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Reduction of systematic dosimetric uncertainties in volumetric modulated arc therapy triggered by patient-specific quality assurance

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ABSTRACT

Background and purpose: Dosimetric patient-Specific Quality Assurance (PSQA) data contain in addition to cases with alerts, many cases without alerts. The aim of this study was to present a procedure to investigate long-term trend analysis of the complete set of PSQA data for the presence of site-specific deviations to reduce underlying systematic dose uncertainties.

Materials and methods: The procedure started by analysing a large set of prostate Volumetric Modulated Arc Therapy (VMAT) PSQA data obtained by comparing 3D electronic portal image device (EPID) based *in vivo* dosimetry measurements with dose values predicted by the Treatment Planning System (TPS). If systematic deviations were present, several actions were required. These included confirmation of these deviations with an independent dose verification system for which a 2D detector array in a phantom was used, and analysing calculated with measured PSQA data, or delivery machine characteristics. Further analysis revealed that the under-dosage correlated with plan complexity and coincided with changes in clinically applied planning techniques.

Results: Prostate VMAT PSQA data showed an under-dosage gradual increasing to about 2% in 3 years, which was confirmed by the measurements with the 2D detector array in a phantom. The implementation of new beam fits in the TPS led to a reduction of the observed deviations.

Conclusion: Long-term analysis of site-specific PSQA data is a useful method to monitor incremental changes in a radiotherapy department due to various changes in the treatment planning and delivery of prostate VMAT, and may lead to a reduction of systematic dose uncertainties in complex treatments.

1. Introduction

When Intensity Modulated Radiation Therapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) are used clinically, it is strongly recommended to perform patient-specific quality assurance (PSQA). A large variety of measurement- and calculation-based patient-specific IMRT and VMAT pre-treatment quality assurance (QA) techniques is used in clinical practice as elucidated in various reports [1–4]. Patient-specific *in vivo* dose measurements may in addition provide information about differences between measured and planned dose distributions due to changes in patient anatomy and variation in patient setup [1,5–7]. The analysis of IMRT PSQA measurements of a specific patient group can be used to demonstrate that IMRT dosimetry was stable over time and within accepted tolerances [8]. However, information about long-term statistics on PSQA results for a large population from various treatment sites is limited. Pulliam et al. [9] analysed plan records and observed statistically significant differences in both point dose and planar dose verification measurements as a function of treatment site and measurement date. Other groups [10,11] analysed their IMRT PSQA results to identify similarities and differences between treatment plans of different treatment sites with the aim to define site-specific tolerance levels for QA approval.

If a PSQA result of a specific VMAT (or IMRT) treatment fails, and if this plan has more modulation than similar plans of the same site, it is common practice in many institutes that the case is re-planned to achieve the planning objectives with less complex intensity patterns [2]. However, such an approach may lead to a non-optimal treatment plan with respect to target coverage or dose in organs at risk, and we have therefore chosen another approach in which the planning objectives were not changed, as explained in the following section.

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In a radiotherapy department a continuous incremental change in the clinical use of techniques for imaging, planning and delivery occurs. Very often it concerns minor modifications that were introduced, for instance because in the planning team new personnel starts and experienced staff leaves, without extensive examination or supplementary end-to-end tests. PSQA data therefore contain in addition to alerted data also records of treatments that do not produce an alert but nevertheless include clinically relevant information *for a group of patients* that is not immediately evident when considering only flagged treatments *for individual patients*.

PSQA can be performed by means of 3D *in vivo* transit dosimetry using amorphous silicon (a-Si) EPIDs [12–16]. Such a type of analysis of *in vivo* dosimetry data of a large cohort of IMRT and VMAT has also been provided by several other groups [17–21]. The main objective of these studies was to test the usefulness of the clinically applied metrics and tolerance levels, showing that patient- specific tolerance dose values are dependent on many factors such as curative vs. palliative treatment intent, site, and available resources to track down errors. This is another aim than of our study as elucidated below.

