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Original Scientific Paper

DOSIMETRIC VERIFICATION OF INTENSITY MODULATED RADIOTHERAPY (IMRT) TREATMENT PLANS FOR PROSTATE CANCER PATIENTS

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ABSTRACT: Intensity modulated radiotherapy (IMRT) has become widely used as a standard radiation therapy technique for the treatment of localized prostate cancer. The transition from conformal radiotherapy (3D CRT) to a more complex IMRT technique triggered the need for more thorough verification of the accuracy in the dose delivery. In this work we present the clinical workflow and the results of patient specific quality assurance (PSQA) procedures for 40 prostate cancer patients who have been treated with step and shot IMRT ever since its implementation in our routine clinical practice. PSQA procedures include dosimetric verification of each treatment plan with dedicated rotational phantom and high-resolution matrix detector system Octavius 4D (PTW Freiburg) that allows three-dimensional comparison of the calculated and delivered radiation dose distribution. Our results proved the compliance with the universal tolerance limits recommended for those procedures (1), assuring the safety of the treatment and providing the possibility for the adoption of more stringent constraints in the future.

Key words: *prostate IMRT, patient specific QA*

Introduction

External beam radiotherapy (EBRT) in prostate cancer patients has been used as a treatment modality since the early ages of two-dimensional (2D) radiotherapy when the four-field box technique was a typical beam arrangement. Over time, with advances in technology, it has been mostly replaced by three-dimensional conformal radiation therapy (3DCRT) that relies on linear accelerators with multileaf collimators (MLC) for treatment delivery and computed tomography (CT) simulator scans used in treatment planning. 3DCRT has led to improved beam shape and dose distribution conformity to target volume while allowing for better sparing of the main organs at risk, rectum and bladder. A few decades ago, even more advanced IMRT technique was introduced that has now become a standard choice in prostate radiation treatments (2). Depending on the treatment machine capabilities, IMRT can be delivered with static photon beams from several directions consisting of small MLC field segments that modify the beam intensity (step and shot IMRT), or as a volumetric arc radio-

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therapy (VMAT) during which the MLCs are changing their shapes while the linac head is continuously rotating around the patient.

Measurement-based verification of the calculated dose distribution in radiotherapy treatment plans for individual patients has been advocated in many papers and international guidelines, especially for advanced radiotherapy techniques such as IMRT/VMAT (1). Highly conformal IMRT plans yield areas of very steep dose gradient where minor differences between calculated and delivered dose distributions might have a significant impact. The mismatch between the distributions can mainly result from a poor beam model in the treatment planning system or the instability of any of the linac mechanical or dosimetric parameters, such as MLC positions, dose output, beam profiles and many others. Applying inappropriate parameters during treatment planning, such as grid size, a large number of small field segments, or an extremely low monitor unit (MU) per segment can also be a source of disagreement. As of this year, a dosimetric verification is required by the law for every patient treatment plan in advanced radiotherapy techniques, prior to beginning the treatment. There are many ways to perform such verification using various kinds of detectors and phantoms for measurement, and all these procedures are commonly known as patient-specific quality assurance (PSQA). It has been proven that the results of PSQA depend on the equipment used for verification, comparison metrics (1,2,3,8) so it is important to keep that in mind when comparing the results. The main goal of PSQA procedures is to ensure safe and accurate radiation therapy by detecting errors and discrepancies in both treatment planning and delivery.

In this paper, we describe our experience in the utilization of a commercially available dosimetric system, PTW Octavius 4D, for dosimetric verification of step-and-shoot IMRT treatment plans for prostate cancer patients. The Octavius system was commissioned before clinical use and its performance evaluated in simple and complex fields. Since the clinical introduction of the step-and-shot IMRT technique in our department, over 40 patients with prostate cancer have received their primary or adjuvant/salvage IMRT including different dose prescription schemes depending on the risk group to which the patient belongs and the extent of the disease, i.e., the definition of target volumes.

