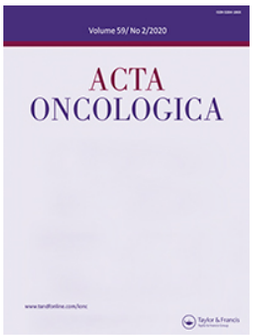

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ORIGINAL ARTICLE

IAEA methodology for on-site end-to-end IMRT/VMAT audits: an international pilot study

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ABSTRACT

Background: The IAEA has developed and tested an on-site, end-to-end IMRT/VMAT dosimetry audit methodology for head and neck cases using an anthropomorphic phantom. The audit methodology is described, and the results of the international pilot testing are presented.

Material and methods: The audit utilizes a specially designed, commercially available anthropomorphic phantom capable of accommodating a small volume ion chamber (IC) in four locations (three in planning target volumes (PTVs) and one in an organ at risk (OAR)) and a Gafchromic film in a coronal plane for the absorbed dose to water and two-dimensional dose distribution measurements, respectively. The audit consists of a pre-visit and on-site phases. The pre-visit phase is carried out remotely and includes a treatment planning task and a set of computational exercises. The on-site phase aims at comparing the treatment planning system (TPS) calculations with measurements in the anthropomorphic phantom following an end-to-end approach. Two main aspects were tested in the pilot study: feasibility of the planning constraints and the accuracy of IC and film results in comparison with TPS calculations. Treatment plan quality was scored from 0 to 100.

Results: Forty-two treatment plans were submitted by 14 institutions from 10 countries, with 79% of them having a plan quality score over 90. Seventeen sets of IC measurement results were collected, and the average measured to calculated dose ratio was 0.988 ± 0.016 for PTVs and 1.020 ± 0.029 for OAR. For 13 film measurement results, the average gamma passing rate was 94.1% using criteria of 3%/3 mm, 20% threshold and global gamma.

Conclusions: The audit methodology was proved to be feasible and ready to be adopted by national dosimetry audit networks for local implementation.

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Introduction

During the last decades, intensity-modulated radiotherapy (IMRT) and volumetric-modulated arc therapy (VMAT) have become widespread around the world. At the same time, external auditing capabilities for radiotherapy (RT) institutions in many countries are limited to the measurement of the absorbed dose to water in reference conditions, which is provided by several dosimetry audit networks (DANs) including the International Atomic Energy Agency (IAEA) in collaboration with the World Health Organization (WHO) [1–3]. Meanwhile, implementation of modern RT techniques leads to optimal patient treatment outcomes when supported by comprehensive local quality assurance (QA) programs and external audits [4–8].

The IAEA has developed several auditing methodologies which involve measurements of absorbed dose to water for high-energy photon and electron beams in non-reference conditions including end-to-end audits for 3D conformal and intensity modulated RT treatments [9–13]. Although these audits are not provided directly by the IAEA as a regular service, their methodologies are available for implementation at a national level by a local DAN with the IAEA support [14–17].

End-to-end testing is a suitable approach for checking the RT chain from imaging through treatment planning to the plan delivery using anthropomorphic phantoms [18–20]. It is particularly useful for checking IMRT and VMAT techniques since they largely rely on automatic processes such as

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Supplemental data for this article can be accessed here.

inverse treatment planning, network data transfer, dynamic multileaf collimator (MLC) based dose delivery with variable gantry speed and dose rate (for VMAT) as well as multiple handovers between different professionals. On the other hand, in case a discrepancy is found, an end-to-end test is of limited use for a root cause analysis and thus should be accompanied by evaluation of the main influencing parameters. These parameters include the beam output in the reference conditions, small beam output factors (OFs), small beam profiles, MLC characteristics and several treatment planning system (TPS) specific features. In particular, it is important to check how heterogeneities are accounted for in TPS calculations since IMRT is performed by the use of superposition of small beam segments in heterogeneous media, which currently represents a major dosimetry challenge [21,22]. One of the anatomic sites that benefits the most from IMRT treatments is head and neck (H&N), which is highly heterogeneous and contains multiple organs at risk (OARs) located close to the planning target volumes (PTVs). Furthermore, IMRT allows simultaneous delivery of different doses to different PTVs within a single fraction, an approach called simultaneous integrated boost (SIB). Both, the SIB approach and dose constraints to nearby organs at risk often cause high degrees of MLC modulation, making it a challenging site for RT treatment planning and delivery.

