BJR

Received: 24 March 2015 | Revised: 22 June 2015 | Accepted: 1 September 2015

doi: 10.1259/bjr.20150251

Cite this article as:
Clark CH, Aird EG, Bolton S, Miles EA, Nisbet A, Snaith JA, et al. Radiotherapy dosimetry audit: three decades of improving standards and accuracy in UK clinical practice and trials. *Br J Radiol* 2015; **88**: 20150251.

REVIEW ARTICLE

Radiotherapy dosimetry audit: three decades of improving standards and accuracy in UK clinical practice and trials

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ABSTRACT

Dosimetry audit plays an important role in the development and safety of radiotherapy. National and large scale audits are able to set, maintain and improve standards, as well as having the potential to identify issues which may cause harm to patients. They can support implementation of complex techniques and can facilitate awareness and understanding of any issues which may exist by benchmarking centres with similar equipment. This review examines the development of dosimetry audit in the UK over the past 30 years, including the involvement of the UK in international audits. A summary of audit results is given, with an overview of methodologies employed and lessons learnt. Recent and forthcoming more complex audits are considered, with a focus on future needs including the arrival of proton therapy in the UK and other advanced techniques such as four-dimensional radiotherapy delivery and verification, stereotactic radiotherapy and MR linear accelerators. The work of the main quality assurance and auditing bodies is discussed, including how they are working together to streamline audit and to ensure that all radiotherapy centres are involved. Undertaking regular external audit motivates centres to modernize and develop techniques and provides assurance, not only that radiotherapy is planned and delivered accurately but also that the patient dose delivered is as prescribed.

INTRODUCTION

The need for dosimetric and geometric accuracy in radiotherapy is well established.[1–5] Recommendations by the International Commission of Radiation Units and Measurements in 1976[1] state that the dose delivery to the primary target should be within ±5% of the prescribed value (but in some special circumstances ±2%). These are based on assessments of clinical accuracy requirements and set the tolerances for process and equipment performance and quality assurance, as well as audit tolerances. There has been a discussion of the exact statistical meaning of these figures, but it has been generally recognized that delivery of the prescribed dose to within ±5% may often be difficult to achieve, requiring careful consistent attention to quality assurance of every step contributing to final delivered dose to the patient. Similarly, awareness of patient positioning and other geometric uncertainties has been mandated, in terms of target coverage and organs-at-risk (OARs) avoidance, but also because geometric uncertainties translate directly into dosimetric uncertainties, increasingly so as techniques become more complex.[5] The value of 5% consists of contributions mainly from dose-calculation accuracy, patient positioning including target and organ definition and treatment machine mechanical tolerance.

One tool in ensuring consistency in dosimetry is the use of dosimetry audit. This may range from postal audits, based on the use of thermoluminescent dosemeter (TLD) or optically stimulated luminescent dosemeter methods, *e.g.* as organized by the International Atomic Energy Agency (IAEA),[6] to on-site visits using ionization chambers and appropriate phantoms. They may be linked to general dosimetry infrastructure, to support for implementing advanced methods, or to clinical trials. Thus, the audits may cover various levels from basic reference dosimetry through to *in vivo* dosimetry on patient treatment or

advanced radiotherapy techniques. Audit is also sometimes referred to as intercomparison. A formal definition of the two terms would define "dosimetry intercomparison" as the physical process of comparing measured doses with predicted doses, whereas "dosimetric audit" implies a wider framework within which this is used as a tool. However, the two terms have historically merged and are sometimes used interchangeably. In this article, we refer to both according to the use at the time, but "audit" is used for consistency as a general term. Techniques for audit can range from straightforward output measurements at a single point on the central axis using an ionization chamber or TLD through a range of complexities for detectors (ion chambers, TLDs, film, arrays), phantoms (homogeneous blocks, inclusion of inhomogeneous material, semi- or full anthropomorphic phantoms) and approaches (single measurement through to full end-to-end testing of the complete scan, plan, deliver process). The dose can also be measured as absolute or relative. Each audit will be designed with an appropriate combination of the above variables, according to the aim of the audit.

The IAEA introduced the first postal dosimetry service in 1966/1967 using (lithium fluoride) TLD and has published periodic updates on results from these audits.[6–10] The World Health Organization joined this programme in 1968. In the same year, the Radiological Physics Centre (RPC), MD Anderson, Houston (now called the IROC-H, the Imaging and Radiation Oncology Core—Houston) first received funding to carry out dosimetry audits within the USA, with their first on-site review being carried out in 1969.[11] They then initiated their TLD programme for photon beams in 1977.[12] In Europe, the ESTRO (European Society for Radiotherapy and Oncology) Quality Assurance Network for radiotherapy (EQUAL), established in 1998, grew out of previous preliminary audit networks developing from the early 1990s.[13–15]

Within the UK, the first comprehensive national photon dosimetry intercomparison was carried out in the late 1980s[16] and laid the basis for the development of a national dosimetry audit network, which began to evolve in the early 1990s.[17–19] The first national electron beam dosimetry intercomparison was carried out in the UK in 1994–1996[20] and was extended to cover all megavoltage (MV), electron and kilovoltage (kV) treatment units within Ireland.[21] The UK Interdepartmental Dosimetry Audit Network grew out of the structure of the original national study and was formally established by 1993. It is now co-ordinated by the Institute of Physics and Engineering in Medicine (IPEM) and consists of nine co-operative regional groups.[19] In 1995, the National Physical Laboratory (NPL) began reference audits within the UK at the invitation of IPEM, initially to link the regional audit network groups. Within this network, the basic audit methodology and phantom design followed that of the national intercomparison. However, more recently, most of the groups have evolved more complex methods to extend the audit scope, including the development of phantoms to simulate various clinical treatment situations, audits of kilovoltage X-ray beams and electron beams, and brachytherapy dosimetry. The UK Radiotherapy Clinical Trials: Quality Assurance Group has also evolved, beginning circa 2000 and supporting quality assurance (QA) for specific three-dimensional conformal radiotherapy (3DCRT) and later intensity-modulated radiotherapy (IMRT) clinical trials.[22–27] This activity gave rise to the Radiotherapy Clinical Trials: Quality Assurance Group, known as RTTQA, in 2003.

