Audits for advanced treatment dosimetry

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Abstract. Radiation therapy has advanced rapidly over the last few decades, progressing from 3D conformal treatment to image-guided intensity modulated therapy of several different flavors, both 3D and 4D and to adaptive radiotherapy. The use of intensity modulation has increased the complexity of quality assurance and essentially eliminated the physicist’s ability to judge the validity of a treatment plan, even approximately, on the basis of appearance and experience. Instead, complex QA devices and procedures are required at the institutional level. Similarly, the assessment of treatment quality through remote and on-site audits also requires greater sophistication. The introduction of 3D and 4D dosimetry into external audit systems must follow, to enable quality assurance systems to perform meaningful and thorough audits.

1. Background
In recent years the approach to treating cancer patients with radiation therapy has evolved considerably. In the past, it was common for clinicians to base treatment decisions on their individual prior experiences, but now it is more common to employ “evidence-based medicine” and derive prescriptions from data obtained through clinical trials [1]. The highest-level evidence for any type of therapy originates from systematic reviews of randomized clinical trials.

As an example, according to data from the Imaging and Radiation Oncology Core-Houston (IROC-H - formerly the Radiological Physics Center, RPC), nearly 70% of all US radiation therapy centers participate to some degree in cooperative group clinical trials [2]. About 25% of the centers collectively enrol more than 1,000 patients per year on protocols managed by one or more of the clinical trials groups. For a treatment center to join and continue membership in the cooperative groups, the institution’s physics staff must perform specific quality assurance (QA) procedures. For protocols that require or permit radiation therapy, there are particular radiation therapy quality assurance and data submission requirements for each patient entered into the trial. Participation in certain advanced technology protocols such as those requiring three-dimensional (3-D) conformal treatment, intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), stereotactic radiation therapy, or brachytherapy require a substantial physics effort to qualify the institution to enter patients. Further physics effort often is necessary to submit the required data for each patient treated under protocol.
The quality assurance procedures required for participation in clinical trials establish a baseline for institutional QA and as one component they include external audits of dosimetry, planning and delivery. As advanced technologies and treatments are often involved in leading edge clinical trials, significant audit development for such treatments has often been in the context of trial QA. It is critical that these are built on previous ‘simpler’ levels of audit, as those levels must be fully verified before moving on to more complex levels. However increasingly such advanced treatment audits have moved away from auditing single parameters, or sets of parameters, towards comprehensive ‘end-to-end’ testing, considering the whole treatment chain as experienced by a patient and using phantoms that are more representative of patients. Clinical trial audits have often also helped to widen adoption of advanced treatments, as this QA has provided confidence in their implementation and delivery. The auditing used in clinical trial QA can augment a hospital’s own QA program by bringing and imposing an independent review of the work performed by clinical medical physicists. A recent review of dosimetry for audits and clinical trials can be found in Kron et al [3] and more generally for QA of clinical trials in Ibbott et al [4], some of which has been used as the basis for parts of this summary. It may be noted that dosimetry is taken here in its widest sense to encompass dose measurement, dose performance of the equipment and the whole treatment process, dose determination (eg.treatment planning dosimetry) and dose delivery, i.e. all areas of clinical dosimetry.

More generally, intercomparisons and audits have been developed over at least the last 5 decades at the local, national or international level, not specifically linked to trials, but rather to support the development and improvement of quality and safety in radiotherapy, to avoid errors, to provide confidence in the accuracy of treatment dosimetry generally and to provide a process for centres to ensure new machines and processes can be independently verified before wider clinical use [5]. To varying degrees, such systems have developed through time to audit more complex dosimetry and treatments, with the aim of providing testing and verification that reflect the development of clinical practice, although in general audit sophistication lags behind practice [3, 6-9].