Taking into account the considerations above, the IAEA has developed an on-site, end-to-end IMRT audit methodology using a commercial anthropomorphic H&N phantom. This work describes the details of the methodology and summarizes the results of the international pilot testing.

Material and methods

Audit package

The 'Shoulders, Head And Neck, End-to-end' (SHANE, CIRS Inc., Norfolk, VA, USA) phantom was designed based on the IAEA specifications during the audit development stage and is commercially available now. It represents an H&N region of a typical RT patient with complex anatomy modeled using plastic materials equivalent to soft tissues, bones and teeth (Figure 1). It has four parallel cylindrical hollow channels in the cranial-caudal (CC) direction accompanied with a set of sleeves and spacers for positioning of ion chambers (ICs) along them. The SHANE phantom may also be disassembled along the mid-coronal plane to accommodate a film. In addition, the caudal part of the phantom contains four calibrated reference plugs (cortical bone, trabecular bone, lung inhale, lung exhale) and a vial with water for obtaining a computed tomography (CT) number to relative electron density (RED) conversion curve (CT-to-RED curve).

A reference set of CT images of the SHANE phantom was obtained with 1 mm slice thickness, 120 kV, 545 mAs. PTV and OAR contours and planning objectives and constraints have been developed for the SHANE phantom by a team of experts in a similar way to RTOG 00-22, RTOG 0615 and PARSPORT trials [23–25]. In accordance with clinical practice, three PTVs are prescribed to 70, 60 and 54 Gy in 30 fractions and defined as PTV_7000, PTVn1_6000 and PTVn2_5400, respectively. Organs at risk are the parotid glands, brain stem and spinal cord. The brain stem and the spinal cord have expanded planning risk volumes with additional dose constraints (Supplementary Table 1). The structure set also contains the delineations of the four IC cavity volumes positioned in pre-defined measurement locations inside the PTVs and the spinal cord (namely, IC_PTV_7000, IC_PTVn1_6000, IC_PTVn2_5400 and IC_SpinalCord, Figure 2) in order to calculate the dose to a chamber volume and for the dose homogeneity assessment. A small volume (0.125 cm^3) PTW 31010 Semiflex ion chamber (PTW Freiburg Inc., Breisgau, Germany) was chosen for this audit and therefore its adapter is included in the phantom package and its active volume contours in measurement positions are included in the structure set. However, the IC itself was not a part of the package in the pilot study. For the consistency of results in national audits, the national auditing organization uses its reference IC for measurements in all participating institutions. EBT3 Gafchromic film (Ashland Inc., Covington, KY, USA) was chosen for film measurements.

Figure 1. The disassembled SHANE phantom.

