance criteria, inhomogeneous media, calculation algorithm, patient safety

INTRODUCTION

Absorbed dose distribution to be delivered during radiation therapy treatment is a prerequisite for successful treatment outcome and patient safety. Therefore, calculated absorbed dose distributions accuracy should be verified along with the feasibility of the delivery, during overall radiation treatment which may last several weeks. The technological advances led to development of modern and highly sophisticated radiation oncology techniques, which has further increased the ability to conform dose to target volumes and spare surrounding tissues. Nevertheless, this has increased the complexity of the treatment process, making constant upgrade and evolution of the quality assurance (QA) program crucial. An important part of the QA program is verification of calculated absorbed dose distributions [1-4]. The consistency of absorbed dose delivery could be ensured by performing pre-treatment verification of calculated absorbed dose distribution. As this is performed individually for each patient undergoing advanced radiation therapy treatment, it is referred to as patient specific dosimetry (PSD). Main task of PSD is to verify calculated absorbed dose distribution which fulfilled requests on target volume coverage and restrictions related to functionality of irradiated organs of the patient. This can be performed by assessing agreement of calculated and measured absorbed dose distributions. A common method for PSD is evaluation of calculated absorbed dose distribution, according to gamma method, using 2-D detector and a homogeneous phantom, to obtain measured dose distribution [5, 6].

This research was actuated by changes in international recommendations regarding tolerance levels [7]. Besides this, the recent studies [8, 9] have shown that common tolerance criteria used is still 3 % dose difference and 3 mm distance-to-agreement. Thus, the first part of our research investigates how changes in tolerance influence gamma passing rates. Results of PSD, performed on around 3500 patient's absorbed dose distributions, analysed with both tolerance criteria, will be presented. Additionally, the PSD concept was evaluated through inhomogeneous media. The

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goal was to analyse the agreement between absorbed dose distributions when inhomogeneity is introduced.

MATERIALS AND METHODS

This research was performed using devices which are in clinical use for preparation, calculation, and delivery of radiation therapy treatment. Setting up and performing PSD begins at the CT simulator Somatom Open (Siemens Healthineers, Erlangen, Germany) with imaging of the detector along with the phantom in measuring setup. The detector IBA Matrixx is a 2-D array detector with 1020 ionization chambers (IBA Dosimetry GmBH, Schwarzenbruck, Germany). Calibration of the 2-D detector in absorbed dose was performed using measurements obtained by Farmer-type ionization chamber (TW30013, PTW Freiburg, Germany) in reference conditions. The effective depth of 2-D detector measurement plane has been determined to be 3.6 mm from the surface of the detector [10]. Dose calculations, for this phantom and detector configuration, were performed using treatment planning systems Monaco v. 5.11, used for step and shoot intensity modulated radiation therapy (IMRT) technique (Monte Carlo based algorithm – MC) and XiO v. 5.10 (both Elekta, Stockholm, Sweden) for forward *field in field* technique (FiF) (standard superposition algorithm – SS). All the calculations by Monaco were performed as dose to medium in medium ($D_{m,m}$). Herewith, calculation is based on electron density data which can be related to Hounsfield units acquired using CT simulator [11, 12]. Due to detector and phantom design, dose delivery was performed in vertical geometry with beam central axes perpendicular to the measuring plane. Other treatment parameters remained unchanged. Two linear accelerators were used: Oncor Impression with 6 MV and 15 MV X-ray beams, equipped with an 82-leaf collimator (LA1) and Oncor Expression with 6 MV and 18 MV X-ray beams, equipped with a 160-leaf collimator (LA2) (both Siemens Healthineers, Erlangen, Germany). For IMRT, only the 6 MV beam of LA2 was used. All the devices are under comprehensive QA program, developed according to international recommendations [13-15]. The IBA OmniProI'mRT (IBA Dosimetry GmBH, Schwarzenbruck, Germany) was used to verify agreement between absorbed dose distributions.