There are currently a range of other national and international QA groups supporting radiation oncology trials, where QA for the trial acts at the same time as a quality audit for the participating centre, *e.g.* European Organisation for Research and Treatment of Cancer (EORTC)[28–30] and the Trans Tasman Radiation Oncology Group (TROG).[31] In Europe, the EORTC began a mailed TLD dosimetry audit pilot for clinical trial participants in 1988.[32]

Overall, the track record of the UK audits has demonstrated confidence in dosimetry for clinical practice and for trials and continues to do so. The audit system is one strand in a regulated dosimetry infrastructure in the UK, providing a system of dosimetry with high consistency which consists of: the national dosimetry standards (NPL); the UK dosimetry codes of practice, specifying defined transfer instrumentation and procedures (with one specific recommended secondary standard chamber and consistently specified and used tertiary dosimeters); the national quality assurance recommendations (IPEM); and the national audit network.

Many articles have been published on dosimetry audits. Together, their results can identity demonstrable benefits and effectiveness and can contribute to estimates of the currently achieved consistency in radiotherapy dosimetry.[5] They can demonstrate the role of dosimetry audits in helping assure accuracy of advanced radiotherapy techniques, determine their benefits to clinical trials and inform the arguments for further national/international audits. As radiotherapy planning and treatment delivery have become less intuitive and more automated, a willingness to undergo radiation dosimetry audit, as one vital component in wider clinical audit, demonstrates the best practice and transparency in the overall process and is now an intrinsic part of the radiation oncology requirements in the national cancer peer-review standards[33] and of acceptability to enter patients into clinical trials involving radiotherapy.

DOSIMETRY AUDIT JUSTIFICATION AND METHODOLOGIES

With any audit or credentialing exercise, one of the primary considerations, alongside accuracy, should be cost-effectiveness. Pettersen et al[34] have examined this issue and stated that "The number of patients required in a Randomised Clinical Trial may be reduced by introducing appropriate dosimetry QA, as the risk of underpowering the study is minimized. Dosimetry QA in clinical studies is therefore cost-effective". Peters et al[35] have reported on the impact of radiotherapy quality on outcome in a large international Phase III trial evaluating chemoradiotherapy for advanced head and neck cancer and concluded that the protocol required interventional review of radiotherapy plans by a Quality Assurance Review Center (QARC). All plans and radiotherapy documentation underwent post-treatment review by the Trial Management Committee for protocol compliance. The secondary review of non-compliant plans for predicted impact

on tumour control was performed. Factors associated with poor protocol compliance were studied, and outcome data were analysed in relationship with protocol compliance and radiotherapy quality. The results clearly demonstrated the critical importance of radiotherapy quality on outcome of chemoradiotherapy for head and neck cancer and that poor QA/compliance can negate the worth of an otherwise well-designed clinical trial.

A number of classification systems have been proposed for different audit types, generally based on the level of complexity. As an example, Table 1 lists the dosimetric services offered by the Australian Clinical Dosimetry Service (ACDS).[31]

Various methodologies have been used worldwide, ranging from postal TLD audits of reference beam calibration to on-site visits aiming to investigate advanced radiotherapy techniques.[9,30,36,37] The audits have either been run from a single-centre or as a "round-robin" approach with different centres taking it in turns to audit each other. Different treatment modalities have been investigated, including photons (MV and kV) electrons, protons, brachytherapy, as well as audits of systems such as planning systems, imaging systems and image registration algorithms.[36] Tolerances applied should take into account the required dosimetric accuracy at the level of the dosimetry chain being assessed and the uncertainties of the measurement methods employed. As one example, the RPC methodologies[11,37] include monitoring beam calibration, dosimetry data, calculation algorithms used for treatment planning and institutions' quality control procedures. The monitoring includes on-site dosimetry as well as a variety of remote audit tools. They also conduct a variety of credentialing activities, which provide mailable anthropomorphic phantoms to verify tumour dose delivery for special treatment techniques and clinical trials.

The overall evidence from dosimetry audits is that results improve with time, in part owing to the impact on centres participating in the audits and dealing with any issues identified.[6,10,11] Thus, repeated audits directly demonstrate their effect in improving dosimetry consistency and hence the quality of radiotherapy dosimetry was applied in clinical practice. As one example, within the UK, repeated reference dosimetry audits have demonstrated that standard deviations (SDs) of the distribution of differences between measured and expected doses and the incidence of out-of-tolerance discrepancies have decreased, indicating improved consistency at the level of beam calibration in the UK. The reasons for this are likely to include the introduction of simple and direct absorbed dose-to-water codes of practice,[38,39] the impact of the audits themselves, the implementation of quality management systems in radiotherapy and regular clinical and dosimetry quality audits *via* the peer-review standard process and the regional dosimetry audit network, respectively. The options for audit groups are therefore to either tighten tolerances for standard audits or continually develop to include more complexity when it is observed that the original levels are met. In general, the latter is likely to gain the most cost-benefit from the limited resource available for audit,[40] as more complex audits move closer to representative clinical treatment delivery situations and test more steps and systems in the overall process, but also typically inherently include a reference beam dosimetry audit as part of higher level audits (for further details, see the National Physical Laboratory's involvement in audit section).