Methods

All patients were scanned with a large bore CT simulator Toshiba Aquilion, with 3 mm slice thickness, as per local protocol for pelvic region. The clinical protocol of the Department for IMRT treatments of prostate cancer was developed relying on international guidelines, clinical trials, and local experience. Patients were instructed to prepare for simulation with empty rectum and bowel and to drink enough water to fill up the bladder. The planning of target volumes (PTVs) included the prostate for primary RT or prostate bed for adjuvant RT, with seminal vesicles and pelvic lymph node, if involved. The organs at risk (OAR) delineated to meet dose volume constraints for a given prescription were rectum, bladder, small and large bowel, femoral heads and penile bulb. Dose prescriptions with moderate hypofractionation up to 3 Gy per fraction were used. In cases of multiple PTVs, the simultaneous integrated boost (SIB) technique was applied (Table 1).

Table 1. Dose prescription schemes and patient distribution

EBRT	Target volumes	Dose prescription	Number of patients
Primary	prostate and seminal vesicles (SM)	60 Gy in 20 fractions	9
	prostate, SM and involved lymph nodes (LN)	SIB 48 Gy to lymph nodes and 68 Gy to prostate with SM, all in 25 fractions	7
Adjuvant	prostate bed + SM	52,6 Gy in 20 fractions	15
	prostate bed, SM and LN	SIB 44 Gy (or 47Gy if LN involvement proven by imaging) Gy to LN and 52,60 Gy to prostate bed with SM, all in 20 fractions	11
Total			42

Treatment plans were made with Elekta Monaco treatment planning system (TPS), versions 5.10 that was lately upgraded to 5.51. Plans were made with 5, 7 or 9 beam directions, depending on targets and OARs anatomical features. All SIB plans were made with 9 beams. Monte Carlo algorithm with the dose to medium option and 0,7% uncertainty per calculation was employed. Other planning parameters were 3 mm calculation grid size, minimum field segment area of 2 cm^2, minimum segment width of 1 cm and minimum 3 MU per segment. Elekta Synergy S linear accelerator with MLCi2 head was used for delivering static (step and shot) IMRT fields with 6MV photon beams.

Octavius 4D system for PSQA included rotational cylindrical polystyrene phantom, inclinometer for rotation control, 2D detector array, control unit and detector interface connected to analysis software PTW Verisoft 7.2. The insertion of the detector into the rotational phantom allows the perpendicular impact of radiation beam for any gantry angle (Figure 1). 2D detector array, Octavius 1500 containing 1405 vented

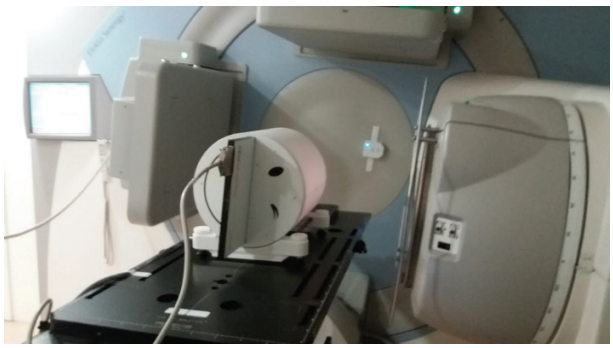


Figure 1. PTW Octavius 4D dosimetric system set up for measurement at linac couch.

ionization chambers, placed 1 cm apart in a checkerboard manner with an offset of 0.5 cm, forming the active detector area of 27x27 cm^2 was used for measurement. The comparison of calculated and measured dose distributions was made with gamma analysis tool (4) that is provided in Verisoft calculation algorithm. Gamma index, γ is a parameter that combines two metrics mostly used in radiotherapy dose distribution comparisons, dose difference (DD) and the distance to agreement (DTA). For each point in evaluated distribution, γ is calculated for specified difference criteria given as DD in percentage and DTA in millimetres. The results depend greatly on the method of dose normalization, which could be global (G) to a maximum dose in referent distribution or local (L) to a dose at evaluated point. In order to exclude low dose regions from comparison, the dose threshold is usually defined, so only the points with the doses higher than that value are taken into evaluation. In order to make the comparison, the evaluated point of dose distribution should have $\gamma \leq 1$. Gamma analysis could be performed on 2D dose distributions in specified planes or in a 3D volume being a special characteristic of Octavius system. The measurements with Octavius solid phantom give 3D dose distribution that is taken as a reference and compared by means of volumetric gamma analysis with the TPS calculated distribution. The reported parameter of such analysis is a gamma passing rate meaning the share of voxels with $\gamma \leq 1$.