The number of PSQA data in our department has increased considerably in the last decade; the number of prostate cancer patients treated per year with VMAT increased almost fourfold between 2010 and 2019. The aim of this study was to present a procedure to investigate long-term trend analysis of a complete set of PSQA data to identify any (gradual) change with time, and to find in a systematic way the reasons for it, which may lead to a reduction of underlying systematic dose uncertainties.

2. Materials and methods

2.1. Study design

Table 1 summarizes the different steps in the proposed procedure, first given as a general description of actions to be performed in each step, followed by the way these actions were implemented in our institute for prostate cancer treatments. Briefly, this study analysed trends in PSQA data of prostate cancer treatments obtained by EPID-based 3D *in vivo* dosimetry, which may lead to a reduction of systematic dosimetric uncertainties in VMAT planning and delivery. In the large set of VMAT PSQA data collected over the last 10 years we have chosen the prostate VMAT PSQA data from the period 2012–2019 to test the general procedure. The reason for this choice was not only that there is a large amount of PSQA data available for this treatment site, but also because we noticed a time-trend in the results in the period 2013–2016 that could initially not be explained, but which was probably due to small incremental changes in the planning and delivery of prostate VMAT.

Table 1
Different steps in the procedure to reduce systematic dosimetric uncertainties in radiotherapy by analysing patient-specific QA (PSQA) data.

Step	General procedure	Details of the method for prostate VMAT PSQA
1	Outline a measurement technique to collect PSQA data	EPID-based 3D *in vivo* transit dosimetry
2	Analyse for each treatment site and/or treatment strategy PSQA data	Assess if systematic deviations or time-trends are present in gamma evaluation metrics and the dose difference at the isocentre for prostate VMAT plans
3	Excludesmall systematic deviations in the measurement system	Dosimetric characteristics of the EPID were re-measured
4	If time-trends could not be explained, confirm the observed deviations with an independent dose verification system	After measuring the dosimetric characteristics of the detector array, absolute dose measurements were performed with this system for the same type of plans
5	Review the modifications in the clinical process that might have influenced the PSQA results	Changes in the prostate VMAT planning and delivery technique during the period 2012–2019 were summarised
6	Identify the major causes of dose changes in the planning and delivery techniques	The effect of MLC type and the single- vs two-arc irradiation technique were investigated
7	Relate the deviating QA results with specific plan or delivery machine characteristics	Plan complexity parameters were correlated with observed dose differences for prostate VMAT plans
8	Improve the deviating TPS or delivery machine characteristics	New TPS beam fits were implemented in 2016, bringing back the prostate PSQA data to the original level in 2012

The commonly applied clinical workflow procedure for PSQA, i.e. to use pre-treatment QA data, could not be used to solve the research question of this study because the number of those measurements was not sufficient to trace statistically significant systematic errors.

2.2. Planning and delivery of prostate VMAT

VMAT of prostate cancer was performed in our hospital since 2009, both on Synergy Sli20 linear accelerators (Elekta AB, Stockholm, Sweden), having an 80 leaf MLCi multileaf collimator (MLC) with 10 mm leaf width, and an Agility MLC having 160 leaves with 5 mm leaf width. More recently Versa HD linear accelerators (Elekta AB, Stockholm, Sweden), equipped with an Agility MLC, were also used for VMAT delivery.

Since their introduction, VMAT plans were generated with Pinnacle V9.0 to V9.16 (Philips Medical Systems, Eindhoven, The Netherlands), which includes the SmartArc module for VMAT plan generation. Prostate VMAT planning used a control point resolution of 4 degrees and was performed with flattened 10 MV beams.

The clinical target volume (CTV) consisted, depending on T-stage, Gleason score and prostate-specific antigen (PSA) level, of the prostate or the prostate including seminal vesicles. Standard plans included in this study used a simultaneous integrated boost of 35 × 2.2 Gy, with an elective dose of 35 × 2.0 Gy. Around 10% of the patients received an alternative fractionation of 19 × 3.4 Gy..