Measurement procedure – homogeneous media

Dosimetric verification of absorbed dose distributions using a homogeneous phantom should be performed prior the first patient treatment [1, 7]. Main steps of such verification are shown in fig. 1. Detector and phantom (Setup 1) were scanned at the CT simulator and acquired data were imported into the treatment planning system. Patient absorbed dose distribution was recalculated as a QA plan using the scanned phan-

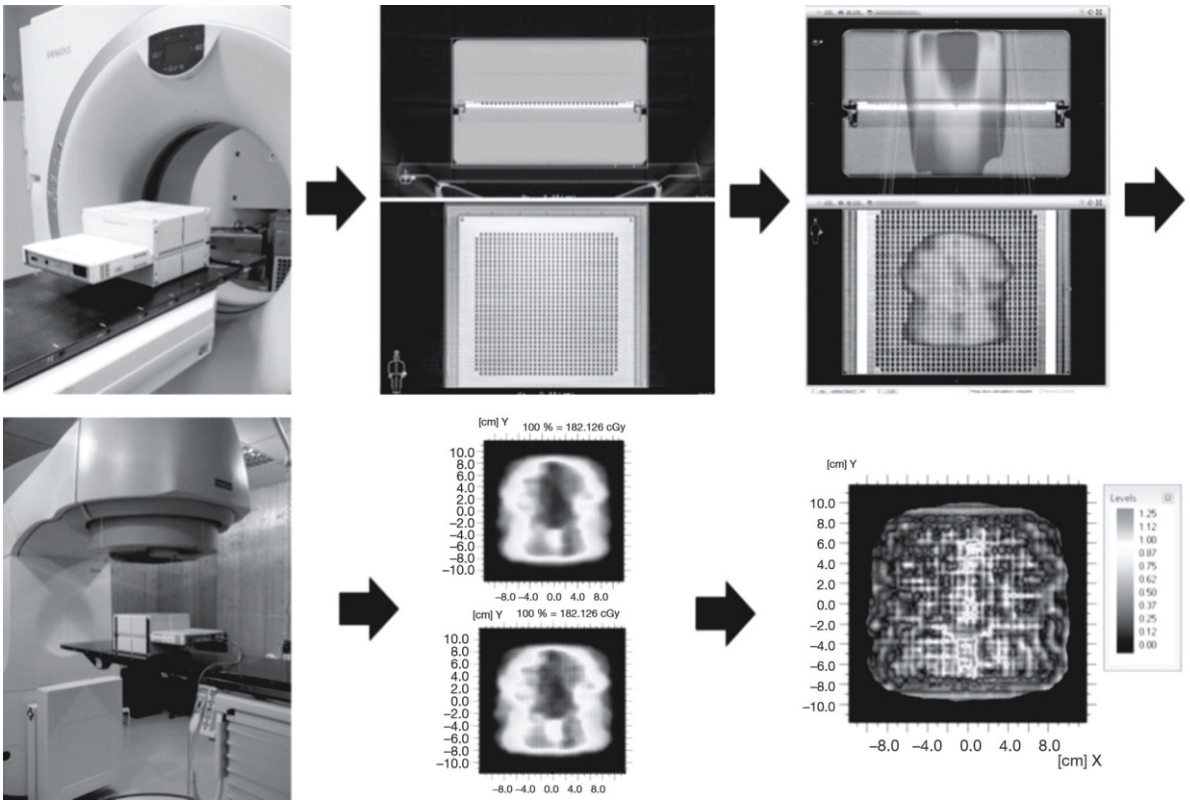

Figure 1. Steps to be performed for PSD in homogeneous phantom: CT scanning of the detector in the phantom, calculation of the 2-D dose distribution, measurement of the dose distribution at the linear accelerator, and evaluation of calculated absorbed dose distribution

tom images. Such QA plan was delivered to the phantom-detector system at the linear accelerator and the absorbed dose distribution was measured. Comparison of measured and calculated absorbed dose distribution was performed and the calculated absorbed dose distribution was evaluated.

Measurement procedure – inhomogeneous media

While the homogeneous phantom represents a standard tool for pre-treatment verification, it does not reflect the different structures of human anatomy. For this reason, measuring setups using a semi-anthropomorphic phantom were introduced. Namely, the conditions when photon beams are passing through different anatomical structures were simulated by CIRS 002LFC phantom (Computerized Imaging Reference System Inc., Norfolk, USA). Phantom is built of water density equivalent, lung density equivalent and bone density equivalent materials.