Before clinical implementation, the Octavius system was commissioned and it showed excellent characteristics in terms of dose and dose rate linearity, and sensitivity to small MLC displacements in accordance with (5). The beam model in Monaco TPS was also confirmed by 2D gamma analysis of specific test fields recommended by TPS vendor (6). In addition, 25 preclinical test IMRT plans were measured and analysed with six different gamma criteria to establish clinical verification procedure and tolerance limits for gamma analysis. Those plans included both head and neck, and prostate patients.

In total, 42 prostate patients were treated with IMRT, and all plans were verified with Octavius 4D system. The clinical workflow was set up as follows: optimized treatment plans were reviewed by prostate oncology team and approved by appointed radiation therapist. QA plan was made in TPS, as a dose distribution of the original plan but calculated on the phantom studyset. The review of the plans and secondary monitor unit calculation with independent software was made by medical physicist who approved the plan for dosimetric verification. The Octavius detector was calibrated against TPS dose on the day of each measurement. The measured dose was compared with TPS by means of gamma analysis, and if the result exceeded adopted tolerances, then further examination of plan features, measurement conditions and recent machine QA data was conducted in order to find the source of disagreement. That can result in remeasuring or replanning until satisfactory results are achieved and final plan approved for patient treatment.

In Octavius system, the dose measurement is re-

constructed to give 3D dose distribution for the comparison with the QA plan. Dose reconstruction is based on previously measured percent depth dose curves with ionization chamber in a water phantom, for different field sizes. Gamma passing rates were calculated according to the recommended universal criteria of 3% DD and 2mm DTA with global normalization to a maximum dose in reference distribution (3%G2mm) and 10% of maximum dose used as a low dose threshold for analysed points (1). Moreover, additional γ passing rates were determined, according to 2%G2mm criteria, and 3%L3mm where gamma index was normalized to a local point dose. Further insight was given by the investigation of γ passing rates according to different dose levels. The points with doses higher than or equal to 10, 50 and 95% of maximum dose were compared. Statistical tools of Kyplot 6.0 free software were used to test for difference in passing rates among the groups of plans with different prescriptions.

Results

The results of volumetric gamma analysis for preclinical test IMRT plans (Table 2) confirmed that the recommended tolerances for γ passing rate of more than 95% points within 3%G2 mm and with 10% low dose threshold (1), could be adopted as a tolerance level in clinical IMRT patient verifications. Based on these results, the criteria of 2%G2mm and 3%L3mm were chosen as secondary criteria for further inspection of clinical plans.

The analysis of the clinical cases showed very good overall results, according to all criteria, and for all kinds of plans (Table 3). When considering the recommended criteria of 3%G2mm with the usual 10% dose threshold, the average passing rate for all plans was 99,5% with standard deviation of 0,4%. Comparing it with more strict criteria of 2%G2mm and 3%L3mm, Figure 3 reveals slightly lower passing rates with larger variability among the results. For the doses higher than 95% of normalization dose, i.e., high dose regions, Figure 3 shows poorer passing rates according to all criteria and even larger variability. When observing the gamma analysis results for one typical SIB plan, simultaneously delivering 44 Gy to pelvic lymph nodes and 52,6 Gy to prostate bed, notable discrepancies in high dose region in all major planes

Table 2. Average volume γ passing rates and standard deviations for 25 preclinical test cases

Criteria	3%G3mm	3%G2mm	2%G2mm	1%G1mm	3%L3mm	3%L2mm	2%L2mm
γ ≤1 (%) SD (%)	99,9 0,1	99,5 0,3	98,4 0,9	78,3 4,6	99,0 0,6	95,7 2,0	93,3 2,6