INSTITUTE OF PHYSICS AND ENGINEERING IN MEDICINE INTERDEPARTMENTAL AUDIT

The initial UK national photon intercomparison, managed by Thwaites et al,[16] considered beam calibration, single-field relative dose parameters and also multifield planned dose distributions in a phantom designed specifically to test inhomogeneities and combinations of other treatment variables. It was largely unfunded (loaned equipment by manufacturers, volunteers carrying out the work and some seed funding for phantom construction and initial travel from the Scottish Health Department), so was set-up to be run by local medical physicists as regional "auditors" in eight different geographical areas. (The term "intercomparison" was used to describe the study in published abstracts from 1988 and in the final publication.[16] The term "audit" was first used to describe the study in a 1991 abstract.). In each group, the measurements were performed by a single auditor who went to

Table 1. Dosimetric services offered by the Australian Clinical Dosimetry Service

Dosimetry level	ACDS	Detector type	Mode	System checked	Comments
Level I	Output under reference conditions	TLD, OSL	Remote	Every radiation beam	Identical to RPC audit
Level IB	Output under reference conditions	Ionization chamber	On-site	Every radiation beam	Offered to new centres prior to opening
Level II	Dose distribution in physical phantoms	Detector array	Remote	Planning system	Can include homogeneity and allows clarification of Level III findings
Level III	Anthropomorphic phantom end to end	Ion chamber, radiochromic film	On-site	Entire treatment chain	Treatment specific—most relevant for clinical trials

ACDS, Australian Clinical Dosimetry Service; OSL, optically stimulated luminescent; RPC, Radiological Physics Centre; TLD, thermoluminescent dosemeter.
Reproduced from Kron.[31]

each centre in the local region, beginning in the Scottish, Northern Ireland and northern England group (the Scottish+ group). The equipment was then taken to a department in the next geographical area, the audit measurement method was carried out there by the previous auditor in conjunction with the next group auditor and the equipment handed on; and so on round the UK's 60+ centres. Discrepancies of ≥5% were investigated by the centre concerned. The intercomparison visit discovered a major calibration error of a cobalt treatment unit, which had resulted in a significant number of patients receiving overdoses of 25%.[16,41] This event lead directly to the introduction of quality management systems in radiotherapy in the UK,[42] being one of the first countries to do so. In addition, the originally drafted audit protocol was to measure multifield irradiations in both isocentric and fixed source-to-surface distance conditions, but owing to limited resources and time available per audit visit, the final protocol allowed a centre to plan and deliver in whichever condition was most frequently used in their then-current clinical practice. In hindsight, a serious treatment planning system (TPS) commissioning error may also have been discovered some years before it was eventually identified, if the original audit had been resourced sufficiently to support measurements in both conditions.[43] These two observations demonstrate not only the direct value of dosimetry audit but also the need for adequate resources for such activity. It is noteworthy that a subsequent bid for funding to the Department of Health for the national electron dosimetry intercomparison[20] was successful and that the study employed a full-time auditor to carry out the measurements, thereby achieving a much more rapid national audit. From the experience of the initial audit, a number of the regional groups continued to develop and carry out audits, and from this, the regional interdepartmental audit network developed, based roughly on the original audit's regional structure and with a steering group set-up and co-ordinated by IPEM to provide an organized and continuing approach to audit between different centres. This National Interdepartmental Audit Network consisted of 8 co-operative regional groups (now 9 groups) each with between 5 and 12 centres and covered all UK departments.[16,17,44]

One of the key strengths of the interdepartmental audit system is that every National Health Service (NHS) department in the country is involved and has an opportunity to compare itself with its peers. Modern radiotherapy is complex to plan and deliver accurately, and departments need to demonstrate that the risk to patient safety is managed. New treatment techniques are typically developed and first implemented in a few centres, often as the prelude to, or as part of, a clinical trial. Audit may begin as specific clinical trial audit and develop into more routine approaches. Thus, interdepartmental audit ensures that standards are maintained as the technique becomes routine. In the UK, this has happened with 3DCRT, through IMRT, image-guided radiotherapy (IGRT) and volumetric arc therapy (VMAT) and will continue with image-guided brachytherapy, adaptive radiotherapy, MR only planning and proton therapy. Each regional IPEM group works autonomously and can therefore design and conduct its own audits, as well as implementing national audits. This group arranges interdepartmental audits between each of the centres, whilst the national audit steering group meets annually to review and co-ordinate audit activity across the UK. The requirement to participate in the national dosimetry audit network is now also incorporated into the National Cancer Peer Review standards.[33]

THE NATIONAL PHYSICAL LABORATORY'S INVOLVEMENT IN AUDIT

The NPL is the UK's primary standards laboratory. The Radiation Dosimetry Group is responsible for maintaining the primary standards for external beam radiotherapy. All UK NHS external beam radiotherapy treatment doses are traceable to the primary standards *via* NPL's dosimetry calibration services. The current UK Code of Practice for MV photon beam dosimetry is the Institute of Physical Sciences in Medicine (IPSM) 1990 code of practice.[38] This was the world's first direct absorbed dose-to-water-based protocol. It was developed in collaboration between the NPL, IPSM (now IPEM) and hospital medical physicists and was based on a pioneering national standard using graphite calorimeters. This code of practice moved away from exposure or air kerma-based standards, which had been in place since the 1960s, to a more relevant quantity, directly in terms of the dose delivered to the patient. A similar approach was taken for electrons in the early 2000s, with a new direct absorbed dose-to-water code of practice[39] replacing the earlier air kerma-based approach.[45]

In 1994, NPL was invited to participate in the national audit network group to provide the link between each of the regions *via* conducting reference dosimetry audits. Initially, there was one audit per region per year. The original audit covered MV photon dosimetry, and the protocol consisted of a measurement of beam quality, machine output and calibration of the hospital's tertiary standard chamber. Other specific areas that were examined included the implementation of ion recombination corrections,[46] testing accurate measurement of temperature and pressure, as these directly impact on ion chamber beam calibration dosimetry, and checks on relevant practical issues such as laser alignment, front pointer agreement and storage conditions for equipment. Since 1995, this has involved approximately 100 audits, some two-thirds being MV photon audits with the remainder being made up of a range of electron (both air kerma- and absorbed dose-based protocols) and kV X-ray audits. The basic NPL audit structure for all reference dosimetry audits includes an independent check of beam quality, beam calibration and field instrument calibration.