Two measurements setups were created using parts of CIRS 002LFC phantom: 5 cm (Setup 2) and 10 cm (Setup 3), were placed on top of the 3 cm RW3 plates (PTW, Freiburg, Germany), which are used to ensure dose build-up, fig. 2. [1]. Detector was scanned at the CT simulator in both setups. Patient dose distributions were recalculated for two setups with inhomogeneity.

Gamma method

Measured and calculated absorbed dose distributions were compared using gamma analysis [5, 7, 16]. To perform the gamma analysis, two tolerance criteria were set. One criterion refers to low dose gradient regions with the emphasis on dose difference between dose distributions at the same interest point. The other tolerance criterion, DTA, refers to high dose gradient regions and focuses on finding two closest interest points with the same dose. Gamma is evaluated according to following equations [17]

$$\gamma(r_r) \quad \min_{r_e} \Gamma(r_r, r_e)$$
$$\Gamma(r_r, r_e) \quad \sqrt{\frac{(r_e \quad r_r)^2}{d^2} \quad \frac{[D_e(r_e) \quad D_r(r_r)]^2}{D^2}} \tag{1}$$

where, r_r, r_e denote the reference and evaluated dose points, D_r, D_e denote the reference and evaluated dose levels, d, D denote distance-to-agreement and dose difference criteria.

The AAPM TG-218 recommends tolerance criteria to be 3 % dose difference and 2 mm DTA with tolerance limit set at gamma passing rate 95 % [7]. Before, standard for gamma passing was 3 % dose difference and 3 mm DTA which was originally recommended by Low *et al*. [18]. To compare the results according to both criteria, data collected between 2016 and 2018 were retrospectively analysed using 3 %/2 mm criteria. Data collected between 2018 and 2021 were analysed using the previously established 3 %/3 mm criteria, also retrospectively. Parameters used for analysis, built-in IBA OmniProI'mRT were set as: global gamma normalization to a point with maximum dose, search distance to 4.5 cm, dose threshold to 10 % of the maximum dose, dose maximum to 100 % as recommended by Miften *et al*. [7]. All dose distributions were analysed in terms of absolute dose. The spatial resolution of detector was limited by the size and the distance between the central axis of adjacent ionization chambers and linear interpolation was used to *improve* resolution. Measured absorbed dose distribution was taken as the reference according to which calculated distribution is evaluated [19].

Dose distributions selection and statistical analysis

At our department, PSD is regularly performed using the detector with the homogeneous phantom (Setup 1). Gamma analysis was performed for 2974 FiF (in the period between 2016 and 2021) and 499 IMRT (in the period of 2018 and 2021) calculated absorbed dose distributions, for different treatment sites. This resulted in 3473 dose distributions processed and analysed in terms of gamma analysis. During this period, dosimetric verification of each calculated absorbed dose distribution (IMRT and FiF) was standard practice at our department.

Additionally, dose distributions were separated in five different treatment plan complexities (TPC), which are related to different treatment sites, for either FiF or IMRT. Treatment plan complexity was determined considering treatment volume size and treatment unit

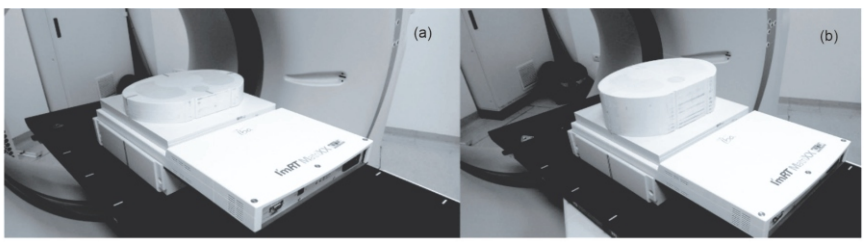

Figure 2. Measurement set-ups created with bottom part of MultiCube phantom, ImRT Matrix detector, 3 cm of RW3 plates and plates of 5 cm (a) and 10 cm (b) of CIRS 002LFC phantom

Table 1. Relation between treatment site and plan complexities; treatment planning technique, treatment unit and calculation algorithms are shown in the last three columns

