Original Article

Validation of Three-dimensional Electronic Portal Imaging Device-based PerFRACTION™ Software for Patient-Specific Quality Assurance

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Abstract

Purpose: PerFRACTION™ is a three-dimensional (3D) *in vivo* electronic portal imaging device-based dosimetry software. To validate the software, three phantoms with different inserts (2D array, ionization chamber, and inhomogeneity materials) were constructed to evaluate point dose and fluence map. **Materials and Methods:** Phantoms underwent independent computed tomography simulation for planning and received repetitive fractions of volumetric modulated arc therapy, simulating prostate treatment. Fluence and absolute point dose measurements, PerFRACTION™ reconstructed doses, and the dose predictions of the planning system were compared. **Results:** There was concordance between ionization chamber and PerFRACTION™ 3D absolute point dose measurements. Close agreement was also obtained between X- and Y-axis dose profiles with PerFRACTION™ calculated doses, MapCHECK measured doses, and planning system predicted doses. Setup shifts significantly influenced 2D gamma passing rates in PerFRACTION™ software. **Conclusions:** PerFRACTION™ appears reliable and valid under experimental conditions in air and with phantoms.

Keywords: EPID, *In-vivo* dosimetry, PerFRACTION™, Phantoms, Validation

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Introduction

Radiotherapy is a major modality in cancer management for about 50% of all patients.[1] The objective of radiotherapy is to provide sufficient target dose to reliably achieve a desired tumor control probability while providing the lowest possible dose to surrounding normal and especially critical structures, thereby securing a relatively high therapeutic ratio of potential benefit compared with hazard.

Technological developments in engineering and computing have greatly improved the methods of radiation delivery over the past few decades.[2] To take full advantage of this, treatment planning systems (TPSs) use powerful optimization tools to generate clinical treatment plans for intensity-modulated radiation therapy, volumetric-modulated arc therapy (VMAT), and stereotactic radiosurgery or body radiation therapy. These complex plans entail significant dose gradients around and within both target volumes and tissues at risk of adverse events. Consequently, the International Commission on Radiation Units and Measurements recommends a specific dose-volume histogram analysis,[3] and additional guidelines promote dose constraints for tissues at risk[4] that must be maintained over a course of radiotherapy through reliable and consistent delivery of radiation (planned at baseline or modified during the course such as in adaptive radiotherapy). Typically, radiation dose is delivered over 4–6 weeks in 20–30 fractions. This takes advantage of biological differences between cancer cells and normal tissue cells. Hence, it is imperative to consistently reproduce patient position and internal anatomy relative to the baseline computed tomography (CT) simulation. In reality, patient organ motion, anatomical changes due to weight

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loss, tumor response, uncertainty in the delivery system, and patient setup variation make it very difficult to achieve this ideal condition. It is possible to use adaptive radiotherapy to accommodate these, providing that dose distribution within the patient can be captured accurately by *in vivo* dosimetry.

Typical *in vivo* dosimetry is done by placing radiation dosimeters directly on the patient skin at the time of treatment. This provides a point dose which can validate the delivery system performance but may not capture any other variation. A more robust and rapid quality assurance (QA) in dosimetric verification is needed. With the introduction of modulated treatments, many QA procedures have been introduced to verify dose before treatment. A pretreatment QA ensures calculated dose for treatment which can be delivered. Recently, PerFRACTION™ was developed by Sun Nuclear Corporation as a three-dimensional (3D) *in vivo* dosimetry software to provide near real-time and online verifications of radiation dose delivered during clinical treatment. This software uses monitor chamber dose rate and output data coupled with exit fluence from the patient as captured by the electronic portal imaging device (EPID) during treatment. It reconstructs the 3D dose distribution in the pretreatment planning CT or an acquired cone-beam CT (CBCT).[5]

The purpose of this study was to validate the PerFRACTION™ software, an important process before clinical use. The first step in this study is a basic comparison of measurements by PerFRACTION™ software compared with those of a standard 2D array MapCHECK system and an ionization chamber placed inside an appropriate phantom. The second introduces known table shifts to an inhomogeneous 3D phantom to check the capability of detecting inaccuracies by PerFRACTION™ software.

