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Current Perspective

Radiotherapy quality assurance: time for everyone to take it seriously

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Abstract

Like high-risk industries, radiotherapy requires intense attention to detail, alertness, precision, and adequate human and material resources to minimise the risk of irreversible consequences. Clinical trials data such as that generated by the Quality Assurance programme of the Radiotherapy Group of the European Organization for Research and Treatment of Cancer (EORTC) in this issue of the Journal have been instrumental in identifying problems with technical quality, the understanding of which can have a direct impact on improving the quality of care in the community. Consistency in absolute dosimetry, dose delivery, volume definition and reproducibility are paramount in radiotherapy quality assurance and have become even more important with the advent of conformal therapy. Extension of these principles to other oncological disciplines has added an additional dimension of improvement. Waiting times and measures of access must also be monitored if overall quality at the population level is to be assessed and enhanced. Lessons should be learned from clinical trials methodology in the use of intervention-specific guidelines, physician education and real time audit of treatment planning decisions. In the future, novel approaches, such as web based systems may further improve education and audit. Wider application and audit of evidence-based management guidelines about the use radiotherapy will bring to standard clinical practice the quality benefits that are considered a basic minimum standard for clinical trials.

Keywords: Quality assurance; Radiotherapy; Treatment planning; Clinical trials; Guidelines

1. Radiotherapy quality assurance in context

The hypothetical flight was to take two hours. In a matter of fact tone the captain announced to the passengers a prediction of safe arrival for everyone of 97% with a further prediction of serious (if not injurious) error of 6.7%. Berwick and Leape challenge whether any of us would stay aboard [1].

The statistics for healthcare differ substantially from the airline industry. While current statistics for the airline industry show dramatically safe rates [1], information for leading hospitals indicates precisely the statistics that were announced by Berwick and Leape's hypothetical captain, and over half the incidents are preventable [2,3]. The airline situation provides a useful analogy with radiotherapy practice. Radiotherapy also serves a sizeable population and there is immense reliance on skill in domains analogous to air traffic control (e.g. medical physicists), technical machine operation (e.g. dosimetrists, radiation therapists), and pilot flight design and assessment (e.g. radiation oncologists and other oncology disciplines). Add the quality of machines, informatics and support systems and we are forced to consider the plight of the pilot required to fly badly designed or maintained aircraft, entering poorly monitored airspace and using inadequate runways in airports lacking appropriate security.

In this issue of the *Journal*, Kouloulias and colleagues provide a powerful dissertation on the process and needs for quality assurance of radiotherapy practice [4,5]. Drawing from a wealth of experience of the Quality Assurance programme of the Radiotherapy Group of the European Organization for Research and Treatment of Cancer (EORTC), they demonstrate a resolute,

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comprehensive, and pragmatic approach to the critical needs of this aspect of the health industry. What can we learn from their experience, and can we challenge their unique system to bring us to another level? For example, a pressing need in the contemporary era of greater sophistication in treatment delivery with intensity modulated radiation therapy (IMRT) and image guided radiotherapy (IGRT) is the provision of additional and different quality assurance procedures.

2. The EORTC quality programme

For more than two decades, the EORTC has attempted to improve the technical quality of radiotherapy delivery in the context of multicentre clinical trials [4,5]. Variations in technical standards among institutions including planning decisions by physicians have been identified and processes have been introduced to deal with these problems. The EORTC quality assurance programme is ground-breaking methodical work built sequentially one step upon its predecessor. Although the initial focus is on clinical trials, Kouloulias and colleagues recognise that there is much in their work that has and will continue to benefit non-trial patients as knowledge gained is applied to the wider oncology community [4].

3. Philosophy of radiotherapy quality assurance

Kouloulias and colleagues' classification of systematic protocol deviation is as informative as it is useful: (1) deviations due to protocol ambiguity; (2) deviations about which an institution may be completely oblivious; (3) deviations related to the inability of an institution to provide a required protocol prescription (e.g. constraints at the technical and resource levels or in skill and knowledge where there is inadequate opportunity and time for professional development). They remind us that the purpose of quality assurance is to improve the quality of clinical practice. The process should be welcomed and above all must not involve aggressive censuring of individuals or institutions [4]. Taking a leaf from the book of the high-risk industries, it is clear that the stunning progress in safety is not related to a climate of fear, reprisal and admonishment. The evidence is that safer care requires safer systems including equipment, work-places, human resources, support systems and a proper organisational structure [1].