2.3. Dose verification of VMAT

All accelerators are equipped with an a-Si EPID (PerkinElmer XRD 1642 AP), which was used in combination with in-house developed MV image acquisition and transit dosimetry software. The *in vivo* dosimetry system used EPID images acquired behind a patient in combination with planning computed tomography (CT) data to reconstruct 3D dose distributions within the patient anatomy. For VMAT verification, cine-mode image acquisition was used and separate EPID frames were continuously acquired during delivery. The reconstructed 3D dose distributions of all frames were then summed to obtain the 3D dose distribution of the total VMAT arc. The raw data were corrected for possible errors during image acquisition. This was done by omitting those measurements having a dose difference at the isocentre larger than 10%, i.e. 5 times the standard deviation of about 2%, in the dose difference. In case measurements for more than one fraction were available, only the fractions with the highest pass rate were included in the analysis for data reduction and to have equal weighting of plans. By doing this, 36 plans (1.8 %) out of a total of 2001 plans were excluded and did therefore not insert an unintended bias in the data.

A possible cause for the deviating measurement results might have been an under-response of the EPID caused by a change in ghosting effects linked to the dose rate [22,23]. We therefore performed an extensive set of EPID measurements for 10 MV beams by irradiating a 30 × 30 × 20 cm^3 polystyrene phantom with 10x10 cm^2 fields to investigate such a possible under-response of the EPID. Five different dose rates (100%, 50%, 25%, 12.5% and 6% of the maximum dose-rate) were used, and the dose linearity of the EPID response was measured over the range 5–1000 monitor units (MUs), while absolute dose

measurements were performed with a microDiamond detector (PTW-Freiburg, Freiburg, Germany) [24]. For this purpose a calculation of the plan on a phantom was performed.

The first two steps in our study present VMAT PSQA data of a set of 1965 prostate patients performed in the period March 2012 to March 2019. Step 3 concerned the exclusion of (small) systematic deviations in the measurement system (EPID) used for this study. Because the observed time-trend in PSQA data could not be explained by changes in EPID characteristics, the deviations had to be confirmed with an independent dose verification system, for which the Octavius 1500 2D array (PTW-Freiburg, Freiburg, Germany) was used (Step 4). The array was inserted in the PTW Octavius 4D phantom which is a cylindrical phantom made of polystyrene with a slot to hold the detector array. The phantom rotates along with the gantry ensuring that the detector remains perpendicular to the beam at all times during delivery. 3D dose distributions were reconstructed within the Octavius 4D phantom geometry using the Verisoft 7.1 software (PTW-Freiburg, Freiburg, Germany). In some experiments the 2D array was replaced by a slab of polystyrene holding a calibrated microDiamond detector for absolute dose measurements. In all these phantom experiments a calculation of the plan on the phantom was necessary. For the determination of the dosimetric characteristics of the detector array, the same measurements as described above for the EPID were performed for a set of 17 prostate VMAT plans. Over the years, the class solution, number of VMAT beams and beam fit model were changed (Step 5). For instance, since mid-2018 the standard protocol changed to 20 × 3 Gy (without a boost). In addition the effects of MLC type and the single-vs two-arc irradiation technique were investigated (Step 6). Step 7 concerned a possible correlation between the number of MUs per cGy and the difference between the measured and planned dose at the isocentre. Apart from that we have also considered more complex metrics including beam modulation and aperture irregularity, as well as the modulation complexity score, but the results were highly correlated. (Data not shown). New TPS beam fits were implemented in 2016 (Step 8).