Materials and Methods

Phantom constructions

Typical to most clinical programs, pretreatment patient-specific VMAT QA includes point dose verification by ionization chamber-based measurements and gamma index[6] fluence evaluation by 2D array-based measurements. Two polymethylmethacrylate (PMMA) 1-cm slab phantoms were constructed[7] [Figure 1]: phantom 1 with an ionization chamber (Sun Nuclear, SNC125c) inserted at 5 cm from the anterior (ANT) surface with the backscatter of 5-cm PMMA slaps and phantom 2 with a diode detector array (Sun Nuclear, MapCHECK 2), each positioned along the central axis. The third PMMA phantom (phantom 3), with two polystyrene ("thermocol") sheets (7.5-cm thickness) lining the inside of the slab cavity, was constructed to test the accuracy of detecting setup errors by the PerFRACTION™ software.[5] To determine the 2D gamma response, various inhomogeneity materials were designed and inserted into the thermocol sheet in appropriate locations to simulate a pelvis model: vinyl-based gel bolus (near to water equivalent) as a prostate tumor; pressed bones (readymade bone rawhide) for both lateral sides; another vinyl-based gel bolus superiorly placed to simulate the bladder; shredded wood to simulate the rectum was placed inferiorly; and a raw chicken leg bone inserted posterior (POST) to the prostate in the model to simulate the sacral vertebra [Figure 2].

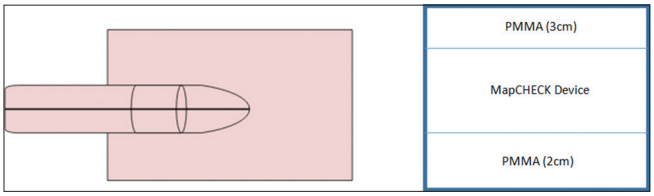

Figure 1: First two phantoms with ionization chamber and two-dimensional MapCHECK device between the polymethylmethacrylate plates

Scanning and treatment planning

A general electric light speed Pro 16 CT scanner was used for simulation. All three phantoms were individually aligned using CT lasers; the isocenter of the first two phantoms was placed at the center of the respective detectors, while the center of the "prostate" (as tumor) was used with the inhomogeneous phantom. Each phantom was scanned with a CT slice thickness of 1.25 mm. The DICOM CT images were exported to Monaco 5.10 TPS, one set of images for each phantom. Surface outlines were contoured for each phantom. 3D structures were created for the first two phantoms using the margin tool in Monaco 5.10 to provide the reference volumes for the planning. Two VMAT plans were generated individually for the first and second phantoms using two full arcs with a prescribed dose of 30 Gy in 15 fractions at 2 Gy per fraction to the prostate volume. A single-arc VMAT plan was generated for the inhomogeneous phantom. A Monte Carlo algorithm and dose-to-medium settings were used for the VMAT calculations. Plans were exported separately to the PerFRACTION™ server and to the Mosaiq Oncology Information System to deliver the "treatments."

Measurements

The delivery machine was an Elekta Infinity with Agility head. The MapCHECK device was calibrated to the absolute

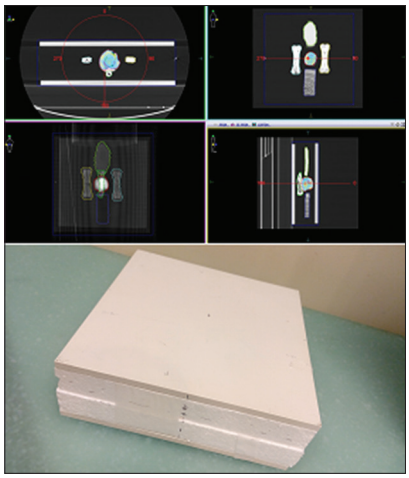

Figure 2: In-house made three-dimensional inhomogeneous phantom with various density inserts

dose before the measurement. In PerFRACTION™, there are two schemas to verify radiation dose delivered to the patient: Fraction 0™ and Fraction n™. Fraction "0" (zero) is essentially a 3D pretreatment dose delivery capture in which the treatment plan is delivered directly into the EPID. Captured images are reconstructed to calculate the 3D dose to check the point dose and gamma analysis within the PerFRACTION™ software. Fraction "n" is the daily *in vivo* monitoring for use during treatment and includes captured exit fluence patterns from the patient matched with treatment log files. The reconstructed doses can be verified each day.[8]

Initial measurements were made without any phantom on the treatment couch, directly irradiating VMAT plans onto the EPID. These were set as Fraction 0. Then, fractions 1–15 were delivered to the first and second phantoms separately and set up as in the CT simulation. The third phantom was irradiated with no shifts introduced on the couch and then with 1.0-cm couch shifts applied over inferior/superior, left lateral/right lateral, and ANT/POST directions. Exit fluences from the phantom were recorded for all fractions. Each exit fluence was reconstructed in PerFRACTION™ software to calculate 3D dose and fluences. The ICOM tool in Elekta iView application captured multileaf collimator segment images.