4. Scope of quality assurance

When considering the scope of a quality assurance programme, one must decide whether we are interested in: (1) guaranteeing the validity of clinical trial results; (2) minimising the risk of errors in routine practice; or (3) increasing the likelihood of desired health outcomes at the population level [6]. The latter has a much wider scope than pure technical quality and introduces concepts of equality of access, consistency, etc. Ultimately, in varying ways, we should really be interested in all three.

Clinical trials programmes, including trial eligibility, represent pure technical quality assurance and wider issues, such as access to care, are generally not considered. The predominant focus is on the reduction of the number of non-evaluable patients. This is achieved by ensuring the accurate delivery of the treatments under investigation. In this way, the result of the trial properly reflects the relative efficacy of the treatments being compared and any perceived differences between the arms are not obscured by errors in treatment delivery. Obviously at face value this focus is narrow, and there could even be theoretical problems generalising the results of such audit laden activity to the community. None the less, in evaluating the practice of radiation therapy, technical excellence must come first and there is much for the wider community to learn from the clinical trials experience.

5. Variability during radiation treatment

5.1. Dosimetric error

Dosimetric errors may result from uncertainty in primary calibration or relative dosimetry, planning system failure, or treatment unit problems. Early work by the EORTC comparing absorbed dose in a water phantom demonstrated variation between centres for both photon and electron treatments [7]. The EORTC has shown how repeated phantom measurement in the context of trial participation is associated with a reduction in variation of absorbed dose [8]. Extension of this to non-trial patients is equally valid using thermoluminescent dosimetry (TLD) as part of the EQUAL programme [9]. Similar postal TLD programmes are conducted by the International Atomic Energy Authority (IAEA) [10] and an Australian survey has shown good conformality with the IAEA reference dose for most centres [11].

Surveys employing test irradiation of anthropomorphic phantoms can also identify multiple points of error along the planning and delivery chain [12] and have been used to demonstrate areas for technical improvement among multiple centres [13]. In the Trans Tasman Radiation Oncology Group (TROG) [14], a study of 10 centres demonstrated that correct dose delivery to the reference point was usual, but that the treatment technique and beam energy chosen resulted in differences doses to critical organs. Therefore, comparative TLD-based

dosimetry using anthropomorphic phantoms is feasible, and the use of such quality assurance techniques could be useful as IMRT is more widely adopted [14].

5.2. Target uncertainty

Volumetric errors result from poor decisions made during treatment planning, treatment set-up variation, or organ motion during or between fractions. An issue of increasing importance, is the growing body of knowledge concerning inter-fraction iso-centre and target organ movement [15–20]. This uncertainty factor (the fourth 'D' of radiotherapy planning and delivery) is highly relevant with greater selection of target volumes and avoidance of other tissues [21]. The geometry of the target volume will often vary during treatment because of daily set-up variations and patient internal organ movement [22]. Hence, planning target volume modification from accepted standards first requires documentation of the degree of target uncertainty on a centre-by-centre and technique-by-technique basis.

5.3. Practitioner-determined uncertainty

Significant inconsistency in the choice of planning target volume between individuals participating in head and neck cancer trials has been demonstrated by the EORTC dummy runs. A review of the non-trial literature shows that inter- and intrapractitioner difference in volume selection is widespread. A sample of such variation is evident in the planning for cancers of the bladder, oesophagus, prostate, lung, paranasal sinus, in addition to Hodgkin's disease, non-Hodgkin's lymphoma, and brain tumours [23–30]. Clearly, the implications of such variation are potentially serious.

The first step in minimising interphysician variation in clinical trials is the use of a detailed clinical trial protocol, the format of which can be refined and standardised to increase its utility [31]. In addition, the EORTC employs case review and individual feedback. Educational sessions and real time review of trial patients has been shown to achieve increased consistency and compliance [32]. The importance of achieving consistency and accuracy in a clinical trial is not questioned. In non-trial practice, this must surely be of equal or greater importance to population outcomes given the known steepness of tumour control and normal tissue complication probability curves.