Whilst maintaining audits of reference dose, NPL has broadened its involvement in dosimetry audit to cover clinical dose delivery of typical treatment modalities, *via* the use of its alanine measurement system, including the national rotational IMRT audit,[47–49] stereotactic ablative body radiotherapy (SABR) audit and brachytherapy audit, in some cases in collaboration with the RTTQA group to support centre accreditation for inclusion in clinical trials. From the point of view of a standards laboratory, benefits of involvement in audit include ensuring the correct implementation of the traceability chain to the patient and closer interaction and understanding of the end users' requirements.

DOSIMETRY AUDIT IN CLINICAL TRIALS

The timing for development of clinical trial audit in the international setting has varied. In the USA, this development ran

alongside general support for technical radiotherapy. Several groups developed, including, amongst others, RPC, Radiation Therapy Oncology Group, QARC, which have now joined together to become the IROC. The experience within North America illustrates how a number of centres with different expertise can come together to form a valuable consortium providing the means of evaluation and assessment of performance for credentialing centres for entering radiotherapy trials with more and more complexity within the trial.

European clinical trial audit developed through the EORTC in the 1980s, with the use of questionnaires and dosimetry audit.[13,28,32] Similar programmes then ran in the UK associated with large multicentre clinical trials such as CHART (Continuous Hypofractionated Accelerated RT Trial for Lung and Head and Neck Cancer),[22] RT01 (a randomised controlled trial of high dose *vs* standard dose conformal RT for localized prostate cancer)[25,50] and START (UK Standardisation of Breast Radiotherapy trial)[27,51] using physicist and therapy radiographer expertise (with advice and support from clinicians), primarily at the Mount Vernon Cancer Centre and the Royal Marsden Hospital. From 2003, collaborative work between these individual centres led to the RTTQA being set-up, that has now become the UK Centre for QA in Clinical Trials (funded through the National Institute for Health Research Clinical Research Network, see website: www.rttrialsqa.org.uk). The EORTC meanwhile has become established as a group responsible for the conduct of clinical trials, with the Radiation Oncology Group being the section which is responsible for radiotherapy trials.[28,52]

Initial dosimetry audit in UK trials

The CHART trial was the first UK trial to have an associated comprehensive audit programme with the emphasis on machine-based measurements.[22] This consisted of a full review (using a standard set of measurements) of one linear accelerator and simulator within each centre participating in the trial, performed at a visit to the centre by the QA team (therapy radiographer/physicist/engineer). At the same time, phantom measurements were made using an ion chamber, in order to obtain immediate measurement results that allowed reconciliation against the calculated doses whilst the team were still in the centre. Anthropomorphic phantoms of thorax and head and neck were developed and built (by St Bartholomew's Hospital) for these measurements.[22] The approach for the START[27,53,54] trial was more process focused as, by this time, it was recognized that all UK centres were following a high standard of checks on their linear accelerators. The main goals for START were: establishing the dose at a reference point, *in vivo* dosimetry, establishing a "Help Desk" for interpretation of the protocol and use of participants' meetings to discuss issues within the trial. Visits included the following checks: a limited set of linear accelerator checks; two-dimensional phantom measurements; and three-dimensional (3D) phantom measurements.[27]

Intensity-modulated radiotherapy dosimetry audit in clinical trials

A further role of dosimetry audit is as a valuable resource to facilitate the implementation of new technology and development of techniques within a department. Often, the confidence gained by having an external audit is considerable. Also, the use of a new technology within a clinical trial can allow a combined experience level to develop more quickly, leading to shared knowledge of what can be achieved. Collaborative relationships between centres with the same equipment can also help to understand more quickly what can be expected, where any issues may lie and how to address them. At each stage of technological advancement, it became obvious that new audit techniques would be necessary.[23–25,50,55] It also became clear that the breadth of expertise needed to support a portfolio of technical trials needed to be expanded to include expertise from other major radiotherapy trial centres. A key stage was the introduction of IMRT in the UK around 2000 and the audit for the trials which were developed in order to provide the evidence base for further expansion of the technique. Since then, many multicentre trials[23,24,55] have included IMRT. These have led to a need for more complex phantoms, multiple dose point measurement and complex dose distribution analysis with techniques such as gamma index analysis. The RTTQA group also set up a nine-point IMRT credentialing programme[23] which was used for all IMRT trials and has since been streamlined to minimize the workload for the contributing centres as well as any repetition which may occur between trials.

The development of the Radiotherapy Clinical Trials Quality Assurance group under National Cancer Research Institute

In 2009, Clinical and Translational Radiotherapy Research Working Group (CTRad) was formed under the umbrella of the NCRI. This group, the "Clinical and Translational Research Working Group" has a broad strategic remit to develop an extensive portfolio of "practice changing" trials. CTRad is responsible for ensuring co-ordination across all aspects of radiobiology and radiotherapy research and for actively promoting translation of new discoveries into practice. The group consists of four work streams (WS1 science base; WS2 Phase I/II trials; WS3 Phase III trials and methodology; WS4 New Technology, Physics and Quality Assurance). WS4 leads on technical aspects of radiotherapy development and QA for clinical trials.[56] Therefore, at this time, WS4 became tasked to provide a National QA programme for all National Institute for Health Research (NIHR) Cancer Research Network (CRN) Clinical Research Portfolio Trials which include a radiotherapy component. The main objectives were to ensure that the remit of providing audit for every UK CRN study portfolio trial including radiotherapy was fulfilled, to develop the concept of trial complexity with appropriate levels of associated QA and to form links with other expert groups, *e.g.* NPL, IPEM, where required.

The RTTQA group is now a multidisciplinary group active on four hospital sites (Mount Vernon Cancer Centre, Royal Marsden Hospital, Clatterbridge Cancer Centre and Velindre Cancer Centre). A management group incorporating clinicians, physicists and therapy radiographers is responsible for the strategic planning. Staff working within the group develop and implement audit programmes which include comprehensive data collection and dosimetry audit. With increasing numbers and complexity of trials and the need for more diverse QA programmes, individual task groups or subgroups were formed.