Evaluation

Evaluation included direct comparison between measurements in the phantoms with PerFRACTION™ reconstructed doses and planning system distributions. A full, 3D absolute dose volume was calculated in PerFRACTION™, and from this, the point doses corresponding to the ion chamber location and along MapCHECK axes (X and Y) were extracted for comparison. In phantom 1, repeated measurements by ion chamber were done through 15 daily setups for the central axis point. Measured values were tabulated [Table 1] and plotted [Figure 3] to compare measured absolute point doses, and differences were calculated. In phantom 2, the 2D planar profiles in orthogonal X- and Y-directions were measured through 15 daily setups. The means of each fraction (with standard deviations [SDs]) for each array point were tabulated and plotted for comparison [X-axis array points, Table 2 and Figure 4; Y-axis array points, Table 3 and Figure 5]. Similarly, for phantom 3, the one no shift and the four combinations of shifts were each measured through 5 daily repetitions [plotted with error bars in Figure 6]. Statistical tests were conducted with Stata 14.2 (College Station, TX). One linear regression compared the dose provided by PerFRACTION™ and by the ionization chamber at the central axis. A multilevel mixed-effects regression was conducted to compare dose provided by PerFRACTION™ and MapCHECK at the 2D array points across the repeating fractions. All *P* values were two-tailed for coefficients in these comparisons.

Three-dimensional dose reconstruction process

Reconstructing 3D dose to a patient/phantom requires knowledge of the delivered beam intensities (as a function of time/gantry angle) and the position of the patient. For the first, PerFRACTION™ combines time-based gantry angle and output information from the machine log file with cine EPID data for leaf positions to derive the delivered beam intensity values. The delivered beam intensities are then forward projected into the patient/phantom volume (planning CT or CBCT if available) using a superposition/convolution graphics

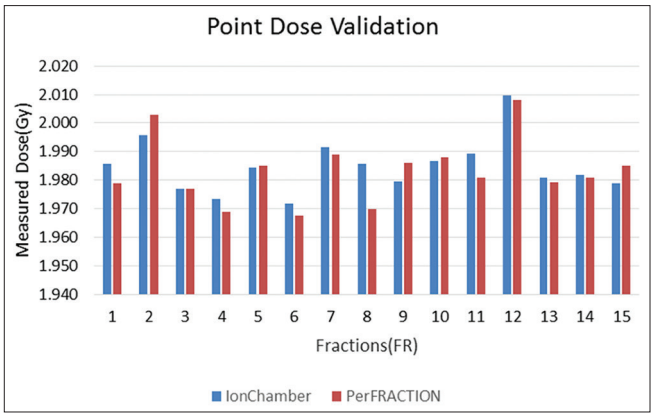

Figure 3: Comparison of measured doses by ionization chamber and PerFRACTION™ for each delivered fraction in the phantom 1

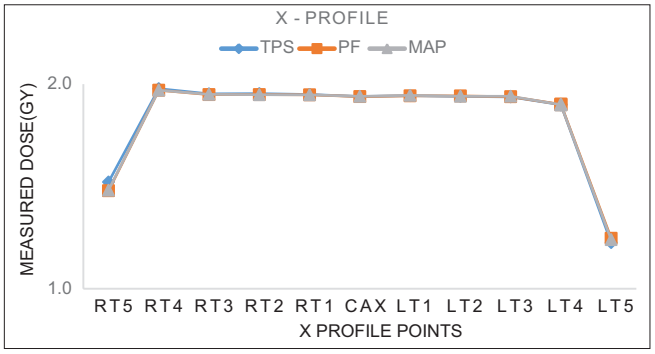

Figure 4: X-axis profile. Legend: TPS: Treatment planning system, PF: PerFRACTION™, MAP: MapCHECK, RT: Right, CAX: Central axis, LT: Left. Standard deviations on each point are fully encompassed within the data points