2. Role of audits in radiation therapy clinical trials and link to credentialing for trials
Multi-center clinical trials operated through co-operative clinical trial groups (CCTGs) such as the Radiation Therapy Oncology Group (RTOG, now part of the NRG Oncology Group), European Organization for Research and Treatment of Cancer Radiation Oncology Group (EORTC-ROG), Trans-Tasman Radiation Oncology Group (TROG) etc. generally have the greatest impact on changing clinical practice as these groups set high standards for trial design, QA, and management, resulting in high quality data to support trial results that can be reproduced in the clinic. Although the process of developing a clinical trial may vary among the groups, the same general principles apply which in turn provides an opportunity for clinical trial groups to collaborate to increase patient recruitment [10]. QA programs should be set up to meet the specific needs of the trial and considering the effect of predicted intercenter variability in treatment delivery [11] on the trial analysis. It may be noted that, whilst hospital participation in clinical trials varies, it has been shown that patients treated at hospitals that contribute larger numbers of patients to trials do better than those with low contribution rates [12], implying a wider effect on quality that may well also affect routine clinical practice in those centres. Thus participation in clinical trials and associated QA may affect the way many patients, locally, nationally, and on the international scale, are treated.

A clinical trial may incorporate a credentialing program in an effort to minimize the number of protocol violations and improve the overall quality of the trial [13] and one part of that is satisfactory achievement of the relevant dosimetry audit requirements. Credentialing offers the opportunity to confirm investigators have read and understood the trial protocol and have the necessary resources to treat the patients in all arms of the trial in accordance with the trial’s specifications. When trials allow the introduction of a new technique, credentialing is also an opportunity to provide education, peer review and an external formal assessment that the new technique has been appropriately commissioned prior to clinical implementation. For example, the UK trial PARSPORT allowed many centers to implement IMRT for head and neck cancers as a result of participation in the trial [14].
Human error has been identified as one of the major contributing factors in patient treatments and therefore some clinical trial groups will require process maps to be developed and submitted for approval prior to a center opening a clinical trial [15].

Clinical trials that require the use of advanced technologies such as IMRT and prostate brachytherapy are considered sufficiently challenging that institutions are required to demonstrate their ability to use these technologies before being permitted to register patients [16-18]. The IROC-H and other QA offices participate in the credentialing process for clinical trials through several cooperative groups. Credentialing for such clinical trials generally involves an evaluation of most if not all of the following aspects:

- Attestation to use of the particular advanced technology to treat patients previously
- Facility Questionnaire
- Knowledge Assessment Questionnaire
- Benchmark case or phantom
- Patient-specific plan QA review
- Electronic data submission
- QA & dosimetry review
- Clinical review by radiation oncologist
- Reviews of Patient Treatment Records

3. External audits of general dosimetry and QA performance

3.1 Remote audits of treatment machine output

Many national or international organizations conduct regular independent audits of treatment machine output calibration with mailed dosimeters. This is a critical first step for all audits, whether of simpler or advanced treatments. The main systems providing international coverage include:

- The International Atomic Energy Agency (IAEA) based in Vienna, which began its TLD service in 1969, aimed at supporting a wide range of lower income per capita UN member states [19, 20];
- IROC-H based in Houston, Texas, which has the largest program and monitors all of the institutions (>2000 institutions as of early 2014) that participate in NCI sponsored clinical trials, both within the USA and internationally [13, 21]. The IROC-H initiated its TLD program for photon beams in 1977 [22]. In 1982 electron beams were included, and in 2007, measurements of proton beams were initiated. In 2010, the IROC-H adopted the use of optically-stimulated luminescence dosimeters (OSLDs) and largely discontinued the use of TLDs for photons and electrons [23].
- The EQUAL-ESTRO service (European Quality Assurance Laboratory-ESTRO) located in Paris, now a commercial service not formally linked to ESTRO, although growing out of scientific and audit pilot studies aimed at supporting quality in radiotherapy in Europe that began within the ESTRO infrastructure in the early 1990s [24-29].