These groups focus on specific technical areas requiring development. The groups are as follows:

- IMRT, including rotational IMRT
- IGRT, to include stereotactic body radiation therapy
- Outlining and imaging, for target and critical structure delineation
- Database solutions and information technology.

Streamlining trial audit processes

The advent of IMRT dosimetry audit brought with it with a need to visit radiotherapy centres to perform dose measurements. This requires local resources to prepare for the tests as well as participate in the visit itself. This workload is in addition to routine service work for physics departments co-operating in clinical trials and many departments find it challenging to manage the work required for the national audit. To alleviate such pressures the RTTQA group implemented streamlining of the IMRT QA processes whereby a centre already credentialed for IMRT use in a particular trial would not be required to undergo the full credentialing for another trial.

Collaborative working has been a key to streamlining workload. The RTTQA Group has co-operated with other groups on projects such as the national rotational IMRT audit[48,49] (NPL, Royal Surrey County Hospital NHS Foundation Trust, RTTQA and IPEM) and the recent national high dose rate (HDR) brachytherapy audit[57] (NPL, Portsmouth Hospitals NHS Trust). The Outlining and Imaging Subgroup has also involved co-operation with the NCRI positron emission tomography (PET) group. Further collaborations are sought where expertise is needed.

International links and harmonization

The Global Harmonisation Group for radiotherapy quality assurance (http://www.rtqaharmonisation.org/) was set up to facilitate harmonization and improvement of the quality assurance of radiation therapy as pertains to multi-institutional co-operative clinical trials implemented worldwide. The steering committee currently consists of IROC (USA), TROG (Australasia), RTTQA (UK), EORTC (Europe), Japan Clinical Oncology Group, National Cancer Institute of Canada Clinical Trials Group and International Atomic Energy Agency (United Nations body based in Vienna). The goals are to collate, homogenize and distribute information regarding the radiotherapy quality assurance standards across audit groups, provide a platform for prospective discussions on new audit procedures, software tools, guidelines and policies and provide a framework to endorse existing and future audit procedures and guidelines across various trial groups.[58] Recent work[59] has included harmonizing the nomenclature for volume naming across international trials.

Audit for clinical trials has created a strong basis for the verification of existing and new techniques in radiotherapy in the UK. The majority of centres now participate in multiple trials and hence have access to a high level of regular audit through the quality assurance processes of these trials.

RESULTS OF DOSIMETRY AUDITS

There have been many audits over the past three decades, in the UK and elsewhere, considering many different combinations of levels of dosimetry audit and testing many equipment, system and process parameters, up to and including audits of dose delivered to a patient using *in vivo* methods.[16–18,20,22,23,27,49,50,53,57,60,61] It is beyond the scope of this overview to review all of these and their results, so the following section limits discussion to two areas only. The first is that of beam calibration audit, being the fundamental reference dosimetry level affecting all patients on any specific machine or in any specific centre; and therefore beam calibration audit is also the most widely carried out audit, by number of beams or by repetitions at different times. Results and observations are summarized from the original national dosimetry intercomparisons up to the current routine dosimetry audit network findings. The second area considered is a brief overview of more recent UK audits to summarize the directions that audit activity has been developing towards and their main results.

Clinically significant discrepancies have been observed in many studies, *e.g.* in the UK, the original national photon audit identified the miscalibration of the Cobalt-60 (Co-60) unit at Exeter.[41] In addition, the general experience demonstrates that repeated audits in the same group of centres, same country etc. show improvements with time, in terms of fewer out-of-tolerance results, smaller ranges and SDs of the distribution of results etc.[6,10,11,15,18,19,37] Although remote TLD audits are less resource intensive, some of the observed discrepancies may arise from inexperience on the part of the local staff carrying out the set-up and irradiation of non-standard phantoms or owing to protocol misinterpretation. On-site visits have less uncertainty and are more likely to find root causes and allow potential resolution of problems at the time of the audit; however, they are significantly more costly.

Initial UK national audits

All of the then 64 radiotherapy centres in the UK participated in the original UK dosimetry intercomparison. For reference point measurements (beam calibration audit) in 61 Co-60 beams, a mean difference between measured to stated dose of 0.2% was observed (*i.e.* a mean ratio between measured and expected dose of 1.002) with a SD of 1.4%, whilst for 100 MV X-ray beams, the corresponding figures were 0.3% and 1.5% with 97.0% within a $\pm$3.0% deviation. Doses were also investigated in planned three field distributions, one in a homogeneous phantom and one with a lung equivalent insert, for one photon machine and beam per centre. Doses were measured at the central point and at four other locations. The mean ratio of measured to calculated doses for all points was 1.008, with SD of 2.7% and 3.5% for the uniform and non-uniform phantoms, respectively. These results were compared with other photon dosimetry audits carried out around the same time.[16]

In the later UK national electron dosimetry intercomparison, 52 radiotherapy centres were visited, making measurements on 1 treatment unit per centre, and 3 beam qualities per treatment unit.[20] The energy, depth of maximum dose and beam calibration were independently determined. In total, 156 beams were audited. A mean difference of audit-measured to expected (locally stated) dose of $-$0.6% (ratio of measured/stated of 0.994) was obtained with SD 1.8%, and range of +4.6% to $-$5.1%. This study also performed a single-MV photon output

measurement at the same visit to each centre, measuring 16 Co-60 and 36 linear accelerator beams. All measurements were within 3.0% with the mean difference between audit-measured and locally stated doses being 0.3% (SD 1.0%). For photon MV beams, the spread (SD and range) had decreased as compared with the 1988–1991 audit. The Scottish+ Group of the UK regional groups carried out an electron beam audit of a subset of these centres in 2002/2003.[19] In the interim, a new electron dosimetry code of practice had been introduced.[39] In total, 22 beams were audited. The mean difference between audit-measured and locally stated dose was −0.5% with a SD of 0.7% and a range of observed values from −2.0% to +0.5%. Considering only the results from the same centres, it is clear that the consistency in dosimetry between centres had improved between the two audits, and the magnitude of discrepancies had decreased.