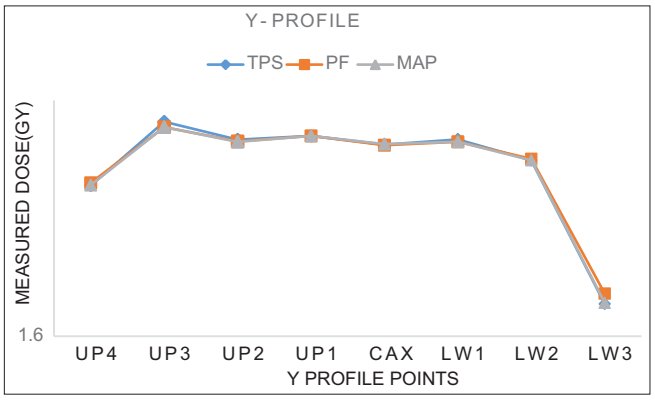

Figure 5: Y-axis profile. Legend: TPS: Treatment planning system, PF: PerFRACTION™, MAP: MapCHECK, UP: Upper, CAX: Central axis, LW: Lower. Standard deviations on each point are fully encompassed within the data points

Table 1: Comparison of three-dimensional absolute point doses by ionization chamber and PerFRACTION™ calculations in phantom 1

Fractions	Ion chamber (Gy)	PerFRACTION™ (Gy)	Difference (Gy)
FR1	1.986	1.979	−0.007
FR2	1.996	2.003	0.007
FR3	1.977	1.977	0.000
FR4	1.973	1.969	−0.004
FR5	1.985	1.985	0.000
FR6	1.972	1.968	−0.004
FR7	1.992	1.989	−0.003
FR8	1.986	1.970	−0.016
FR9	1.980	1.986	0.006
FR10	1.987	1.988	0.001
FR11	1.989	1.981	−0.008
FR12	2.010	2.008	−0.002
FR13	1.981	1.979	−0.002
FR14	1.982	1.981	−0.001
FR15	1.979	1.985	0.006
Mean±SD (Gy)	1.985±0.009 Gy	1.983±0.010 Gy	

SD: Standard deviation

Table 2: X-axis point dose validation

X-axis points	Mean±SD_ PerFRACTION™ (Gy)	Mean±SD_ MapCHECK (Gy)	TPS (Gy)
RT5	1.394±0.017	1.396±0.022	1.436
RT4	1.960±0.011	1.959±0.010	1.969
RT3	1.930±0.006	1.931±0.007	1.935
RT2	1.930±0.006	1.930±0.006	1.937
RT1	1.929±0.006	1.929±0.005	1.931
CAX	1.917±0.006	1.919±0.007	1.918
LT1	1.923±0.006	1.925±0.007	1.923
LT2	1.922±0.007	1.919±0.010	1.919
LT3	1.917±0.006	1.919±0.006	1.915
LT4	1.868±0.007	1.865±0.013	1.865
LT5	1.186±0.020	1.181±0.027	1.170

CAX: Central axis, SD: Standard deviation, TPS: Treatment planning system

Table 3: Y-axis point dose validation

Y-axis points	Mean±SD_ PerFRACTION™ (Gy)	Mean±SD_ MapCHECK (Gy)	TPS (Gy)
UP1	1.934±0.007	1.934±0.005	1.934
UP2	1.924±0.007	1.923±0.006	1.927
UP3	1.950±0.012	1.950±0.012	1.960
UP4	1.850±0.019	1.846±0.017	1.845
CAX	1.917±0.006	1.919±0.007	1.918
LW1	1.923±0.008	1.923±0.008	1.928
LW2	1.892±0.017	1.890±0.010	1.890
LW3	1.666±0.016	1.6516±0.023	1.650

CAX: Central axis, SD: Standard deviation, TPS: Treatment planning system

processing unit-accelerated dose computation algorithm[9,10] to produce a 3D reconstructed dose distribution. By incorporating monitor chamber dose recorded during delivery as well as measured leaf positions (from analysis of EPID images) in the forward calculation, PerFRACTION™ attempts to capture and calculate the impact of machine output and collimation delivery errors to the patient/phantom volume.[5]