It should be noted that steps 1–3 should be repeated periodically, while in case of unexplained changes steps 4–8 should be followed

In order to exclude any deterioration of the EPID panel over the years, weekly end-to-end tests were performed by the therapists by irradiating a 30 × 30 × 20 cm polystyrene phantom on all accelerators using the EPID system for typical “standard” plans. Two VMAT plans were used for this purpose, a 6 MV head-and–neck plan, and a 10 MV rectal plan. If there was a deterioration in EPID response on a specific linac, the calibration factor of that EPID was adjusted. If the image quality of the EPID became too bad for clinical use in the time period of this study, the EPID was replaced by a new one.

3. Results

Fig. 1 shows a gradual lower measured dose at the isocentre of about 2% in the period 2013–2016, accompanied by a gradual lower gamma pass rate shown in Fig. 2. It should be noted that the under-response for the majority of cases was still within the acceptance level: 3% dose difference at isocentre and 85% pass rate.

Phantom measurements indicated that all EPID reading per MU ratios had a difference less than 1% compared to the value for the maximum dose rate, and the dose linearity of the EPID response was within 1%, relative to the value for 100 MUs. The absolute dose at the isocentre measured with the microDiamond detector also agreed within 1% with the EPID-based values. (Both set of data not shown).

The results of the measurements with the detector array were very similar to those observed for the EPID, with differences less than 1% for the dose-rate dependency and the dose–response linearity. The dose at the isocentre agreed also within 1% with the microDiamond values for field sizes of 5x5cm^2 and larger.

VMAT plans vary considerably in their complexity depending on the number of arcs, size of target volume, and related quantities such as leaf speed and number of MUs. Fig. 3 shows that indeed a correlation between the number of MUs per cGy and the difference between the measured and planned dose at the isocentre existed. Further analysis demonstrated that there was no difference between the two MLC types used. (Data not shown).

New beam fits were implemented in the TPS in 2016 , restoring the prostate PSQA results approximately to the level of 2012 (see Figs. 1 and 2).

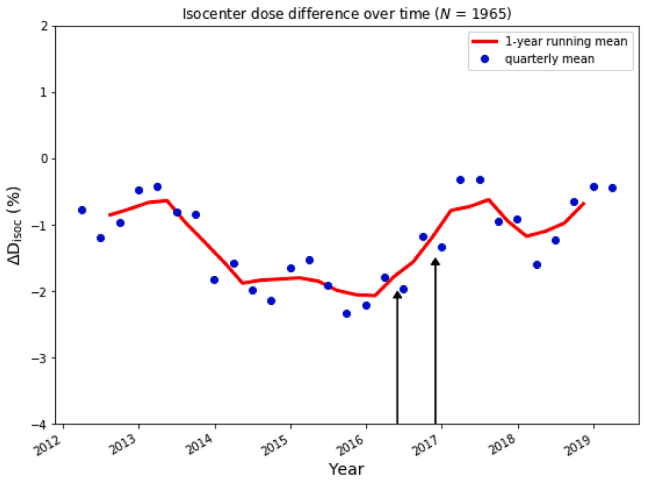

Fig. 1. Time dependence of the 3D *in vivo* dose verification results of prostate VMAT in the period March 2012 to March 2019. Shown are the mean 3-month dose differences per fraction at the isocentre. The red line indicates the running mean over 4 points, and the arrows indicate the clinical use of new beam fits in Pinnacle; the June 2016 beam model was for the Agility MLC and the December 2016 beam model for the MLCi. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