Treatment plan complexity	Treatment site	Code	Treatment planning modality	Treatment unit	Calculation algorithm
Large volume, low complexity	Rectum	TPC1	FiF	LA1	SS (XiO)
Large volume, medium complexity	Breast	TPC2			
Small volume, medium complexity	CNS	TPC3		LA2	
Large volume, high complexity	Lung, H&N Prostate	TPC4			
Large volume, high complexity	Prostate	TPC4	IMRT	LA2	MC (Monaco)
Small volume, medium complexity	CNS	TPC3			
Large volume, extra high complexity	H&N	TPC5			

Table 2. Arithmetic means of gamma passing rates and respective standard deviations for four different complexities for FiF and three different plan complexities for IMRT dose distributions when 3 %/3 mm, 3 %/2 mm tolerance criteria are applied

Treatment planning modalities	Treatment plan complexity	$\bar{\gamma}$ (SD) % points passing with gamma <1	
		3 %/3 mm tolerance criteria	3 %/2 mm tolerance criteria
FiF	TPC1	97.64 (1.79)	95.22 (4.12)
	TPC3	99.34 (1.18)	98.39 (2.01)
	TPC2	98.85 (1.18)	96.99 (1.67)
	TPC4	99.25 (1.04)	98.12 (1.81)
IMRT	TPC3	98.84 (1.51)	97.09 (1.87)
	TPC4	97.80 (2.92)	95.78 (1.89)
	TPC5	97.24 (3.19)	96.35(3.95)

multileaf collimator resolution. Additionally, fluence maps modulation degrees were considered for IMRT. For FiF, the number of additional fields and their size and shape were considered. Dose distributions were analysed for the three above specified phantom set-ups. Relation between treatment site and plan complexity is shown in tab. 1.

Statistical analysis was performed by using the TIBCO Statistica v. 14.00.15. One-way analysis of variance (ANOVA) was applied as a parametric test and Kruskal-Wallis test as a non-parametric test. The significance level was set at p-value <0.05.

RESULTS

A summary of the obtained passing rates is shown in tab. 2 for different treatment plan complexities. The average value of gamma passing rates and respective standard deviations for absorbed dose distributions of different treatment plan complexities are reported for different tolerance criteria.

The lowest average value was obtained for TPC1 (FiF), with 97.64 % (3 %/3 mm) and 95.22 % (3 %/2 mm). Considering IMRT dose distributions, lowest average gamma values were 97.24 % for TPC5 (3 %/3 mm) and 95.78 % for TPC4 (3 %/2 mm). When the 3 %/3 mm and 3 %/2 mm criteria were applied, all average gamma passing rates were within tolerance for both planning techniques, shown in fig. 3.

For absorbed dose distributions per different TPC, average values of gamma passing rates were shown, tab. 3, with corresponding standard deviations, separately for a homogeneous setup (Setup 1) and two levels of inhomogeneity (Setup 2 and 3), obtained using 3 %/3 mm and 3 %/2 mm.

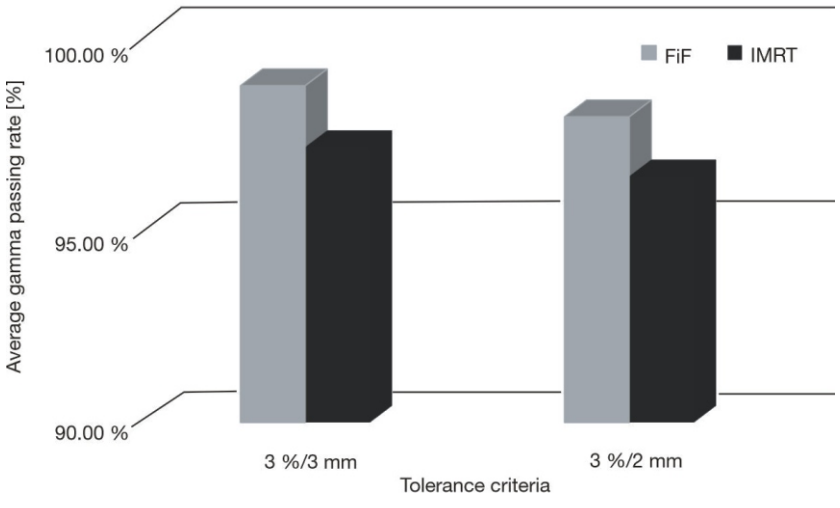

Figure 3. Average gamma passing rates for two planning techniques (FiF and IMRT), and two tolerance criteria (3 %/3 mm and 3 %/2 mm)