Table 3. Average volume γ passing rates as percentage of points with γ ≤ 1 within given criteria and standard deviations for 4 IMRT plans

γ passing criteria	3%G2mm			2%G2mm			3%L3mm		
Dose level (% of maximum dose)	10%	50%	95%	10%	50%	95%	10%	50%	95%
Plan dose prescription	Average γ passing rate ± standard deviation (%)								
52,6 Gy / 20 fr	99,4 ± 0,2	99,1 ± 0,3	98,6 ± 1,3	98,0 ± 0,5	96,9 ± 1,3	91,4 ± 6,4	99,0 ± 0,4	99,5 ± 0,3	99,3± 0,8
60 Gy / 20 fr	99,4 ± 0,5	99,2 ± 0,7	99,5 ± 0,6	98,4 ± 1,0	97,8 ± 1,4	96,9 ± 2,0	99,0 ± 0,7	99,6 ± 0,5	99,9 ± 0,1
SIB: 44 (47) Gy and 52,6Gy / 20 fr	99,4 ± 0,4	99,5 ± 0,3	94,6 ± 5,3	97,6 ± 0,9	97,5 ± 1,1	80,7 ± 11,2	98,5 ± 0,5	99,6 ± 0,3	96,6 ± 3,4
SIB: 48 Gy and 68 Gy / 25 fr	99,7 ± 0,3	99,8 ± 0,3	98,8 ± 2,3	98,8 ± 0,8	98,8 ± 1,2	90,6 ± 9,9	98,5 ± 0,4	99,7 ± 0,4	99,2 ± 1,6
Total	99,5 ± 0,4	99,4 ± 0,5	97,8 ± 3,5	98,2 ± 0,9	97,7 ± 1,3	90,1 ± 9,8	98,8 ± 0,5	99,6 ± 0,4	98,7 ± 2,3

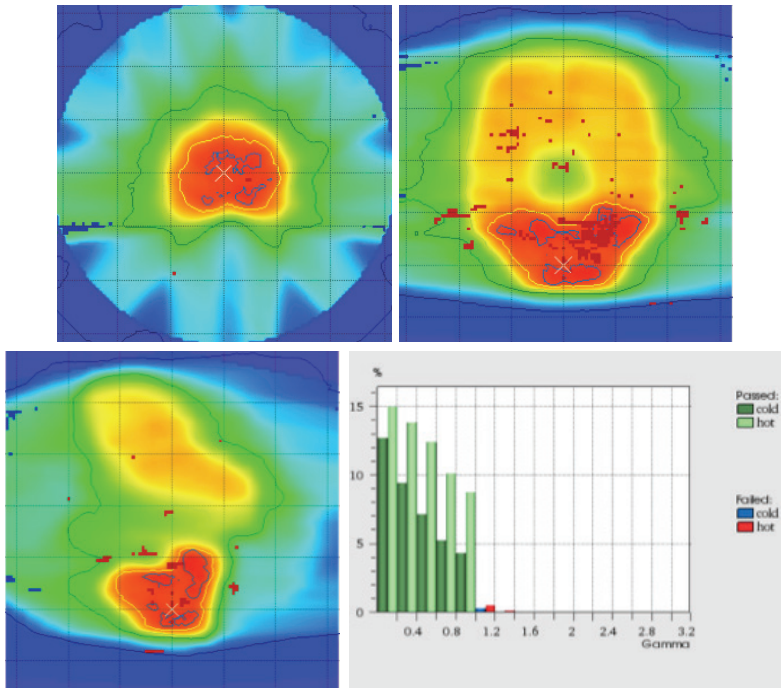
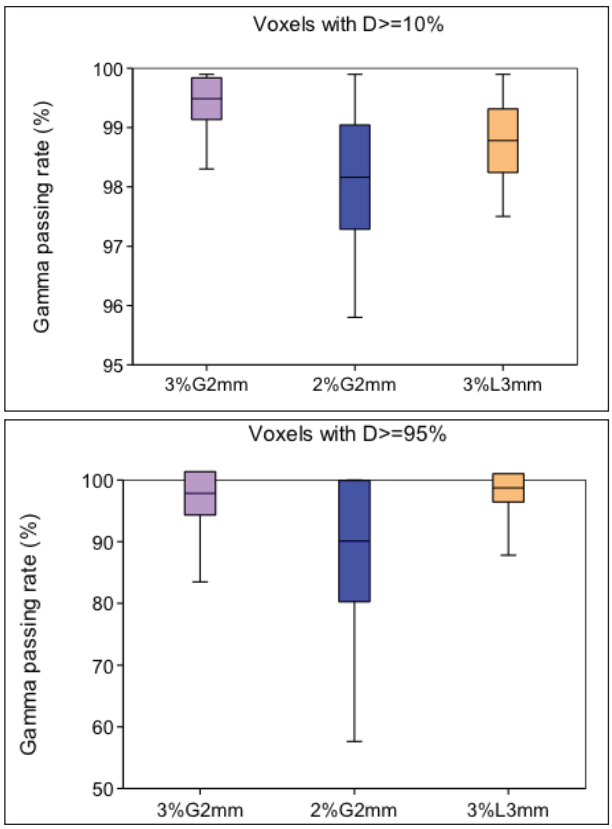