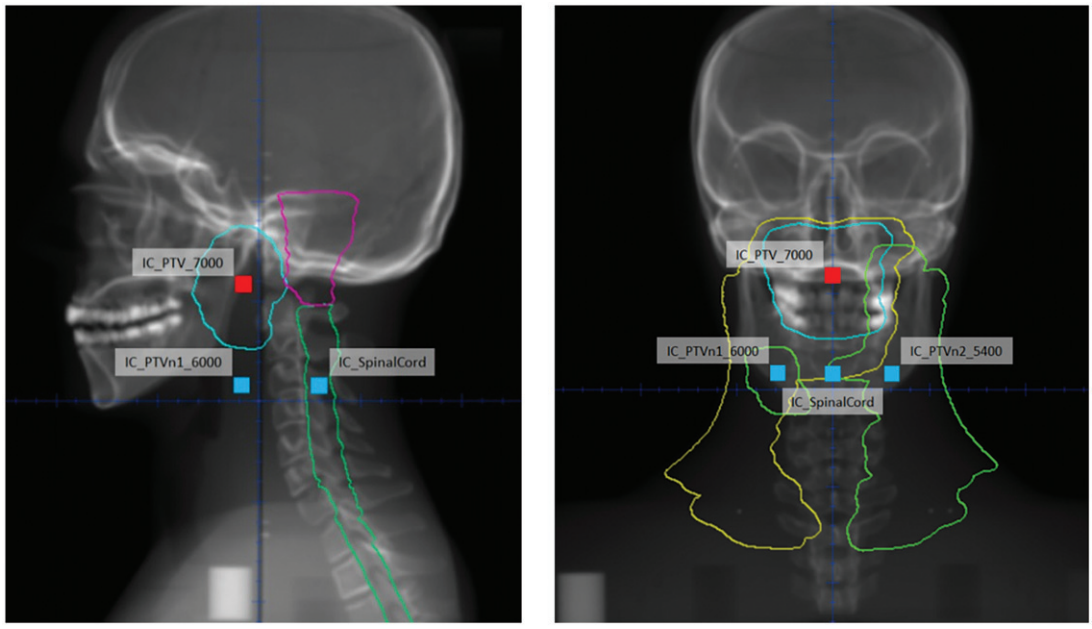

Figure 2. Anterior and lateral projections of the SHANE phantom and some of the delineated structures. Location of the IC measurement points inside the SHANE phantom is indicated with square symbols.

Overall, the package developed for the on-site, end-to-end IMRT/VMAT audit consists of the SHANE phantom, the DICOM CT image set, the associated DICOM RT structure set, a list of planning objectives and constraints, a detailed audit methodology description, step-by-step instructions for the auditor and the institution being audited, data reporting forms, and a set of reference data for the tested parameters [26].

Audit methodology

The audit consists of a pre-visit phase and an on-site visit phase. During the pre-visit phase, the audited institution is asked to prepare a clinically acceptable treatment plan using the reference SHANE CT and structure set following the audit guidelines, to perform local pre-treatment QA as well as MLC testing and to undertake several computational exercises. The on-site visit takes place only if the pre-visit phase was completed successfully and any potential discrepancies have been resolved. During the on-site visit, the audited institution's staff together with auditor performs CT scanning of the SHANE phantom, registers the acquired images, copies the structure set and the pre-visit phase plan onto the new CT images, recalculates and if needed, re-optimizes the plan, and irradiates the phantom. The details of the pre-visit and on-site visit activities may be found in the Supplementary Material.

The irradiation of the SHANE phantom is performed as if it were an actual patient. After the phantom is aligned on the treatment table, its position is verified according to the local set-up procedure using volumetric or planar imaging. Ion chamber measurements are performed at least three times in each of the four measurement points and the average is calculated. The measured doses are compared with the mean TPS calculated doses in the corresponding IC volumes. Film irradiation is done with three consecutive fractions per film to be in the useful dose range of 2–8 Gy for EBT3 films. Film measurement results are compared to the 2D coronal dose distributions exported from the TPS using gamma analysis [27] with 3%/3 mm criteria, 20% threshold, global gamma, and with normalization to a point within a high-dose low-gradient region in the central part of PTV_7000.

As such, the on-site visit is planned for two days. The data collected during the on-site visit are analyzed by the auditor and the audit report for the institution is prepared.

Audit testing

Testing of the audit methodology was initially performed at the Medical University of Vienna/Vienna General Hospital, Vienna, Austria (AKH) and then at the international level with the group of the IAEA consultants. Some steps of the methodology in the preparatory phase such as small field output and profile calculations and MLC QA were tested previously during IAEA-organized Coordinated Research Projects (CRPs) [10,11]. Therefore, the main focus of the audit testing was on assessing the suitability of the SHANE phantom for the audit process and the end-to-end methodology.