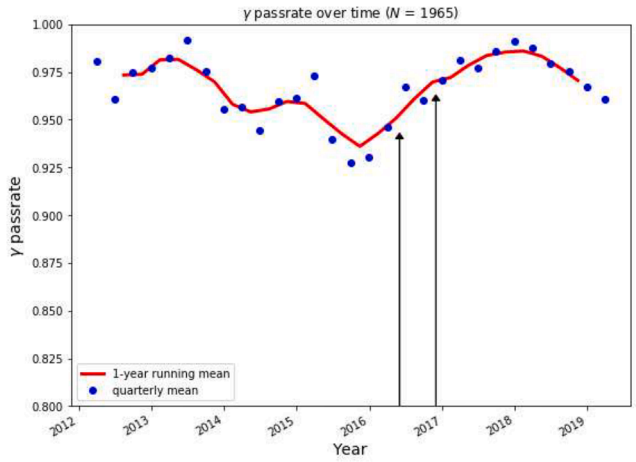

Fig. 2. Time dependence of the results of *in vivo* 3D dose verification of prostate VMAT in the period March 2012 to March 2019. Shown are the mean 3-month passing rates of 3D gamma evaluation per fraction. The red line indicates the running mean over 4 points, and the arrows indicate the clinical use of new beam fits in Pinnacle; the June 2016 beam model was for the Agility MLC and the December 2016 beam model for the MLCi. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

An 8-step method was proposed for long-term trend analysis of PSQA data to identify site-specific systematic dose uncertainties. Using this method, a systematic under-dosage was detected and corrected.

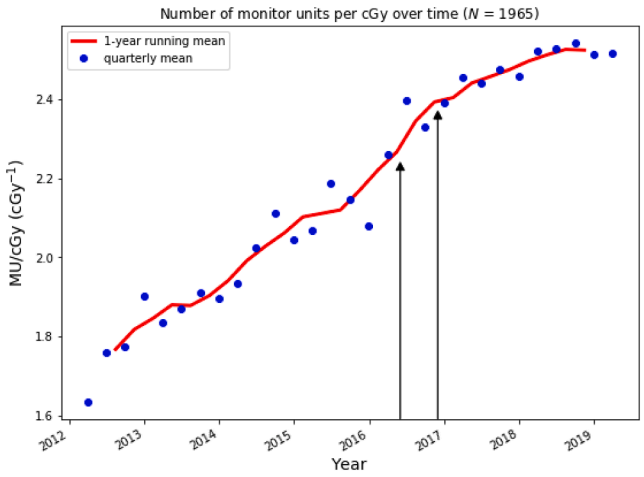

Fig. 3. Number of MUs per cGy as a function of time of prostate VMAT in the period March 2012 to March 2019. Shown are the mean 3-month monitor unit per cGy values per fraction. The red line indicates the running mean over 4 points, and the arrows indicate the clinical use of new beam fits in Pinnacle; the June 2016 beam model was for the Agility MLC and the December 2016 beam model for the MLCi. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

EPID-based 3D *in vivo* transit dosimetry PSQA results of a large patient population (1965 prostate VMAT treatments) were analysed (step 1–2). The measurements of the dose-rate dependency, the dose linearity and the absolute dose indicated that the dosimetric characteristics of the EPID were sufficiently accurate to be used for *in vivo* 3D dose verification of prostate VMAT, and did not require a modification (step 3). Furthermore, as pointed out in step 4, in a stable geometry the EPID-based dose verification measurements and the detector array data are in good agreement. Unfortunately, when we collected the detector array data for a set of 17 prostate VMAT plans, we did not perform phantom measurements with the EPID system for the same set of prostate plans. However, in another study performed in that time period, we proved that for 68 VMAT plans the agreement between the reconstructed 3D dose distributions obtained with EPID dosimetry and the detector array was very good; the average γ-pass rate (2% local/2 mm) was 92.2 ± 5.2% (1SD).

Various changes in the treatment planning and delivery of prostate VMAT in the period 2012–2019 may have influenced the PSQA results and have been reviewed (steps 5 and 6). The most important changes concerned the introduction of multiple arcs having more modulation, and the use of the Auto-planning module, but it cannot be ruled out that other changes like a small change in the template objective function or a change in the bladder filling protocol have also occurred. The change from one to two arcs happened gradually in the period October 2012 to September 2014. Auto-planning was introduced in March 2016 for the 35 × 2.2 Gy fractionation scheme, and in December 2016 for the 19 × 3.4 Gy fractionation. The reason that the Auto-planning module resulted in more MU/cGy was that it effectively performed 6 consecutive warm start optimisations, where the segmented result of 1 optimisation was the starting point for the next one. During each run the complexity increased slightly, leading at the end to a more complex plan compared to standard use which typically consisted of 1 or 2 warm starts. This was reflected in the increase in the number of MUs per cGy as a function of time (see Fig. 3).