Table 3. Arithmetic means of gamma value and respective standard deviations for absorbed dose distributions for five treatment plan complexities. Analysis was performed for homogeneous setup (Setup 1) and two different levels of inhomogeneity (Setup 2 and 3) using 3 %/3 mm and 3 %/2 mm tolerance criteria

Treatment plan complexity		$\bar{\gamma}$ (SD) % points passing with gamma <1	
		3 %/3 mm	3 %/2 mm
TPC1	Setup 1	97.23 (0.49)	95.06 (0.58)
	Setup 2	93.67 (1.50)	85.19 (1.73)
	Setup 3	90.54 (1.95)	83.22 (3.39)
TPC2	Setup 1	98.79 (0.26)	97.35 (0.97)
	Setup 2	97.27 (0.91)	92.19 (1.48)
	Setup 3	93.35 (1.83)	90.88 (2.15)
TPC3	Setup 1	98.96 (0.74)	98.04 (1.06)
	Setup 2	97.04 (0.89)	96.61 (1.29)
	Setup 3	96.15 (1.34)	93.84 (2.02)
TPC4	Setup 1	98.21 (0.75)	96.39 (2.59)
	Setup 2	96.15 (2.49)	92.47 (4.10)
	Setup 3	92.00 (3.51)	89.73 (5.77)
TPC5	Setup 1	97.30 (0.31)	96.87 (1.03)
	Setup 2	95.72 (0.20)	93.96 (0.08)
	Setup 3	92.34 (0.48)	92.36 (1.06)

Gamma passing rates for different TPC were shown to be dependent on the level of heterogeneity of the treated volume. As expected, the highest average gamma passing rates were obtained using a homogeneous phantom (Setup 1), while the lowest gamma passing rates were obtained for Setup 3.

Highest average gamma passing rates were obtained for TPC3. When 3 %/3 mm tolerance criteria is applied, mean gamma value was higher than 95% for all setups. Lowest values were obtained for TPC1, with average gamma passing rate being 90.54 % (Setup 3). Using 3 %/2 mm criteria, the highest mean gamma value was obtained for TPC3 with 98.73 % (Setup 1) and the lowest result for TPC1 with 83.22 % (Setup 3).

Comparing average gamma passing rates for Setup 1 and Setup 3 (3 %/3 mm), the largest gamma deterioration is observed in TPC1 ($\bar{\gamma}$ = 6.69 %). Treatment plan with smallest gamma deterioration is TPC3 with $\bar{\gamma}$ = 2.81 % (3 %/3 mm).

Applying 3 %/2 mm criteria, the largest drop in mean gamma value between Setup 1 and Setup 3 is found for TPC1 with $\bar{\gamma}$ = 11.84 % and the lowest drop for TPC5 with $\bar{\gamma}$ = 4.51 %.

Additional analysis was performed for two calculation algorithms: standard superposition algorithm for FiF and Monte Carlo based algorithm for IMRT, regarding the deterioration of gamma passing rates when inhomogeneity is introduced. Deterioration of gamma passing rates calculated between Setup 1 and Setup 3, is shown in fig. 4. Deterioration of gamma passing rates for 2 mm/2 % was also considered in this case.

Deterioration of gamma passing rates between Setup 1 and Setup 3 is lower for IMRT absorbed dose distributions for all tolerance criteria, with $\bar{\gamma}$ = 4.48 %, $\bar{\gamma}$ = 4.90 % and $\bar{\gamma}$ = 4.70 %, consecutive for tolerance criteria 3 %/3 mm, 3 %/2 mm and 2 %/2 mm. The largest deterioration is observed for FiF and tolerance criteria 2 mm/2 % with $\bar{\gamma}$ = 8.74 %.

DISCUSSION

Intention of this research was to investigate the deterioration of gamma passing rates when calculated with recommended [7] stringent criteria. It was shown that gamma passing rate deteriorates when calculated with 3 %/2 mm tolerance criteria but, average gamma passing rates remain higher than 95 %, tab. 2 and fig. 3, when PSD is performed, using the homogeneous phantom.