Treatment planning review

A review of the treatment planning part of the audit was organized to ensure that the time needed to create a clinically acceptable treatment plan for the audit was representative of a typical planning time for similar cases in the participating institution. Participants were requested to prepare an IMRT/VMAT plan recording the time needed to create it, ask a local radiation oncologist to check the plan for clinical acceptability, perform the local pre-treatment QA and submit the plan for review to the IAEA. The treatment plans were analyzed in terms of quality (using PlanIQ, Sun Nuclear Corp., Melbourne, FL, USA) by comparing the calculated plan doses for PTVs and OARs with their corresponding planning constraints. Each dose constraint achieved was added on to

the total plan score in such a way that the maximum plan quality value was 100. The participants did not know about the scoring method beforehand. Technical deliverability of plans was verified by the local pre-treatment QA procedure. In all cases, it involved 2D dose comparison between calculations and measurements using either film or a detector matrix; 3%/3 mm/global gamma criteria were used.

Fourteen institutions from Argentina, Austria, Estonia, Hungary, Portugal, Russia, Slovakia, Slovenia, Spain and the UK submitted 42 treatment plans (Supplementary Table 2). In terms of IMRT delivery modes, 21 plans were for dynamic MLC IMRT (dMLC), 12 for VMAT, six for Step and Shoot IMRT (SnS) and three for Tomotherapy.

Multicenter study

After the initial feasibility testing of the audit methodology, a multicenter pilot study with a broad complement of participants having different RT equipment was organized. Participants were supplied with the same SHANE phantom, instructions and datasheets, and asked to follow the on-site visit part of the methodology and thus perform the SHANE phantom CT scanning, treatment planning and IC and film measurements. In total, six RT institutions from Austria, Belgium, Estonia, Spain and the UK participated in the multicenter pilot study with several combinations of treatment unit, TPS, dose calculation algorithm and IMRT delivery technique (Supplementary Table 3). All combinations were commissioned for IMRT treatment planning but some of them were used only for research. Therefore, these modalities were not covered with a routine clinical QA program, which became the reason for separating 'clinical' and 'research' modalities into different groups. This allowed the assessment of the influence of a regular clinical QA on the audit results. Altogether, 17 sets of IC measurements and 13 film measurement results were collected. Films were evaluated by the institutions participating in the pilot study following their best practices and audit-specific recommendations provided by the IAEA. Differences related to scanners, film analysis methods and software packages used were investigated before [28] and considered during the analysis of the aggregated pilot study results. The IC and film measurement results obtained during the multicenter study were used to establish the audit tolerance levels. Additionally, the relationship between the number of monitor units (MUs) as a plan complexity descriptor and IC measurement results was analyzed and a dose homogeneity index ($HI=(D_{max} - D_{min})/D_{average}$) within IC structures was assessed as these easily computable metrics can provide useful information for the interpretation of the measurement results [29]. This analysis was performed for a subset of results where the required treatment plan related data were available.

Statistical analysis

A Wilcoxon signed rank test was used to test whether the average values of the ratios of the IC measured dose to the TPS calculated dose (D_{IC}/D_{TPS}) in four measurement points were equal to 1. The test was carried out separately for clinical and research modalities.

A regression analysis was conducted to investigate the statistical relationship between D_{IC}/D_{TPS} and the number of MUs in the plan, as well as the dose homogeneity index (HI).

Results

Treatment planning review

The results of the treatment planning review are summarized in Figure 3. The planning time varied from 1 to 12 hours with the average of 3.5 hours. About 80% of the plans achieved a quality score >90 with nine plans fully satisfying the planning constraints (score 100). None of the centers used autoplanning strategies. 95% of plans passed the local pre-treatment QA while in two cases the tolerance level was marginally exceeded. The analysis of the data showed that there was no correlation between the time necessary to carry out the plan and the plan quality score ($p=.97$).