A study of non-small cell lung cancer treatment planning by Bowden and colleagues [33] showed that interphysician volume selection variation can be reduced by application of clear planning protocols. Similarly, written treatment policies for radiotherapy of head and neck cancer can dramatically reduce the proportion of cases treated with inadequate radiotherapy coverage [34] and this can be almost entirely eliminated by the use of real-time audit at the time the radiotherapy course commences [35]. Improvement in radiotherapy plan acceptability rates over time emphasises the need to maintain such processes as a component of ongoing quality assurance [35].

Similarly, in a non-clinical trial community oncology setting [36], treatment prescription audits employing protocol-generated checklists showed that approximately 10% of lung cancer and prostate cancer plans were rejected because of target volume coverage problems [36]. Subsequently, at least three-quarters of these rejected plans were modified by the treating physician. In contrast, only 1.4% of breast cancer plans were queried, half of which were subsequently altered. In this way, real-time audits of treatment planning decision-making appears useful and feasible and allows random audits of sites with good compliance (e.g. breast) while continuing to audit the majority of lung and prostate patients. As yet, no formal cost-benefit analysis has been performed on these particular data, although the safety of such a sampling methodology for initial review of clinical trials patients appears to increase cost efficiency without increasing the proportion of protocol violations [37].

Esik and colleagues documented improved practices following bi-monthly common audits of radiotherapy plans within neighbouring departments and recommended that follow-up audits occur. Prerequisites to a successful audit include written treatment policies and involvement and acceptance by staff [38].

Overall, it would seem that increased use of detailed planning protocols within departments, improved physician education by anatomical disease site and radiotherapy technique, and real-time audit of planning decision-making should be considered part of routine practice. Furthermore, the proposal by Kouloulias for web-based radiation treatment planning system offers the potential for novel approaches to education and audit [5].

6. Variation in dose/fractionation

Unjustified variation in prescribing practice implies excessive treatment of some patients and under-treatment of others; it also potentially wastes resources [39]. Despite this, widespread inter- and intradepartmental variation in the choice of dose and fractionation exists [40,41]. In certain circumstances, there may be appropriate reasons for fractionation variation. For example, unreported use of other modalities may be relevant (e.g. concurrent chemotherapy or the use of surgery combined with radiotherapy) and could explain practice variability. Thus, while standard fractionation administered with concurrent chemotherapy is an appropriate strategy in locally advanced head and neck cancer [42],

altered fractionation to augment dose delivery without chemotherapy appears to also be justifiable [43]. However, in the absence of apparent explanations, pure physician-driven variation in dose and fractionation is hard to justify on clinical grounds and is particularly difficult to explain to funding agencies. The responsibility lies with the radiation oncology community to conduct clinical trials to resolve fractionation controversies and in the meantime develop consensus-driven approaches to minimise variation.

7. Regular activities in a radiotherapy department

Weekly clinical review of treatment of patients undergoing radiotherapy may identify aberrant radiotherapy response in normal tissues or evidence from acute radiation responses that the dose is not adequately encompassing the intended target area. Viewing initial patient 'set-ups' on the treatment unit may uncover positional errors (including left/right discrepancies in unilateral treatments), malpositioning of beam modifying accessory devices including tissue isodense bolus material, shielding, missing tissue compensators or wedges. Departmental procedures should be appropriate to resolve problems relating to transcription errors (including writing, reading and interpreting treatment-related prescriptive orders and identifying their authors). There should also be procedures to eliminate problems in radiotherapy planning, such as left/right or other localisation errors in radiologically-defined targets (e.g. adjuvant radiotherapy following complete responses to chemotherapy, where the radiological hallmarks of the tumour may no longer be present). In addition, an efficient no-fault process to handle incident reports relating to identified errors in radiotherapy delivery should be in place.

8. Towards comprehensive quality assurance

Accepted quality improvement standards (e.g. International Standards Organisation (ISO) 9001) and World Health Organization (WHO) standards must include appropriate departmental quality structure and optimal treatment planning and delivery processes and involve quality audits to identify areas needing programme enhancement (see Table 1) [4,44–46]. Vigilance is important in maintaining appropriate licensing credentials for personnel and equipment to observe regulatory standards for the jurisdiction [4,45–47]. The role of quality management also includes all aspects of patients' treatment experience, including both technical and interpersonal facets of care [47]. Kouloulias and colleagues comment on the breadth of a process extending across technical delivery, human resources,

Table 1
Key components of a comprehensive quality programme, adapted from Thwaites and colleagues [44]