Figure 2. Transversal, coronal, and sagittal planes of TPS Monaco calculated dose (isodose lines) and measured dose (color wash) for SIB prostate plan analysed in Verisoft. Dose prescription was 44 and 52.6 Gy in 20 fractions. Points failing 2%G2mm (γ >1) criteria are presented in red (hot) and blue (cold) colours. Last image showing an γ index histogram.



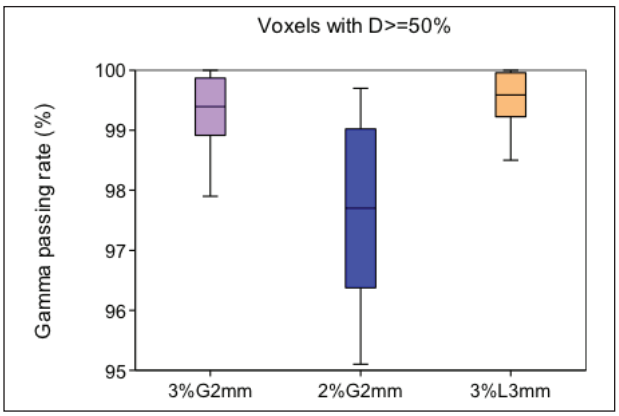


Figure 3. Comparison of gamma passing rates for different criteria for all analysed plans regarding selected dose threshold. First image shows the results for all evaluated voxels with low dose threshold set at 10%, the second one is for medium dose range, doses higher than 50%, and the last one, for high dose regions, voxels with doses larger than 95% of the maximum dose. Larger scale range at the last image should be noticed. The data are presented in box and whisker graph where a box central line represents mean value, box size is given by standard deviation of data and whiskers are showing the range from minimum to maximum.

are shown in Figure 2, although 98,9% of evaluated points passed the 2%G2mm criterion with 10% dose threshold. Gamma values histogram shows that most of the failed points have γ only slightly higher than 1. In most failed points, the calculated dose was higher than measured.

The investigation of the results obtained in patient groups with different dose prescriptions was limited to most rigorous 2%G2mm criteria, allowing better discrimination between the results.

As Shapiro-Wilk test did not confirm the normality of data distribution, a non-parametric Kruskal-Wallis test was used to check the hypothesis of the difference existing between the mean values of gamma passing rates for plans with different prescriptions. When 10% dose threshold was applied, the test brought back the p value of 0,4 which could imply the existing difference ($p < 0,05$). However, for high dose regions, the doses ≥ 95% of D_{max}, the test revealed significant difference in mean passing rates among the groups, with p value of 0,0021 ($p \leq 0,001$).