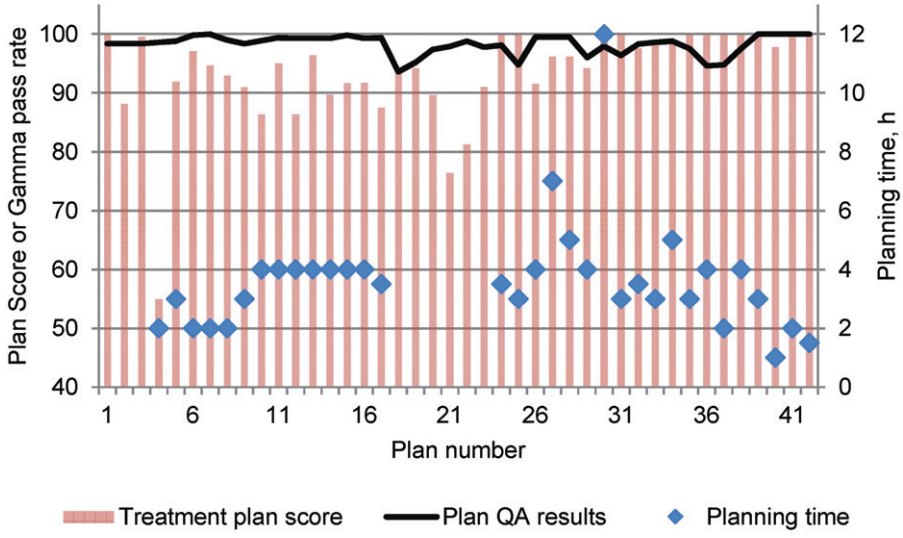

Figure 3. Calculated treatment plan scores and corresponding local QA results in terms of gamma passing rates in comparison with the total planning time for all participants.

Multicenter pilot study

In Figure 4, the IC measurement results for seven clinical IMRT modalities and 10 research modalities in terms of D_{IC}/D_{TPS} for the four measurement points are shown and the averaged results are given in Table 1. According to the Wilcoxon signed rank test, the IC results for clinical IMRT modalities were not significantly different from 1 and had a standard deviation (SD) ranging from 0.9% to 1.8%. At the same time, in the group of results for the research modalities, there was a significant difference ($p<.05$) from unity of the D_{IC}/D_{TPS} in the IC_SpinalCord measurement point with SD of 3.2%. Of 13 film measurement results obtained, eight belonged to clinical IMRT modalities and the average gamma pass rate for this group constituted 95.9% (1.5% SD) while for research modalities it was 91.1% (1.8% SD). Based on the results of the multicenter study, the following tolerance levels were established: 5% in PTVs and 7% in OARs for IC measurements, and a 90% gamma pass rate with 3%/3 mm criteria, 20% threshold, global gamma, normalized to a point within high-dose low-gradient area in PTV for film measurements. 2/17 IC results and 1/13 film results of the multicenter study were out of the established tolerance levels.

The regression analysis showed that neither the number of MUs nor HI have correlation with the IC results D_{IC}/D_{TPS} ($p=.16$ for the average of four points and $p=.23$ for the spinal cord point, respectively). There was also no difference found ($p=.12$) between results for clinical and research modalities in the observed range of MUs (Supplementary Figure 1). D_{IC}/D_{TPS} ratios were within approximately ±4% as long as the HI was lower than 0.15 (Supplementary Figure 2).

Discussion

The multicenter pilot study together with the treatment planning review allowed the validation of the audit methodology and the establishment of the tolerance levels for both IC and film measurement results.

Initial concerns about achievability of the treatment planning goals within a reasonable time were not supported by the results of the treatment planning review. Participants generally reported that the case was similar to those routinely treated in their institutions and they were able to create clinically acceptable plans within four hours. At the same time, during standardized analysis of treatment plans using PlanIQ, it was found that not all of the submitted plans were close to satisfying all the plan acceptability criteria (i.e., plan score >90). In general, some slight differences in the PlanIQ score may be attributed to the differences in the dose grid sizes between the participant's TPS and the PlanIQ and thus different dose-volume histogram calculations during the plan quality assessment. In some cases, poor plan scores were related to insufficient experience of the planner who was not able to achieve the prescription stated in the methodology (as can be seen in Figure 3, plan number 4). Nevertheless, even the poorest quality plans were reported to be clinically acceptable by the local radiation oncologist and passed the local pre-treatment QA, which means they could be used for treating a hypothetical patient. This raises the issue of clinical training in IMRT treatment planning and use of independent treatment planning process QA tools [30].