The trend of diminishing SD within a given type of audit has continued. Since the introduction of the 2003 electron dosimetry code of practice,[39] the NPL have carried out audits on electron beams. The mean difference in the dose measured by NPL and stated by the centre was 0.3% with a SD of 0.4% (compared with 1.8% in the original electron audit and 0.7% in the Scottish+ group). Similar reductions in SDs can be summarized by examining the results of the national MV photon audits in Table 2.

The audits demonstrate the consistency of the mean ratio between audit-measured and hospital-stated doses and that it is close to unity, *i.e.* that the overall mean radiotherapy doses across the country are as expected. In addition, the repeated audits demonstrate the improvement in the SD, *i.e.* improved consistency of dose across centres. This is most likely a result of the developments in measures implemented to provide the UK with a robust and rigorous radiotherapy dosimetry framework, such as in absorbed dose primary standards, dosimetry codes of practice, the use of quality management systems in radiotherapy and the audit network and audit exercises themselves.

The audit network progressed from the early 1990s with each regional group carrying out its own audits, to suit the local resources and requirements, linked by the NPL intergroup audits and liaising through the national (IPEM) steering group.[18] The first nationally co-ordinated audit within the current structure of the IPEM interdepartmental audit groups was an MV photon audit in 2008. The purpose was to reset a baseline whereby all radiotherapy departments in the UK would have demonstrated that they had achieved a clearly documented and comparable dosimetry standard. This consisted of a single-wedge beam, planned to deliver 2 Gy at a specified field size and depth to provide a clinically relevant situation. The auditor measured the absolute dose and compared with the local centre's TPS calculated dose. 93.8% of measurements were observed to be within the ±3.0% tolerance set. The following year a national electron audit against the 2003 code of practice[39] was run. The (beam calibration) doses at the recommended reference depths from the code of practice were all within the pre-set 2.5% tolerance (95.0% were within 1.5%). Apart from some minor systematic errors that were resolved, the results of all audits of dose in reference conditions have been within protocol tolerances, confirming the long-term stability and agreement of basic radiation dosimetric parameters nationally. There is further overall evidence of improvement in radiation dosimetry with time, including with the adoption of newer codes of practice,[44] as shown in Figure 1.

In addition to the basic electron dosimetry parameter audits in the more recent nationally co-ordinated study, a planned cut-out rectangular field of 5 cm by 7 cm was also considered. Here, the differences were significantly greater between audit measurements and TPS calculated or department-stated doses; 90.0% were within 5.0% and the range of results was much broader. Generally, the measured dose was less than calculated and in a few cases was >4.0% different. A number of reasons for this discrepancy were explored, including approximations made in the calculation process. Three departments with output difference >10.0% in this cut-out were asked to investigate the cause of the discrepancy.

Recent national radiotherapy dosimetry audits for more advanced techniques

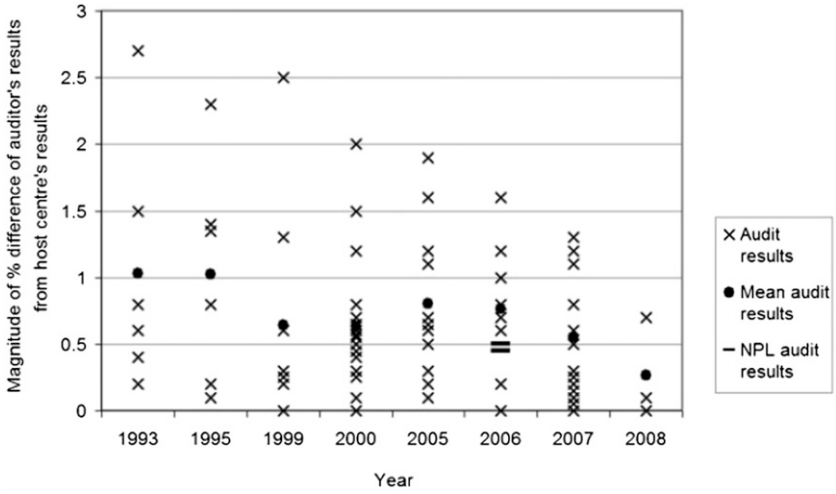
In the past 5 years, there have been several national UK audits carried out which have helped to support the implementation of, and set the standards for, advanced techniques. These have included a national IMRT audit[60] which was designed to be independent of linear accelerator, TPS and treatment delivery method and suitable for a plan from any clinical site. The aim was to provide an independent check on the efficient implementation of IMRT in the UK, identify problems in the modelling and delivery of IMRT and act as a pre-clinical independent check for centres starting IMRT or moving to new treatment sites. It also provided a snapshot of the range and complexity of IMRT being practiced in the UK and satisfied the need for independent IMRT audit methods being proposed in national guidelines and standards.[62] This was a postal audit with a relatively simple design and methodology. Centres were sent alanine pellets and film and asked to select a plan from their own centre

Table 2. A summary of the results of UK megavoltage audits carried out at the national level since 1987

Audit	Dates	Mean difference (%)	Standard deviation (%)
Thwaites et al[16]—measured/centre-stated	January 1987 to January 1991	0.3	1.5
Nisbet and Thwaites[20]—measured/centre-stated	From 1994 to 1996	0.3	1.0
NPL—measured/centre-stated	Since 2003	0.3	0.7

NPL, National Physical Laboratory.

Figure 1. The improvement in results of radiation dosimetry audit over time. Reproduced from Palmer et al[44] with permission from the British Institute of Radiology.



which had already had local quality processes run on it and to deliver an individual field to blocks of solid water with the film and alanine in place. 57 centres participated and, for the film measurements, all fields from the less complex IMRT plans (including prostate and breast plans) achieved over 95.0% pixels passing a (local dose normalization) gamma criterion of 3%/3 mm within the 20% isodose. For the more complex IMRT plans (mainly head and neck), 96.7% of fields achieved >95.0% pixels passing a 4%/4 mm gamma criterion. For the alanine measurements, 94.9% of beams were within the pre-set 5.0% tolerance from the dose predicted by the treatment planning system. Three of these were large deviations of 77.1%, 29.1% and 14.1%, respectively, which were traced to human error associated with carrying out the audit measurements and not affecting patient treatment. Excluding the three measurements outside 10%, the mean difference was 0.05% with a SD of 1.5%. The results of this audit showed that the overall standard of beam modelling and delivery was within national guidelines.