In addition, there is a wide range of national or regional systems. Many of these were initially supported by IAEA, or linked, developmental projects [7, 9] and using similar TLD methods; others developed independently, eg the Section of Outreach Radiation Oncology and Physics at the National Cancer Center of Japan, in Tokyo, using glass dosimeters [30]. Descriptions of many of these can be found, for example, in proceedings of IAEA dosimetry symposia, available at http://www.iaea.org/Publications/, eg [31].

Most external audit systems for beam output verification are relatively simple, eg the IAEA’s simple-assembly TLD stand to be placed in a water phantom [19, 20]. The IROC-H’s OSLD system is
described here as an example. Each year, institutions receive a package containing a lightweight platform and acrylic mini-phantoms containing several OSLD “nanoDots” (Landauer, Inc., Glenwood, IL) for irradiation with each radiation beam. Instructions are supplied that explain the irradiation procedure and ask the institution to describe their calibration procedure. The blocks and other equipment are returned to the IROC-H where the OSLDs are analyzed. The IROC-H applies corrections for the differences in scatter between the institution’s calibration conditions and the OSLD irradiation, and for fading, dose linearity and energy dependence of the OSLD system [23, 32].

The uncertainty of the system for measuring output of accelerators remotely has been evaluated to be 1.5% [32], expressed as the standard deviation of measurements of dose. Consequently, the IROC-H’s measurement of an institution’s output can be stated at an uncertainty of less than 5% using a 99% confidence interval and this (5%) has been established as the threshold for acceptability. When the OSLD measurement disagrees with an institution’s stated dose by more than 5%, the IROC-H initiates further steps to resolve the discrepancy. If the discrepancy cannot be resolved through telephone call discussion and the review of procedures and documentation, an on-site dosimetry visit is scheduled.

Remote audits of machine calibration have been described by many other investigators [3, 7-9, 19, 20 24-28, 30, 31, 33, 34]. For example, the experience at the International Atomic Energy Agency (IAEA) in Vienna is comparable to that of the IROC-H in terms of numbers of separate institutions audited, although the frequency of audits is typically lower [19, 20]. Williams et al described the early experience of the Australian (ACDS) dosimetry audits using TLDs and OSLDs [35]. Other systems have used dosimeters made of a thermoluminescent glass rods [18, 34], alanine [36], lithium formate [37], etc. It may be noted that some audit systems have developed methods to use remote auditing for a much wider range of dosimetry parameters than just beam output, eg the IAEA-supported system of linked national audit networks has piloted, and in some cases routinely implemented, remote audits of field size output variation, beam quality, field symmetry, asymmetric outputs, tests of small fields, tests of dose changes under inhomogeneities and other planning system tests etc. [7-9, 19, 20].

3.2 Results of remote audits of machine calibration
As one of the two largest examples, the IROC-H has described results from a large series of annual calibration audits [2, 38]. Consistently each year, 5% to 6% of the US megavoltage beams audited with TLD have fallen outside of the IROC-H’s ±5% dose or 5 mm electron depth dose criteria on the first measurement. The analysis indicated that the incorrectly-calibrated beams are distributed among approximately 10% to 20% of the institutions monitored by the IROC-H. This observation has been confirmed by on-site visit measurements using ion chambers; among institutions visited by the IROC-H, approximately 10% to 15% had one or more beams outside of the IROC-H’s criteria on an annual basis that required an investigation by the IROC-H [2, 38].

The precedent for performing TLD audits annually was established by the IROC-H early in its development and all current trial data and results are based on having this level of QA. A review of EORTC trial results indicated that decreases in tumour control probability were associated with discrepancies in the beam calibration, as measured by a TLD audit program [11]. At the same time, increases in normal tissue morbidity were associated with discrepant high TLD measurements. The article also indicated that sequential TLD audits improved the uniformity of the clinical outcome and that small deviations in beam output might lead to clinically important variations in outcome. Mailed TLD audits were deemed to be an integral part of quality assurance for trials. Other studies have shown the importance of independent audits to assure clinical trial quality [12, 39].