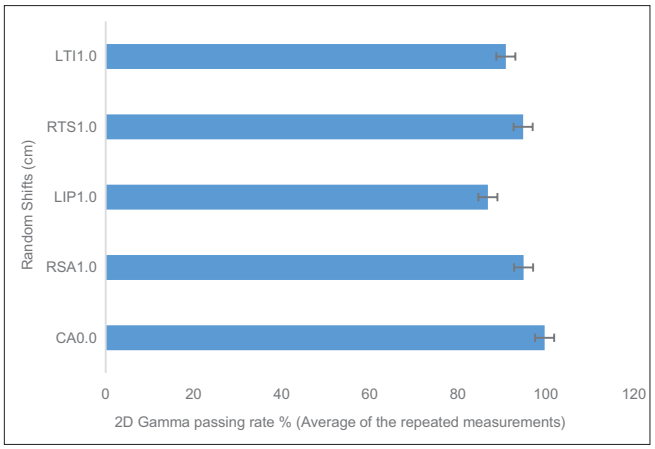

Figure 6: Two-dimensional gamma results in PerFRACTION™ with inhomogeneous phantom's shift measurements. Legend: CA0.0: Central axis 0.0 cm (No shifts), RSA1.0: Right lateral, superior, anterior shifts 1.0 cm, LIP1.0: Left lateral, inferior, posterior 1.0 cm, RTS1.0: Right lateral, superior 1.0 cm, LTI1.0: Left lateral, inferior 1.0 cm

Results and Discussion

Three-dimensional point dose comparison in phantom 1

The point dose calculated by the TPS at the ionization chamber location in phantom 1 was 1.989 Gy. For PerFRACTION™ for Fraction 0, it was calculated to be 1.989 Gy; no difference was noticed between the TPS point dose and Fraction 0 measurement. For fractions 1–15, the PerFRACTION™ calculated 3D point dose is compared [Table 1] with the point dose measured by the ionization chamber, and the differences between both estimations are presented according to each fraction. The greatest difference was − 0.016 Gy, with the other 14 differences being ≤ ±0.008 Gy. For all 15 fractions, the mean ± SD for the ionization chamber was 1.985 ± 0.009 Gy; it was 1.983 ± 0.010 Gy for PerFRACTION™. There was a close and linear relationship between both measurement methods for fractions 1–15 [Figure 3].

X–Y-axis point dose comparison in phantom 2

An X-Y grid was used to compare doses in phantom 2. Results for the X-axis [Table 2 and Figure 4] and Y-axis [Table 3 and Figure 5] are shown, with table columns for PerFRACTION™, MapCHECK, and the TPS. Each row corresponds to one point along the X- or Y-axis. [Note that the identical data corresponding to the central axis are presented in both Tables 2 and 3 and both Figures 4 and 5.] There is a visual correspondence between the mean doses at each point when comparing PerFRACTION™, MapCHECK, and the TPS. Quantitatively, only 2.2% of 270 differences between dose measured by PerFRACTION™ and MapCHECK exceed the absolute difference in dose of 0.05 Gy, and the highest value of difference was −0.074 Gy at Y-axis LW2 point.

Shift measurements in phantom 3

A reduction in the PerFRACTION™ 2D gamma pass rate, relative to the baseline, was observed for all introduced shifts. Pass rate differences ranged from 5% to 13% with a high degree of reproducibility across all repeated measurements [Figure 6]. Some introduced shifts resulted in heterogeneities within the phantom having a greater impact on dose distribution, producing greater reductions in the gamma pass rate.

Regression analysis

The regression comparing PerFRACTION™ and ionization chamber values at only the central axis gave a difference in dose between PerFRACTION™ and the ionization chamber of +0.002 Gy for PerFRACTION™ with a 95% confidence interval (CI) of +0.01497 Gy to −0.010965 Gy (P = 0.75, not statistically significant). The multilevel mixed-effects regression comparing PerFRACTION™ and MapCHECK demonstrated that, controlling for fractions and array points, the difference in dose was +0.00126 Gy for PerFRACTION™ with a 95% CI of −0.00090 Gy to +0.00342 Gy and two-tailed P value for a difference of 0.25. These regressions demonstrate that PerFRACTION™ did not provide point dose estimates that statistically differed from those provided by the ionization chamber or MapCHECK.

Conclusion

This study demonstrates that for central axis, off-axis point doses in a static scenario with the first two phantoms and 2D gamma passing effects and in shift positions with a more complex third phantom, PerFRACTION™ dose estimates are in agreement with measurements acquired with MapCHECK diodes, with an ionization chamber and with predictions provided by the TPS to the same spatial locations. The study also demonstrated influence on the 2D gamma passing rates in PerFRACTION™ software due to the introduction of errors in phantom setup.