Discussion

Our commissioning results and also many studies (5,7,8,10) have proven that PTW Octavius 4D system and particularly Octavius 1500 array with high resolution, is a suitable and reliable equipment with excellent performance for PSQA. It is not an easy task to choose the right metric, criteria, and tolerances for gamma analysis that would be appropriate for given treatment delivery technique, linac technical capabilities, TPS calculation algorithm and other features, and finally PSQA equipment in use. There are many different approaches and published results that only recently resulted in universal recommendations (1). Our preclinical results for 25 plans where we tested several different passing criteria, showed that our system complies adequately with recommended tolerance of 3%G2mm, with mean passing rate of 99,5% and 0,3% SD. The results according to more strict criteria of 2%G2mm were still very good with 98,4% but with 1%G1mm, the mean passing rate dropped to 78,3% which was in accordance with (8) and (11) for different detector used. As there is a general tendency for more accuracy and tighter tolerances, the 2%G2mm was chosen as the second criteria, to be assessed in clinical plans. Both of these criteria are based on global normalization that might conceal discrepancies in low and high dose areas (2), so 3%L3mm criterion was selected for the inspection of local γ.

Our clinical data for 42 prostate cases showed very good results related to the selected criteria and to the similar studies (8-11). Regarding the observed poorer results with higher variability for high dose areas, our results were in agreement with (8). It is also hardly surprising that there are significant differences between groups of plans with different prescription, although larger sample analysis would be more conclusive. For SIB plans, mean passing rates are generally lower for voxels above 95% dose levels (Table 3). This could be explained by higher modulation needed to achieve the planning goals in such plans. Although all plans passed given tolerances, an insight in passing rates for different dose regions was still useful. The dose threshold of 95% is related to target coverage and 50% to OAR doses (8).

Although this study included small number of cases and did not cover extensive period of time, the worth of PSQA was clear. It gives confidence in treatment accuracy, which is important especially for complex treatments where many parameters are involved. These first results should be constantly updated and reviewed periodically, since long term studies with large number of patients could reveal different uncertainties in radiotherapy procedures (9).

Conclusion

The preclinical plan verification results confirmed the adequacy of the local procedures for the use of the Octavius 4D system for PSQA, and it set the basis for the establishment of the reporting gamma metrics and local tolerance levels. O ur clinical results for prostate cancer patients agreed with similar studies or were even better, if more strict criteria were used. There is no significant difference among the groups of plans with different prescriptions and complexity, leading to possibly more demanding tolerance levels in the future. Due to relatively small number of analysed plans, further investigations into the effects of various parameters on the gamma analysis scores are to be conducted with the unceasing aim to improve the safety and accuracy of IMRT treatments.

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Sažetak

DOZIMETRIJSKA VERIFIKACIJA RADIOTERAPIJSKIH PLANOVA INTENZITET-MODULIRAJUĆE RADIOTERAPIJE U BOLESNIKA SA RAKOM PROSTATE

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Radioterapija moduliranog intenziteta (*eng. intensity modulated radiotherapy –IMRT*) u posljednjem desetljeću je postala uobičajena radioterapijska metoda za terapiju lokaliziranih karcinoma prostate. Prelazak s konformalne radioterapije na naprednu i tehnički složeniju IMRT tehniku, donio je i potrebu za detaljnijom i sveobuhvatnom provjerom točnosti isporuke doze zračenja. U ovom radu predstavljamo provođenje postupaka dozimetrijske verifikacije radioterapijskih planova poznatih pod engleskim nazivom *patient specific QA (PSQA)* te rezultate za 40 bolesnika s karcinomom prostate koji su primili IMRT terapiju. U tu svrhu koristimo posebni dozimetrijski sustav s rotacijskim fantomom i visoko razlučivom detektorskom matricom, Octavius 4D (PTW Freiburg). Pokazalo se kako su sva dobivena odstupanja između planirane i mjerene trodimenzionalne raspodjele doze bila unutar preporučenih tolerancija (1) što nam daje povjerenje u sigurnost provođenja ovakve terapije te otvara mogućnost za primjenu strožijih ograničenja u budućnosti.

Ključne riječi: *radioterapija moduliranog intenziteta (IMRT) karcinoma prostate, dozimetrijska verifikacija plana, patient specific QA (PSQA)*