More recently, the second national IMRT audit took place to focus on the development towards rotational IMRT (VMAT and tomotherapy). This was set up as a collaborative project between the NPL, IPEM, the Royal Surrey County Hospital and RTTQA. The involvement of the RTTQA allowed the centres to choose a clinical case for which they wished to use rotational IMRT and to be credentialed for trial recruitment. The audit also developed a novel approach to audit[48] of using an array of ion chambers such that multiple dose points could be measured simultaneously and results could be given during the on-site visit.[49] Point dose differences gave a mean ± SD of 0.1 ± 2.6% and 0.2 ± 2.0% for a specially designed generic test (3D TPS)[47] and the clinical trial plans, respectively. 42 of 43 centres passed their clinical trial plan with >95.0% of the measured points passing 3%/3 mm criteria, suggesting that in the UK, TPS modelling and delivery can achieve high accuracy for rotational IMRT. However, issues were also identified with the lack of couch modelling in some TPS and overall poorer results being obtained in some centres where the planning and delivery systems came from different manufacturers. A statistically significant difference in gamma pass rates was seen between planning systems where rotational IMRT modelling had been designed for the manufacturer's own treatment delivery system and those designed by different manufacturers to be independent of the rotational IMRT delivery equipment.[49]

Other novel techniques which have been recently audited include intraoperative radiotherapy, using compact mobile kilovoltage X-ray sources for the treatment of breast and other cancers. All seven current clinical sites in the UK were audited by a single visiting group and set of measurement equipment.[61] Measurements were performed using an ion chamber, TLDs and radiochromic film, and the mean difference between measured and planned dose across all centres was −3.2 ± 2.7% (one SD). A national dosimetry audit for SABR in the lung has also recently been completed, co-ordinated by the UK SABR Consortium. In 2013, this group set up a dosimetry audit on an anthropomorphic phantom in collaboration with NPL, the Royal Surrey County Hospital and Clatterbridge Cancer Centre, to provide verification of planning and delivery of the high doses delivered in a few fractions required by this technique. This audit has been accepted as a pre-requisite for the just launched Commissioning through Evaluation (CtE) programme for SABR. CtE have also funded a quality assurance programme, which includes a dosimetry audit, to support this programme.

Brachytherapy has been a technique in radiotherapy which in general has had less audit attention paid to it. However, in 2010, a survey of brachytherapy quality control practices was carried out, linked to the introduction of a new code of practice.[63] A review of dosimetric audit in brachytherapy has also recently been presented by Palmer et al,[64] considering eight international dosimetry audits published over the last two decades in HDR brachytherapy.[65–67] The majority of these were concerned with verification of source strength,[65,66,68–72] although Haworth et al[67] had undertaken a pilot end-to-end audit in Australia, performed in a jig for straight catheters designed to deliver a uniform dose to the measurement point. Within the UK, a recent co-ordinated audit approach has brought together three

brachytherapy audits. These include two that are currently ongoing: a well-chamber audit of source–strength and an audit measuring absorbed dose in a geometric phantom for the INTERLACE trial. The third study conducted by Palmer et al[57] *via* a Working Party of the IPEM Radiotherapy Special Interest Group was the first multicentre fully "end-to-end" dosimetry audit for HDR cervix brachytherapy. It used a novel phantom together with film dosimetry audit methods, obtaining dose maps using triple-channel film dosimetry, to compare TPS planned and measured (delivered) dose distributions around clinical treatment applicators. The audit visits also took the opportunity to review local procedures. 46 of the 47 brachytherapy centres in the UK were audited between May 2013 and August 2014. Deviations between plan and measurement were quantified at the standard Manchester Point A and also using gamma analysis. The mean difference between planned and measured dose at Point A was −0.6% for plastic applicators and −3.0% for metal applicators, at standard uncertainty 3.0% (k = 1). Isodose distributions agreed within 1 mm over a dose range of 2–16 Gy. Mean gamma pass rates exceeded 97.0% for plastic and metal applicators at 3% (local)/2 mm criteria.

Meanwhile, there have also been advances in the techniques, which have been identified for audit within the IPEM interdepartmental audit. These now include SABR, flattening filter-free beams, VMAT and also kV and MV imaging.

RECENT DEVELOPMENTS IN AUDIT

Overall, the greater availability of anthropomorphic phantoms has meant that there has been a move towards more end-to-end audit. This allows the testing of the entire radiotherapy chain, as used for a patient treatment, from imaging, planning and quality assurance processes through to treatment delivery. The greater the resemblance of the phantom to the patient in terms of anatomical shape and composition the easier it is to simulate the whole clinical processes. A greater variety of audit approaches has been facilitated by the recent establishment of the IPEM phantom library which offers the opportunity to borrow complex phantoms from lending centres for specific projects or periods of time and thus allows either multiple centres to use the same phantom, or use phantoms to which they otherwise may not have access.

