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Original article

A virtual dosimetry audit – Towards transferability of gamma index analysis between clinical trial QA groups

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ABSTRACT

Purpose: Quality assurance (QA) for clinical trials is important. Lack of compliance can affect trial outcome. Clinical trial QA groups have different methods of dose distribution verification and analysis, all with the ultimate aim of ensuring trial compliance. The aim of this study was to gain a better understanding of different processes to inform future dosimetry audit reciprocity.

Materials: Six clinical trial QA groups participated. Intensity modulated treatment plans were generated for three different cases. A range of 17 virtual 'measurements' were generated by introducing a variety of simulated perturbations (such as MLC position deviations, dose differences, gantry rotation errors, Gaussian noise) to three different treatment plan cases. Participants were blinded to the 'measured' data details. Each group analysed the datasets using their own gamma index (γ) technique and using standardised parameters for passing criteria, lower dose threshold, γ normalisation and global γ.

Results: For the same virtual 'measured' datasets, different results were observed using local techniques. For the standardised γ, differences in the percentage of points passing with $\gamma < 1$ were also found, however these differences were less pronounced than for each clinical trial QA group's analysis. These variations may be due to different software implementations of γ.

Conclusions: This virtual dosimetry audit has been an informative step in understanding differences in the verification of measured dose distributions between different clinical trial QA groups. This work lays the foundations for audit reciprocity between groups, particularly with more clinical trials being open to international recruitment.

Radiotherapy dosimetry audits allow for the testing of procedures and the identification of deviations. Dosimetry audits range in complexity from measuring machine output under reference conditions to complex radiotherapy such as intensity modulated radiotherapy (IMRT) measurements [1–9]. Currently the verification of the measured dose distribution can vary largely with multiple different commercial hardware and software systems available. There are also different methods of the analysis of the dose distribution such as dose difference and distance-to-agreement (DTA). One of the most widely used techniques is the gamma index method [10]. Various studies have evaluated the response of the gamma index in different commercial systems and shown that it can respond in different ways between different systems [11–13].

Quality assurance (QA) in clinical trials is crucial as lack of compliance can affect trial outcome [14–18]. Different international radiotherapy clinical trial QA groups have developed independent methods of measured dose distribution verification and analysis for various historical and other logistical reasons and the particular

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systems they had access to, all with the ultimate aim of ensuring compliance [19–22].

Individual clinical trial QA groups have methods for streamlining the trial QA for multiple trials to avoid duplication. For example, a centre that has had the dosimetry credentialed for a particular trial may be exempted from repeating the dosimetry QA for the same clinical site or other similar (or less complex) clinical trials. Some clinical trials are now open to international recruitment to increase patient numbers and limit the time to full accrual. Streamlining dosimetry QA in the international setting, such that an institution credentialed by one QA group may be accepted by another, is therefore of interest. To be able to achieve this, it is important to understand how different analysis techniques and tolerances translate between different groups, and the challenges involved. The Global Quality Assurance of Radiation Therapy Clinical Trials Harmonisation Group (GHG) has been established to facilitate the harmonisation and reciprocity of clinical trial QA between different groups and consistency in the dose delivery in the trials [23–26].

This study focuses on the verification of measured dose distributions for complex techniques such as IMRT and volumetric modulated arc therapy (VMAT). The aim was to gain a better understanding of the different gamma index analysis processes between international clinical trial QA groups and to inform potential future dosimetry audit reciprocity within and outside clinical trials.

Methods and materials

Six international radiotherapy clinical trial QA groups, which are members of the GHG, participated in this study. These were the Radiotherapy Trials QA (RTTQA) group in the United Kingdom, the European Organization for Research and Treatment of Cancer (EORTC) Radiation Oncology QA group, the Imaging and Radiation Oncology Core (IROC) in the United States, the Japan Clinical Oncology Group (JCOG), the Trans-Tasman Radiation Oncology Group (TROG), and the Australian Clinical Dosimetry Service (ACDS).