As a result of the multicenter study, 5% tolerance level was adopted for local dose differences between the calculated and the IC measured doses for points inside PTVs. At the same time, it was necessary to widen it to 7% for the IC point in the spinal cord due to the noted higher dose gradient and the increased SD. Although, on average, IC results were in agreement, systematic shifts were noted for the

Table 1. Summary of the ion chamber results in terms of D_{IC}/D_{TPS}.

Measurement point	Clinical IMRT modalities ($n=7$)		Research IMRT modalities ($n=10$)		Total	
	Average	SD	Average	SD	Average	SD
IC_PTV_7000	0.977	1.2%	0.984	1.3%	0.982	1.3%
IC_PTVn1_6000	1.000	0.9%	0.988	2.5%	0.993	2.0%
IC_PTVn2_5400	0.989	1.5%	0.991	1.6%	0.990	1.5%
IC_SpinalCord	1.006	1.8%	1.030	3.2%	1.020	2.9%

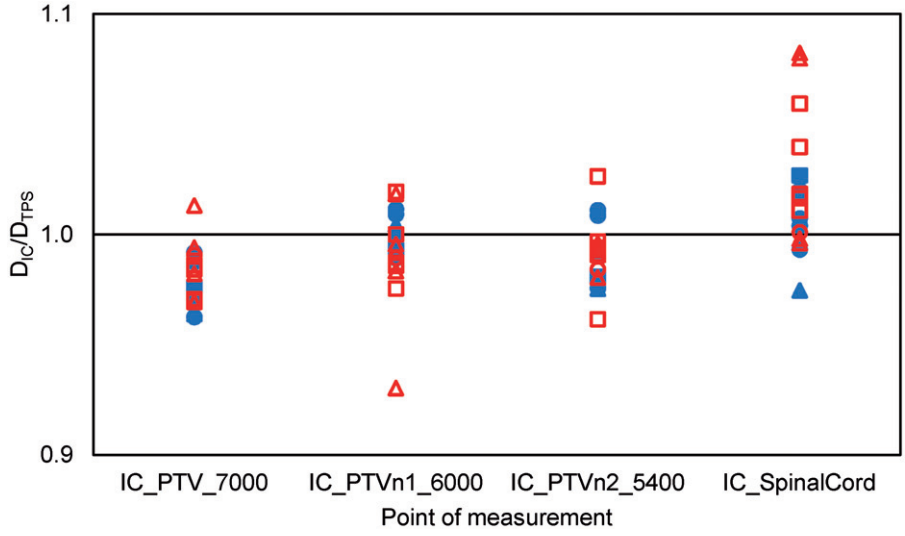

Figure 4. Ratios of ion chamber measured doses to TPS calculated doses (D_{IC}/D_{TPS}) in four measurement points located in the PTVs and the spinal cord. Blue/solid symbols – clinical IMRT modalities, red/hollow symbols – research IMRT modalities. Circles – VMAT plans, triangles – dMLC plans, squares – SnS plans.

IC_PTV_7000 and IC_SpinalCord points, which also contributed to the establishment of the tolerance levels. It is expected that they will be further verified in future national studies and might be adjusted if necessary [31].