In addition, a greater range of detectors and detector configurations have been used, including alanine detectors, which are particularly suitable for the higher doses used in hypofractionated regimens. IROC and ACDS have recently replaced their TLD programmes with optically stimulated luminescence detectors[72,73] in order to achieve a lower standard uncertainty and therefore the ability to reduce the audit tolerance values. A recent study in the UK has tested out the use of glass beads for remote audit which may be particularly useful for countries that have demanding climates,[74] *e.g.* glass rods are used in some Asian national audit systems.[75] In addition, more recent audits, in particular for more complex techniques, are moving from individual ion chambers to the use of arrays and have shown the ability to measure absolute dose in multiple points, thus testing dose distribution as well.[48,49,76,77]

Greater collaboration between audit groups is also taking place. In December 2013, a meeting was held at the NPL, which brought together the main dosimetry audit groups in the UK and other interested parties. As well as providing a forum to share methodologies and results, this meeting saw an agreement to launch the UK Dosimetry Audit Network (www.uk-dan.co.uk) to create a forum to present and discuss current and future audits, link together the active audit groups and focus on strategies for co-ordination, which exist and can be developed between these groups for a more joined-up approach. The main contributors are currently the NPL, RTTQA and the IPEM interdepartmental audit groups; however, there are also links with other international groups such as the ACDS, TROG, EORTC and IROC. On an international level, the Global Harmonisation Group now meets regularly and several co-ordinated projects have been completed[58,59] or are under way.

LOOKING AHEAD

Intensive dosimetry audit activity is resource expensive, and developments are needed to streamline and find new approaches which are efficient, avoid overlap between different groups and activities, yet focus on the important aspects of the quality assurance processes and which can highlight the issues which have most impact on the clinical outcome for the patient. These could include use or development of new equipment (such as detectors or phantoms), sharing of data and protocols with different groups and reducing the workload both for the centre and the QA group by streamlining the processes.

More and more clinical trials are becoming international, and equipment and techniques in radiotherapy are becoming more homogenized. The UK audit groups need to work with our international partners and maintain and develop world-class audit, which can set and support internationally agreed standards, not only in the UK but also in a range of countries who offer radiotherapy, including those who do not have the same level of resource and infrastructure (*e.g. via* IAEA).

The UK has a strong history of supporting the implementation of new technologies through audit (*e.g.* IMRT, rotational IMRT), and this will need to continue with the implementation of advanced radiotherapy imaging and treatment systems and techniques, such as four-dimensional (4D) radiotherapy (4D CT, PET), increased functional imaging into planning, advanced treatment planning methods and tools, advancing online imaging verification such as 4D cone beam CT, MR linear accelerators or proton-induced PET. There is also an expansion of techniques such as stereotactic radiotherapy, electronic brachytherapy and proton therapy.[78] A significant number of centres will be offering these services, and there will be a requirement to identify and support the standards that can be achieved. Future audits and clinical trials will need to address the new technologies which are on the horizon and develop suitable approaches and measurement techniques.

DISCUSSION

Audit is recognized as having a critical role in the development and safety of radiotherapy.[79] National and large scale audits are able to set standards, as well as maintain and improve those

standards. In UK radiotherapy departments, the significance of dosimetry audit must always be highlighted and the importance should be understood beyond the physics department. It is often conducted by physicists out of hours and on a voluntary basis, which means the value can be unnoticed by funders, whereas in fact the opposite is true in that it is so important that physicists are prepared to give their time to ensure that accidents and errors do not happen. It is helpful that Public Health England now indicate that dosimetry audit [U Findlay, Public Health England, 2015, personal communication] is regarded as one of the key influence factors in the UK radiotherapy safety culture. This may support a change in the perception that audit is sometimes simply fulfilling obligations to provide examples of traceability and audit completed. This change of view has recently been supported by the full funding of a dosimetry audit to support the CtE programme.

However, as a community, we should consider audits at many levels as promoting the best practice and high quality treatment, with tight consistency of dose delivered to individuals across patient populations and centres, as it is essential for clinical trials but is also vital for routine clinical practice. A co-ordinated approach between audit groups will help to streamline the measurements made in each department and roll out national audit protocols to interdepartmental local audit. There are significant benefits to both host and auditor, including peer-to-peer interaction, sharing of best practice, reassurance in methodology and correct implementation of codes of practice. Audit also enables the creation of supporting networks and provides both assistance and confidence in the implementation of new technologies.

Dosimetry audit for advanced techniques can also support implementation and facilitate awareness and understanding of issues which may exist, by benchmarking centres with similar equipment. This can lead to an increased understanding and knowledge of what can be achieved from a particular combination of imaging, planning and delivery equipment. Regular audit at different time points can confirm long-term stability and improvement. It also plays an essential role in risk and safety management. Audit completes the circle in ensuring the correct implementation of traceability from the NPL primary standard to the end user and ultimately to the benefit of the patient.

"The implementation of QA in radiotherapy has become vitally important in recent years. Often, as has been demonstrated here, a clinical trial has led the way to the general benefit of all patients receiving radiotherapy. By pursuing QA in the first year of the clinical trial, the standard of treatment was set and any later uncertainties, when analysing the results, were avoided. Wariness at each centre visited was replaced by active co-operation and satisfaction with the high standards that could be achieved and maintained. In addition, these visits gave an opportunity for mutual exchange of ideas".[22] This was written for clinical trials but holds as well for radiotherapy as a whole.

The UK has a strong history of dosimetry audit, much of which has been undertaken on a voluntary basis because of the belief in its value. Over the last three decades, dosimetry standards, performance and consistency have demonstrably improved, and audit has been one significant factor in this, not only providing a quantitative assessment of progression but also triggering improvement and helping to maintain safety by identifying issues and discrepancies that can then be rectified. Over this period, the complexity of audit has also increased, and there is now a need for more end-to-end audit to incorporate the many-stages and multifaceted approaches of modern radiotherapy. When designing a new audit, the apparent ease and reduced cost of postal audit need to be weighed against the advantages of the increased consistency and precision of on-site methods, the personal contact and opportunity to review local practice and data and the ability to investigate and resolve issues immediately, given by an on-site visit audit.

Dosimetry audits can be used to help assure accuracy of both basic and advanced radiotherapy techniques, determine their benefit to clinical trials and inform the arguments for further national/international audits. Undertaking regular external audit allows centres to demonstrate compliance with national standards, provide assurance that patients are receiving the prescribed dose accurately according to protocol, ensure accurate basic radiation dosimetry and be motivated to modernise and develop techniques. Participating in clinical trials is an effective way in which a centre can access external audit and assure accurate dose delivery.

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