The IROC-H data also showed that 41% of the institutions monitored by the IROC-H had exactly one discrepancy detected by the TLD program during the 10 years between 1998-2008 [38, 40]. However, thanks at least in part to the audit intervention, a much smaller percentage had two or more discrepancies during this period, a feature of most audit reporting of experience over time and over repeated audits. As indicated above, while calibration discrepancies were detected for 15 - 20% of the major contributors to clinical trials in any one year, these institutions did not consistently have such discrepancies. Instead, significant calibration errors apparently can occur at any institution at any time.
Approximately 230 new machines are installed each year at institutions participating in US NCI-funded clinical trials and may be subject to calibration errors as they are put into clinical service, with potentially serious results. These errors can occur as a result of changes in procedures and protocols, the recruiting of inexperienced personnel, operating new systems, etc. and are relatively frequently observed with the use of new treatment equipment.

The IAEA experience and that from the linked national groups in its developing national audit network projects is similar [7-9, 19, 20] in general terms. However this can be significantly modified overall, or in individual countries, by the much wider range of resource, staffing, training, equipment, infrastructure, prior audit experience, etc., as the centres audited are in many countries worldwide, with widely varying economic conditions.

3.3 On-site Visits for Dosimetry Audit and Dosimetry and QA Review

A dosimetry review audit has been recommended by several organizations, including the AAPM and the IAEA [41, 42]. In addition, some national audit systems, eg the UK Institute of Physics and Engineering in Medicine national audit network [6], use on-site visits, and not remote audits, as the basis of their regular routine audit. This has grown out of initial experience with ion chamber-based national dosimetry intercomparisons and audits [43, 44] and combines dosimetry audit and QA review at the same visit and enables greater flexibility in the implementation and development of routine audits [6, 45]. An independent on-site audit is especially important for solo practitioners but is a valuable exercise for all practicing clinical medical physicists. It need not be extensive, but should address key activities such as basic calibrations, the overall QA program and documentation.

An independent dosimetry review visit consists of a review of the institution’s QA procedures and documentation; a review of treatment records to ascertain the consistency of the procedures used for treatment planning and monitor unit calculations; and measurements of the radiation beams and radioactive sources [41, 42, 46]. The set of measurements to be carried out should be defined to align with the visit review remit and requirements. For example, depending on the scope of the visit, this should include mechanical alignment and accuracy of position readout devices, light versus radiation field congruency, calibration of treatment machine output, relative field-size dependence, percent depth dose, off-axis ratio, asymmetric jaw and irregular field parameters, and accessory transmission factors. Additional measurements could evaluate the basic data required for delivery of IMRT, including small-field output factors, and the performance of a multi-leaf collimator (MLC). A straight-forward spot-check of image-guided radiation therapy (IGRT) can be performed with a simple phantom [47]. Other modalities, such as brachytherapy source strength checks can also be included. Because of interest in treating protocol patients with protons, the IROC-H and other QA groups have more recently developed and implemented procedures for visits to proton-beam facilities [48].

The IROC-H has conducted on-site audits during its 45-year history, and has accumulated extensive measured data from several thousand photon beams which have been grouped into 96 combinations of manufacturer, model, and beam energy [49]. This database of “Standard Data” enables the IROC-H to provide assistance by comparing an institution’s measured data with the Standard Data. Differences often point to measurement errors and help identify the source of calibration errors detected by a mailed audit.

3.4 Review of QA Programs

Some QA/audit systems, particularly those linked to clinical trial QA, formally review QA and dosimetry procedures and records from the participating institutions, to ascertain compliance with accepted published recommendations. These may change with time as recommendations evolve, but for example IROC-H currently compares to the guidelines in AAPM reports from Task Groups 40 and 142 on comprehensive quality assurance [50, 51]. Significant differences are found frequently, but in some cases these are justified by the institution’s own procedures and measurements. More often, however, the institution has overlooked some component of recommended QA, or has allowed their
program to lapse in some important aspect. A list of common failures or lapses in QA programs found by the IROC-H is given below [2]:

- QA records not available or maintained
- Annual calibrations or monthly checks not performed timely
- No record of comparison to clinical values on annual report
- No record of comparison of daily and monthly checks against annual “baseline” values
- Physicist review of daily checks not documented
- No record of corrective actions and repeat measurements
- Check of electron beam energy not performed as required by applicable regulations and recommendations
- Output or field flatness constancy with gantry angle not checked during annual calibration

3.5 Audits of advanced treatment methods

Whilst a number of advanced treatment audits have been linked to specific clinical trials (section 4) some have been carried out as more general audits of performance for planning and delivery of such treatments (ie not linked to a particular trial). Many of these have grown from earlier audits of 3DCRT, or of other lower level audits. For example, the IAEA is currently developing a TLD and radiochromic film-based IMRT audit, for single field delivery in a planar phantom and for combined field end-to-end tests in a head-and-neck-like phantom within its developing national audit group project [9], having previously developed increasingly complex audit levels involving non-reference and other complex and combined field audits [9]. In the early 2000s, an ESTRO project group developed and ran a general intercomparison of IMRT planning and delivery for a pelvic/prostate-like phantom across a range of centres with diverse TPS and delivery technology [52, 53] and other European advanced technology audits have been reported [54-58] which are not specifically linked to particular trials. Many of these have taken into account experience from earlier audits for 3DCRT [59-61]. The Australian ACDS has carried out some level III audits, building on other trial or general audits for IMRT [3, 62] and other Australian IMRT and advanced technology audits have been run [3, 63]. A general VMAT audit is currently underway [64] based on similar methodology to the UK rotational IMRT audit described below [65]; and pilot audits are currently being carried out in NSW for 4D lung treatment methods (3DCRT, IMRT and VMAT) using a locally-developed moving ‘tumour’ phantom and making dose measurements with both an ion chamber and radiochromic film [66, 67] and for FFF VMAT lung SBRT using an ion chamber and ArcCheck [68].

The UK audit group (RTTQA, www.uk-dan.co.uk) has carried out general IMRT audits [69] and rotational therapy audits [65, 70, 71] as well as national audits for brachytherapy [72] and is currently conducting an SBRT audit [73]. These are within a national interdepartmental audit structure that comprises regular routine audits within an audit network of 8 regional groups, linked by less frequent audits of beam calibration by the NPL and supplemented by one-off audits at the national level, as above. This structure grew out of the original national photon dose calibration and multi-field planning audits in the late 1980s [43] and electron audits in the early 90s [44], with the geographic regional network beginning to take shape in 1991/2 [6]. The latter used a range of simple geometric, semi-anatomic and pseudo-anatomic phantoms for flexibility for 3DCRT audit [5, 6, 43, 45, 74-76] some of which had originally been designed for clinical trial audits [77-80]. Almost all the audits have been via on-site visits and measurement methods have included ion chambers, TLDs, radiochromic film and latterly 2D arrays. Some audits have included in-vivo dosimetry using TLDs [81] or diodes [82] as one component.

Taking the UK IMRT audits as examples:

i) IMRT audit [69]: A mail-based IMRT audit was carried out between 2009-10. Measurements were made for each individual field in institution-selected current clinical IMRT plans. Each field was measured isocentrically in a flat water-equivalent phantom at a depth of 5 cm using film and alanine,
processed centrally, with additional local ion chamber measurements also being made. 57/62 centres participated (78 plans submitted). For the film measurements, all 176 fields from less complex IMRT plans (mainly prostate and breast) achieved over a 95% gamma pass rate (using 3%/3mm for points above a 20% threshold). For more complex plans (mainly head-and-neck) 237/245 fields (98.7%) achieved more than a 95% gamma pass rate, using 4%/4mm criteria. 4/78 (5.1%) of the alanine measurements were > 5% different to the TPS predicted dose, three of which were large deviations (>10%), but which were linked to procedural errors during the audit set-up and dose delivery and not to real clinical errors. All out of tolerance values were found to be within tolerance when repeated. Excluding those three results on that basis, the mean difference was 0.05% (sd 1.5%). The study concluded that the audit in 92% of UK centres supported confidence in implementation of IMRT in the country.