The Kruskal-Wallis test for determination of statistical difference between gamma passing rates for different treatment plan complexities (3 %/2 mm tolerance criteria) has shown that a statistically significant difference exists for TPC1 and TPC2, with *p*-values of $p < 0.0001$ and $p < 0.0025$, respectively. This corresponds to the result reported by Pulliam *et al*., [20] who showed that the patient specific QA results could differ significantly between the treatment sites. Statis-

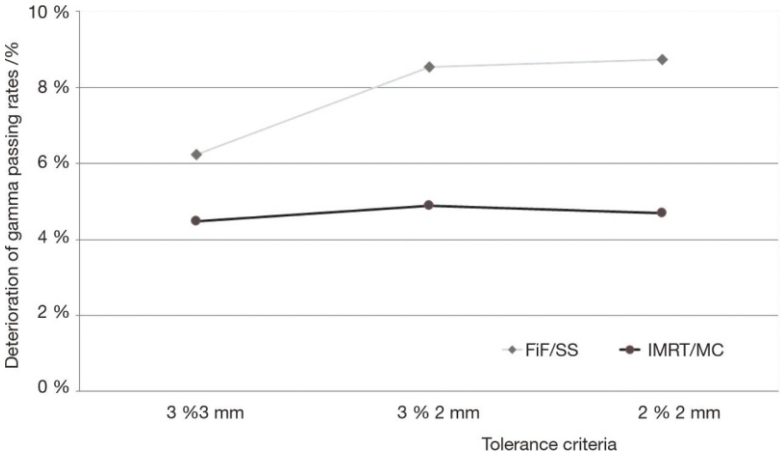

Figure 4. Deterioration of gamma passing rates between homogeneous setup (Setup 1) and setup with 10 cm plates of CIRS 002LFC phantom (Setup 3); deterioration was calculated for two calculation algorithms: standard superposition for FiF and Monte Carlo based algorithm for IMRT, respectively

tically significant difference ($p > 0.2678$) was not found between average gamma passing rates for remaining treatment sites.

At our premises, two linear accelerators are used for patient treatments. They have difference in the multileaf collimator design which define the *resolution* of delivered absorbed dose distribution. The leaf widths at the isocenter are 1 cm and 0.5 cm for LA1 and LA2, respectively. Dose distributions of TPC1 and TPC2 are delivered by the LA1, while other sites are treated by the LA2. There is a statistically significant difference ($p = 0.00029$) between average gamma passing rates for two linear accelerators used, which could be related to the multileaf collimator design, which is also in accordance with Pulliam *et al*. [20].

Comparing IMRT dose distribution gamma passing rates using Kruskal-Wallis test, the difference between treatment plan complexities was not statistically significant for any of the tolerance criteria used: $p > 0.4953$ with 3 %/3 mm and $p > 0.1989$ with 3 %/2 mm.

For measurements performed through inhomogeneous media, average gamma passing rates are the lowest for Setup 3, for all the treatment plan complexities, tab. 3. Similar results were obtained by Smilović *et al*. [21]. This occurs due to the 10 cm plates of semi-anthropomorphic phantom (Setup 3). The treatment plan complexity with the least deteriorating average gamma passing rate is TPC3 (2.81 % for 3 %/3 mm). This was expected, as absorbed dose for TPC3 is typically delivered to a small volume, which allows the beam to pass only slightly through different density areas of the inhomogeneous setup. The largest drop in average gamma passing rates, regardless of Setup and tolerance criteria, is observed for TPC1, 6.69 % for 3 %/3 mm and 11.84 % for 3 %/2 mm tolerance criteria. In these cases, the beams pass through a large area of the inhomogeneous parts of the phantom which causes the deterioration of gamma passing rates. This is also a consequence of larger leaf width of LA1 multileaf collimator.

Generally, deterioration of gamma passing rates from 3 %/3 mm to 3 %/2 mm criteria also suggests that the detector resolution is one of the limiting factors of the analysis, as the distance between two adjacent ionization chambers is 7.619 mm [22]. This is pronounced in the regions of high dose gradients.