The heterogeneous composition of the SHANE phantom increases the uncertainty of both the dose calculation and measurements. At the same time, its commercial availability makes it easier to adopt the audit methodology at a national level as opposed to using self-developed phantoms. It is therefore challenging to directly compare the proposed tolerance levels with other on-site IMRT audits employing different phantoms. For example, the dosimetry audit for the PARSPORT trial [32] adopted tolerance levels of 3% for PTV and 5% for OAR. The Japanese Clinical Oncology Group on-site IMRT audit system in support of clinical trials [33] also utilizes 3% tolerance for dose in the PTV. As for remote IMRT audits, point dose measurement tolerance levels are usually higher than those of on-site audits due to the increased uncertainty of solid state dosimetry systems compared with IC measurements. In addition, there is an advantage of the auditor presence during the on-site measurement session. For example, IROC-Houston utilizes 7% tolerance for point dose measurements with thermoluminescent dosimeters (TLDs) in PTV for IMRT H&N credentialing [34]; the same tolerance is adopted in the national remote IMRT/VMAT audit pilot run using lithium formate dosimeters in Sweden [35]; 5% tolerance is used for alanine point dose measurements in the national IMRT audit using a slab phantom in the UK [36]; and 5% tolerance is also used for the PTV in the IAEA remote audit of IMRT/VMAT head treatments with TLD [13]. Consequently, the tolerance levels of 5% and 7% in PTVs and OAR, respectively, used in the audit methodology here are comparable to those of the existing audit systems using a similar type of audit and phantom.

The film measurement tolerance value of 90% points passing 3%/3 mm gamma criteria, 20% threshold, global gamma, was established in the pilot study. The proposed gamma criteria represent a common practice although there is a concern about the ability to detect errors using them [37,38]. The tolerance proposed here is similar to the ones used in PARSPORT trial and the UK national IMRT audit: 95% points passing 4%/3 mm or 4%/4 mm gamma criteria respectively with 20% threshold [32,36]. According to IROC-Houston analysis of their credentialing results, the 3%/3 mm/90% gamma criteria/gamma pass rates adopted for SHANE would result in only 28% institutional pass rate and 42% institutional pass rate if using 4%/4 mm/95% criteria [39]. Thus, in the context of large-scale dosimetry audits, this approach appears reasonable and even may be considered quite strict. Similar to the IC measurements, the acceptance criterion for film dosimetry results may be adjusted when more data become available.

The established IC and film measurement tolerance level values are slightly higher than those described in recommendations for hospitals performing patient-specific IMRT QA by the European Society for Radiotherapy and Oncology (ESTRO) and the American Association of Physicists in Medicine (AAPM) [40,41]. Nevertheless, it was shown [42] that external audits greatly complement the hospital QA programs by allowing the detection of systematic errors due to their inherent independence and the different dosimetric traceability of the measurement systems used.

Although the results of all participants of the multicenter study were within the established tolerance levels with their clinically commissioned IMRT modalities, inclusion of the results from the research modalities give an estimate of the potential failure rate of 2/17 IC results and 1/13 film results. It also emphasizes the sensitivity of the methodology to limitations in TPS calculation accuracy and the requirement for a special clinical commissioning of algorithms used for IMRT treatment planning and their subsequent regular QA. Special attention should be paid to modeling of MLC collimated small fields including fine-tuning of beam parameters and careful measurement of OFs as well as the dosimetric leaf gap [43]. The pre-visit activities help to identify these kinds of problems before the audit visit takes place.

The results of this study indicate that the number of MUs as a descriptor of the IMRT plan complexity is not related to its deliverability although a higher spread of IC results with the increase number of MUs was observed. Similarly, a higher HI is noted to be a possible predictor of higher IC measurement deviations. Currently, a series of studies show contradictory results for different plan complexity metrics and for different number of institutions involved. For example, in a single-institutional study a significant correlation was found between a small aperture score (used to describe the complexity of 122 SnS IMRT beams) and QA results [44]. At the same time, in the study analyzing the multi-institutional results of IROC-Houston H&N phantom irradiations there was no correlation found between 13 different plan complexity metrics and the average dose inaccuracy in 343 cases employing different IMRT delivery techniques [45]. Different plan complexity metrics will be tested for this audit methodology as more data become available.

Conclusions

This on-site, end-to-end IMRT audit methodology for H&N cancer treatments was developed by the IAEA and has been shown to be feasible. It was successfully tested in an international, multicenter pilot study. The audit was found to be clinically relevant and can be executed efficiently using the two-phase process, a pre-visit preparatory phase and an on-site phase. The audit methodology is currently being implemented at a national level in several countries.

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Disclosure statement

The authors report no conflicts of interest.

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