Virtual 'measured' plan creation

Three individual cases were chosen for the study. These were the three-dimensional treatment planning system (3DTPS) test developed by RTTQA for VMAT & Tomotherapy benchmarking [27], a prostate cancer case, and a head & neck (H&N) cancer case. For the 3DTPS case, a $2 \times 360^{\circ}$ arc volumetric modulated arc therapy (VMAT) plan was generated. The prostate and H&N cases respectively were planned with 5 and 7 fixed field IMRT fields respectively. All plans were generated in the Varian Eclipse TPS (Varian Medical Systems, Palo Alto, CA) and calculated using the AAA v 11.3 algorithm with 2.5 mm dose grid spacing. Screenshots of these cases are shown in Fig. 1.

Using a similar methodology as has been reported previously [11,12,28,29], plans were copied and a range of deliberate errors were introduced to perturb the dose distribution. These included a varying combination of single and whole bank MLC errors ranging from 1 to 5 mm, dose difference errors of +3% and −3% and gantry and collimator errors of 0.5 and 1 degrees. In some of the plans, gravity effects were introduced into the MLC positions based on Carver et al. [30] using Eq. (1):

$$\mathrm{MLC}_{\mathrm{mod}} = \mathrm{MLC}_{\mathrm{orig}} + A\sin(\theta) \quad (1)$$

Where $\mathrm{MLC}_{\mathrm{mod}}$ is the modified MLC position, $\mathrm{MLC}_{\mathrm{orig}}$ is the original position, and A is the specified maximum MLC position change (in this case we used 1–5 mm), and θ is gantry angle [30]. Some plans also had subtle positional errors into the MLC using a Gaussian random number generator in MATLAB. The overall result was a range of virtual datasets that appeared to have simulated 'measured' features. In some of the plans the errors were such that dose-volume histogram constraints are pushed out of tolerance according to the corresponding author's institutional objectives; for example the rectum tolerance for the prostate cancer case and spinal cord for the head & neck case.

In total there were 5 'measured' virtual datasets for the 3DTPS plan, 5 for the prostate plan and 7 for the H&N plan; a short description of the errors introduced into each one is given in Table 1. To ensure consistency all plans were recalculated on the same water-equivalent cylindrical phantom measuring 30 cm diameter by 30 cm length. Example gamma index distributions for a virtual measured plan from each of the three cases are shown in Supplementary Fig. 1.

Gamma index analysis

Each clinical trial QA group was sent the original unedited dose distribution labelled 'TPS dose' and the edited distributions labelled 'Measured Dose 1', 'Measured Dose 2' and so forth, for each of the individual cases. All users were blinded to the specific details of the perturbations (if any) within the 'measured' virtual datasets to avoid subjective bias.

All datasets were sent in 3D DICOM format with 2.5 mm pixel-pixel spacing in the x and y coordinates, and 3 mm in the z (slice spacing) coordinate. Additional 2D coronal planes were sent to allow each clinical trial QA group to import the correct dataset as normal for their practice. For example to facilitate a group whose standard practice was to compare a coronal film measurement against a 2D calculated coronal dose plane.

Gamma index analysis was performed in two ways as described below. All users reported the percentage of points passing with $\gamma < 1$.

Gamma index analysis using each clinical trial QA group's own routine settings

Each clinical trial QA group performed a gamma index analysis with their own routine settings for the following:

- Global or local γ analysis.
- Whether the evaluated and reference dose distributions are rescaled or not
- γ normalisation technique (e.g. max dose/point in high dose region etc.).
- Lower dose threshold as a percentage of the normalisation.
- Passing criteria (% and mm).

Each QA group were requested to provide the details of what was used for the above points, as well as which software and version was utilised.

Standardised gamma index analysis

Each clinical trial QA group then repeated the gamma index analysis using their software with standardised gamma index parameters for the passing criteria, normalisation and low dose threshold. Analysis was performed for the following: 2%/2 mm, 3%/2 mm, 3%/3 mm, 5%/5 mm, 7%/4 mm, global gamma index, no rescaling of the datasets, gamma index normalisation set as the maximum dose point in the 'measured' dataset, and a 20% lower dose threshold. The passing criteria were chosen based on typical criteria used by different groups. Where possible users were asked to perform the gamma index where the reference distribution was the 'measured' dataset and the evaluated distribution (i.e. the distribution that was searched for the minimum γ) was set as the TPS

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