In general, *in vivo* dosimetry of prostate VMAT shows larger uncertainty compared to pre-treatment QA using a phantom due to variation in rectal and bladder filling, patient or organ motion, the presence of metallic hips, contour changes, etc. for an individual patient [6,7]. However, due to the abundance of data and the randomness of the variations, time trends of average values of *in vivo* data for a group of patients do contain reliable information of the underlying dosimetric processes.

In the period of our study, technical aspects of treatment planning were continuously evolving, including modifications in the TPS software, a change from one to two VMAT arcs, and the introduction of Auto-planning. Two new beam fits where implemented in the period 2013–2016. These differed from the previous ones mainly in terms of the leaf offset table (a correction from the physical leaf-tip position compared to the radiological leaf-tip position) and the modelling of the tongue-and-groove width. The changes in the TPS software were generally thoroughly tested, including detector array measurements, but did not result in improved PSQA results in the period 2013–2016. The reason is that some of the TPS parameters, such as the MLC transmission and the tongue-and-groove width, are not physical, but provide dosimetric results which match the delivered dose for simple geometries. As a result long, narrow apertures in VMAT beams tend to cause an overestimation of the TPS output factor, which is difficult to adjust, resulting in a too low measured dose during VMAT verification [25,26].

New beam fits were introduced in June 2016 for the Agility MLC and in December 2016 for the MLCi. The emphasis in 2016 was shifted to improvements in dose calculation for target areas and modeling of the leaves and interleaf transmission following the latest recommendations of the manufacturer, i.e. taking care of the increasing complexity of the plans. After implementing these new beam models in the TPS, the PSQA results were restored to the level at the beginning of this study (see Figs. 1 and 2). The reason the restoring appears more gradual is: first the data shown is averaged over a 3-month period and thus causes some blurring over adjacent points; i.e. the change was not precisely in between two 3-month periods. Second, the red line is a running mean over 4 points and hence is also less sensitive to jumps. The new beam models alone do not fully explain the shape of these curves as also other modifications in the VMAT technique occurred due to changes in fractionation schemes (see Section 2.3) and the introduction of Auto-planning. Furthermore, on average still a small remaining systematic underdosage of 0.5% to 1% can be observed, which is similar to the verification results of VMAT dose calculations by Pinnacle in combination with Elekta linacs as reported by Bedford *et al.* [25] and Louwe *et al.* [26]. According to these authors this under-dosage in dose calculations of VMAT seems to be inevitable because commissioning of the TPS is generally carried out using only a finite set of beam configurations. Obviously, modeling a TPS and carefully checking the accuracy of planned 3D dose distributions for a number of treatment techniques does not guarantee the correctness of the TPS in calculating 3D dose distributions for other sophisticated treatment techniques. It confirms the opinion expressed by Kerns *et al.* [27] that there is a need for regularly checking the beam modeling and dose calculation in a TPS. Periodic checks of class solutions, in combination with time-trend analysis, such as the one described in this paper, should be performed to ensure that a class solution still delivers the same plan quality as during its initial introduction.

In conclusion, long-term trend analysis and data visualization of PSQA data of VMAT were able to trace site-specific deviations due to incremental technical innovations in a radiotherapy department. Application of this procedure unveiled that it could lead to an improvement of the PSQA results and a reduction of systematic dosimetric uncertainties in VMAT .

Informed consent

At the time the study was conducted, our department applied an opt-out procedure for use of patient data, consistent with the code of conduct 'Human Tissue and Medical Research; Code of conduct for responsible use (2011)' that was used in the Netherlands. Patients were informed that data that was collected as part of their standard treatment could be used for scientific research after anonymization. If patients refused this use, they could indicate that they opted out of this.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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