Validating innovative measures and processes occurs in a series of logical steps. This study looked at the most basic arrangement of static phantoms and setup translations in an in-house designed inhomogeneous phantom using VMAT plans. In the most limiting of scenarios, PerFRACTION™ was compared favorably with ionization chamber, MapCHECK and planning system dose values in- and off-axis for VMAT plans, and also with introduced translation errors in the inhomogeneous phantom. PerFRACTION™ reliably identified experimentally introduced errors and estimated their impact. With this initial validation result and recent publications,[11-14] we have introduced PerFRACTION™ into daily clinical practice to further validate this software program using clinical data.

Taking a phantom through an entire course of fractions can provide a high level of "end-to-end" QA.[15]

Further validation of PerFRACTION™ is justified with additional active experiments and with passive analytics during clinical operations across patients and tumor types at different body locations. Such studies would extend validation across the applied technological and clinical space. With PerFRACTION™, actual treatment quality could be determined in relation to machine, attachment, patient, and setup variations arising in practice. This may help direct adaptive (re) planning strategies to optimize therapeutic ratio.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Delaney G, Jacob S, Featherstone C, Barton M. The role of radiotherapy in cancer treatment: Estimating optimal utilization from a review of evidence-based clinical guidelines. Cancer 2005;104:1129-37.
2. Williamson JF, Dunscombe PB, Sharpe MB, Thomadsen BR, Purdy JA, Deye JA, *et al.* Quality assurance needs for modern image-based radiotherapy: Recommendations from 2007 interorganizational symposium on "quality assurance of radiation therapy: Challenges of advanced technology". Int J Radiat Oncol Biol Phys 2008;71:S2-12.
3. International Commission on Radiation Units and Measurements. Prescribing recording and reporting photon beam therapy. Report 83. Oxford University Press. Journal of the ICRU 2010;10.
4. Bentzen SM, Constine LS, Deasy JO, Eisbruch A, Jackson A, Marks LB, *et al.* Quantitative analyses of normal tissue effects in the clinic (QUANTEC): An introduction to the scientific issues. Int J Radiat Oncol Biol Phys 2010;76:S3-9.
5. SunCHECK Patient. On the Matter of Forward versus Back Projection for Radiotherapy 3D Dose Reconstruction. White Paper D072516. Melbourne, FL: Sun Nuclear Corporation; 2016.
6. Low DA, Harms WB, Mutic S, Purdy JA. A technique for the quantitative evaluation of dose distributions. Med Phys 1998;25:656-61.
7. Won HS, Chung JB, Eom KY, Hwang DG, Kang SW, Suh TS. Feasibility study of multi-purpose quality assurance phantom for pretreatment verification of volumetric modulated arc therapy. Int J Radiat Res 2018;16:279-87.
8. SunCHECK Patient. PerFRACTIONTM 3D Pre-Treatment QA and *In-Vivo* Monitoring. D041316. Melbourne, FL: Sun Nuclear Corporation; 2017.
9. Jacques R, Taylor R, Wong J, McNutt T. Towards real-time radiation therapy: GPU accelerated superposition/convolution. Comput Methods Programs Biomed 2010;98:285-92.
10. Jacques R, Wong J, Taylor R, McNutt T. Real-time dose computation: GPU-accelerated source modeling and superposition/convolution. Med Phys 2011;38:294-305.
11. Vinagre F, Rachinhas P, Simoes P, Cavaco A, Balau F, Borrego M. Implementation of a Patient Specific QA *in vivo* Dosimetry Protocol Using the PerFRACTION 3D System. Eposter EP-1764. Vienna, Austria: ESTRO; 2017.
12. Reilly AJ, Haughey A. Implementation of a Forward Projection *in vivo* Dosimetry System for Treatment Verification in a New Radiotherapy Service. The UK Radiological Congress and Radiation and Oncology Congress. Manchester Central; 12-14 June, 2017.
13. Zhuang AH, Olch AJ. Sensitivity study of an automated system for daily patient QA using EPID exit dose images. J Appl Clin Med Phys 2018;19:114-24.
14. Sait AA, Hliziyo F, Figueredo J, McGowan T, Jones G, Thomas RS, *et al*. Validation of PerFRACTION 3D EPID based patient specific QA Software. Med Phy Int J 2016;4:328.
15. IAEA Human Health Series. Accuracy Requirements and Uncertainties in Radiotherapy. International Atomic Energy Agency Rep. Vienna: IAEA Human Health Series; 2016;31:297.