ii) rotational IMRT audit [65, 70, 71]: 34 UK cancer centres with 43 treatment delivery systems (25 Varian and 12 Elekta VMAT 6 helical tomotherapy) took part in the audits in 2013. A complex virtual phantom planning exercise with 5 PTVs and one OAR, designed to test limits of the delivery system [71], and a clinical trial planning exercise were carried out and independently measured in each institution using a PTW Octavius II phantom with a PTW seven29 2D-array [65]. Point dose differences and global gamma index were calculated in regions corresponding to PTVs and OARs. Point dose differences for the virtual phantom test gave a mean (±sd) of 0.1% (±2.6%) and for the clinical trial plans were 0.2% (±2.0%). For the virtual phantom test, 34/43 institutions achieved all measured planes with > 95% pixels passing gamma <1 at 3%/3mm. rising to 42/43 for the clinical trial plans. Again the study concluded accurate clinical implementation in the country.

4. Audits of advanced treatment dosimetry for clinical trials

4.1 Results of treatment planning benchmark tests
Some trial QA systems have developed techniques to credential institutions through the use of a specific treatment planning exercises called a “benchmark case” and this is an increasingly standard requirement, particularly for more advanced treatments, incorporating full ‘dummy runs’ of planning cases to meet trial protocol requirements. Its purpose is to test whether an institution can meet the trial-specified requirements, such as dose prescription, contouring, etc. To comply, an institution must download a standardized CT data set (or comparable imaging information) and generate a treatment plan that complies with the requirements of the relevant trial. This must then be submitted digitally for evaluation, generally consisting of review of target volume contours and DVHs [83, 84]. For IROC-H, it can also include an independent calculation of dose to the target. When benchmark cases fail to meet the criteria, the QA office can contact the institution, explain the discrepancies, and work with the institution to resolve them. The follow-up generally consists of irradiation of an anthropomorphic phantom as a more definitive end-to-end test of the treatment planning capability. The comprehensive EORTC trial QA procedures have emphasised dummy runs for some considerable time as summarised in a range of reviews of their QA activity [85-90], linking generic QA with specific planning QA on virtual phantoms and with practical measurement-based QA.

4.2 Results of anthropomorphic phantom reviews
For the more complex technologies and treatments, clinical trial QA systems are now more frequently requiring institutions to simulate, plan, and treat a geometric or anthropomorphic phantom in ways as close to those used for patients as possible (an “end-to-end test”). If the protocol requires a benchmark treatment plan (section 4.1), some QA offices such as the IROC-H review the institution’s plan and re-calculate the doses at key locations to evaluate the accuracy of the planning system. This calculation is possible because the IROC-H has either measured data collected through visits to the institution, or is able to use its “standard data” [49]. When anthropomorphic phantoms are used, the delivered dose must be compared with the institution’s plan to determine the agreement [21, 91-94] Similar approaches are used by other trial audit systems, eg a range of audits of institutions participating in
trials run by the Trans-Tasman Radiation Oncology Group were reported or summarised by Kron et al. [3, 17] and Ebert et al [63]; and for the UK, for example, Clark et al reported detailed audit methods and results for the PARSPORT head-and-neck IMRT clinical trial [14, 95, 96]. The EORTC has supported a range of specific audits linked to trials including advanced treatments [85-90].