When comparing the two calculation algorithms, lower gamma passing rate deterioration is observed for Monte Carlo based algorithm (IMRT), fig. 4, for all applied tolerance criteria. This is expected, as it was proofed that Monte Carlo based algorithms are superior to analytical algorithms when dose distributions are calculated through inhomogeneous media [23]. Also, all dose distributions were calculated as $D_{m,m}$, which was shown to be in very good agreement with Monte Carlo calculations performed by the *general purpose* Monte Carlo N-Particle (MCNP) code [24].

CONCLUSIONS

Transition from 3 %/3 mm to 3 %/2 mm criteria has shown that gamma passing rates exceed the 95 % tolerance limit for the stringent criteria. This points to optimal calculation and optimization of dose distributions, appropriate commissioning of linear accelerators and treatment planning systems, as well as a thorough performance of a comprehensive QA program. Nevertheless, it is important to be aware of possible limitations of the different part of the system, because each of them may considerably influence absorbed dose delivery and, consequently, the treatment outcome and patient safety.

Furthermore, gamma passing rates depend on the level of inhomogeneity of the region of interest. By increasing the level of inhomogeneity and thus approaching realistic clinical situations, gamma passing rates deteriorate. Having this in mind, it is very important to keep gamma passing rate of standard patient specific dosimetry in homogeneous media as high as possible to obtain higher quality of the absorbed dose delivery and, better outcome of radiation oncology treatment.

AUTHORS' CONTRIBUTIONS

This research was conceived by N. Obajdin and Dj. Smilović Radojčić. Data was collected and analysed by N. Obajdin, Dj. Smilović Radojčić, D. Rajlić and M. Švabić Kolacio. Retrospective analysis was done by N. Obajdin. Statistical analysis was done by Dj. Smilović Radojčić. Manuscript was written by N. Obajdin, Dj. Smilović Radojčić and S. Jurković and reviewed by all authors. N. Obajdin and Dj. Smilović Radojčić have contributed to this work in equal parts.

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Невена ОБАЈДИН, Ђени СМИЛОВИЋ РАДОЈЧИЋ, Давид РАЈЛИЋ, Манда ШВАБИЋ КОЛАЦИО, Славен ЈУРКОВИЋ

УТИЦАЈ ПРОМЕНЕ КРИТЕРИЈУМА ПРИХВАТЉИВОСТИ НА ВРЕДНОВАЊЕ РАСПОДЕЛА АПСОРБОВАНЕ ДОЗЕ У ХОМОГЕНОЈ И НЕХОМОГЕНОЈ СРЕДИНИ

Развој уређаја и система у радијацијској онкологији поставио је додатне захтеве на прорачун и оптимизацију расподела апсорбоване дозе. Учинак радиотерапије темељи се на контроли тумора и избегавању компликација здравог ткива. Обе величине зависе од апсорбоване дозе па је важно тачно одредити њену вредност. То је могуће постићи системом вредновања израчунатих расподела апсорбоване дозе.

У овом истраживању израчунате расподеле апсорбоване дозе за више од 3500 пацијената вредноване су гама методом. Додатно су осмишљене различите мерне геометрије фантома и 2-D детектора, у сврху испитивања утицаја нехомогености средства на одступање израчунате и измерене расподеле апсорбоване дозе. Истражена је и зависност одступања од сложености израчунате расподеле дозе. Прорачун апсорбоване дозе спроведен је коришћењем система за одређивање и оптимизацију расподеле дозе Monaco и XiO. Детектор са 1020 јонизацијских комора коришћен је за вредновање расподеле дозе у комбинацији с хомогеним фантомом и семи-антропоморфним фантомом.

У хомогеном фантому, средња вредност гама индекса, за све вредноване расподеле дозе, виша је од 95 % за критеријум прихватљивости од 3 %/ 2 mm. За мерења у нехомогеном средству, највећа вредност гама индекса добијена је за расподеле дозе средње сложености и малих волумена ($\bar{\gamma}$ = 93.84 %), док је за расподеле дозе ниске сложености и великих волумена добијена најнижа вредност гама индекса ($\bar{\gamma}$ = 83.22 %).

Кључне речи: вредновање расподела апсорбоване дозе, критеријум прихватљивости, нехомогена средина, рачунарски алгоритам, сигурност пацијената