As one example, a review of the IROC-H results was recently reported by Molineu, et al [94]. During the time period 2001 to 2011 the IROC-H mailed head-and-neck phantoms to 763 distinct institutions. The phantom (figure 1) contains a primary and secondary PTV, along with an OAR and can hold point dosimeters and radiochromic film in two orientations. The institutions were instructed to perform imaging, develop a treatment plan using IMRT techniques, and then deliver the treatment to the phantom. A total of 1,139 irradiations were analyzed. Of these, 929 irradiations or 82% successfully met the irradiation criteria of 7% and 4 mm distance-to-agreement. (Had the dose criterion been reduced to 5%, only 69% of the irradiations would have passed.) The passing rate has increased steadily since the phantom’s introduction in 2001 from approximately 69% to a current rate of 91% [94]. It has been noted that some institutions irradiated such phantoms multiple times to improve their initial irradiation results, test different treatment planning system algorithms or test different treatment delivery systems. As a comment on the usefulness of end-to-end measurement audits of this nature, a study can be considered which compared the results from the benchmark case used by the Quality Assurance Review Center as an IMRT treatment planning capability exercise, to the IROC-H IMRT H&N phantom irradiation results from the same group of 113 institutions. All of the institutions passed the IMRT benchmark case (planning study and self-reported IMRT QA measurement) while 20 of these same institutions did not pass the end-to-end independent phantom irradiation. The phantom audit is capable of detecting imaging, data transfer and delivery errors that cannot be detected by the institution’s completion of a benchmark case. In addition, each institution’s own IMRT QA results of their IMRT benchmark plans passed their own QA criteria. An independent end-to-end anthropomorphic QA audit is capable of detecting dosimetry errors that might otherwise go undetected.

Besides the head-and-neck phantom the IROC-H system has developed a range of other specific phantoms, including pelvis, spine, liver, thorax, SRS head [91-93]. Whilst many options for point dosimetry and for radiochromic film dosimetry are possible and routine in such phantoms, and in commercial anthropomorphic phantoms, the use of true 3D dosimeters is not yet routine [97]. The feasibility of using 3D gel [98] and PRESAGE® [99, 100] dosimetry in the IROC-H head phantom has been tested but is not yet easily available. Similarly, some commercial anthropomorphic can be supplied with the option of gel-holding inserts, but these dosimetry systems are still not robust enough for wider audit use.

Figure 1. IROC-H head phantom
5. Final comments
Kron [3] identified some current challenges for audit dosimetry, which included: risk assessment approaches to audit design; scope and frequency for best use of limited resources; limited methods available for image-guided and adaptive radiotherapy, for motion management and for brachytherapy; and the need for access to treatment planning or trials review software [101] that can display dose distributions from a variety of different planning systems for comprehensive and flexible evaluation of dose distributions from measurements against those from TPS. Ebert et al [63] and the EORTC [10, 88, 89] have considered a range of organisational, administrative and financial issues relating to audit and practical aspects of audit measurements and challenges posed by the new technologies [88]. Many commentators and reviewers note that measurement audit cannot exist in isolation and increasingly must be part of a wider set of comprehensive audit of facility and systems performance [42].

6. Conclusions
Radiation therapy technology and techniques have been advancing rapidly over recent years and continue to do so. They have become increasingly complex through the widespread availability and implementation of IMRT, VMAT, other rotational and robotic delivery methods, etc. and all coupled with image-guidance. Increasingly too, other advanced methods are being used, including SBRT, FFF beams, adaptive radiotherapy, 4D radiotherapy, proton and other beams, etc. Institutional commissioning and QA has had to advance with these changes. Similarly dosimetry audit methods have had to evolve to meet the demands of advanced treatments. Many of these have been developed and piloted for clinical trial QA, as it is often in this context that advanced treatments begin to roll out more rapidly. It is critical for optimum trial outcome and confidence that participating centres are QA’d and audited carefully for these treatment methods, to provide comparison between centres of the level of performance consistency against defined external trial standards. A comprehensive trial quality assurance program can define the range of acceptable and unacceptable variations, detect and correct the causes of such variations, and document the frequency of variations. The ability of QA programs to reduce variations in treatment delivery and improve the quality of clinical trials and routine clinical practice in participating institutions has been demonstrated. Measurement and analysis methods for advanced treatment dosimetry QA and audit need to be accurate and precise, in line with demonstrating that the QA standards requirements are met. Ideally for complex 3D and 4D treatments, QA and audit measurement methods should be fully 3D and 4D, but practical systems that fully deliver this are still not available.

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