- Aim of the organisation
  - What is the target population served?
  - Determine breadth of expertise for the organisation
- Structure of the organisation
  - Designated responsibility for quality
  - Appropriately qualified staff
- Obtaining and maintaining the means of delivering radiotherapy
  - Diagnostic modalities (especially imaging)
  - Simulation (physical or virtual methods)
  - Treatment planning systems
  - Treatment machines (i.e. linear accelerators)
  - Procedures to be undertaken in the event of equipment malfunction
- Process control
  - Adequate data for patient staging and treatment decision-making
  - Treatment protocols (radiotherapy-specific and for overall management)
  - Treatment planning and prescription (unambiguous terminology)
  - Waiting for treatment (monitoring and minimising waiting times)
  - Treatment delivery (i.e. patient positioning, accuracy of set-up, etc.)
  - Treatment verification including portal imaging and/or *in vivo* dosimetry
  - Information flow through the radiotherapy process
  - Audit of process and outcome
- Acquisition and maintenance of knowledge and skill within the organisation
  - Departmental policies on continuing education
  - Availability of resources
- Monitoring of quality system
  - Active management processes in place

and biological principles in the application of radiotherapy. Their attention to interdisciplinary quality is also exemplary and includes more recent requirements for pathology, surgery, and also chemotherapy in their audits [4,48]. The contemporary era of image-guided radiotherapy delivery brings additional need to include imaging modalities, so vital to radiotherapy target definitions, into the quality equation.

9. Access to care

Quality delivery in a radiotherapy programme should also include safeguards that ensure that appropriate patients are offered radiotherapy. This applies both to decision-making for patients who are actually referred to the centre for consultation and to those who are not. Non-referral may be due to ignorance about the role of radiotherapy, contrary views about the benefits of the treatment, or may reflect an absolute lack of resources to provide the service [49,50]. Guidelines at the institutional or community level may improve the consistency of decision-making, especially if this includes audit. Comprehensive QA should include monitoring of waiting times for patients referred to the centre and population-based audits of radiotherapy utilisation rates to capture information about access for the entire community.

10. New challenges

Enhanced computer technology may have changed radiation medicine to a greater degree than virtually any other medical specialty. Unprecedented capability to plan and deliver accurate radiotherapy with exquisite dose conformation to intended targets is now possible. While the capability is dramatic, the change is equally so for practitioners in the field. Methods of planning treatment have altered to an entirely volume based system requiring target volumes and organs at risk to be contoured on thin computed tomography (CT) slices to permit target coverage or avoidance [51]. Precise anatomical knowledge is required, but also measures of uncertainty in treatment delivery [22].

The practitioner has traditionally relied intensely on the portal film for correlation with the intended beam position, shape and intensity determined by conventional physical simulation. This is relatively less important in the IMRT era compared with the other complexities involved (see Table 2). Most radiation oncologists are familiar with the troubling scenario of an incorrectly placed beam-modifying wedge, the traditional modulator of radiation intensity. The challenge has always been to recognise that such a problem even arose, and IMRT depends on processes that are similarly difficult to verify. A detailed discussion of IMRT is not intended here, but some of the outstanding quality assurance issues have recently been discussed [22,52]. Clinical trials groups must continue to develop recommendations for this important new modality in radiotherapy delivery.

In addition, when new techniques or complex interventions are introduced, a learning curve must be recognised. Steps should be taken so those patients are not exposed to risks greater than the norm. There should be formal training followed by a period of supervised practice until competence is achieved [53].

Table 2
Selected problems in IMRT quality assurance

Linear accelerator testing
Multileaf collimation (MLC) function
• Leaf calibration accuracy (leaf gap position at closure)
• Leaf travel during leaf motion in dynamic IMRT
• Gravity influences on leaf function during different gantry positions
• Relative radiation intensity for sliding window (velocity, MUs, various leaf pairings)
Dosimetric verification
• Time-dependent nature of dose requires entire radiation sequence for each verification
• Steep multidirectional dose gradients render dose interpolation very problematic
Treatment planning system commissioning
Determine linear accelerator model parameters used by planning system
• Complex computer distribution optimisation that also accounts for leaf leakage
• Dose (MUs) sequence delivery and leaf sequencing
Assessing agreement between measured versus planned dose distributions
• Testing leaf sequence algorithms and linear accelerator operation
• Multibeam IMRT plan tests in geometric and anthropomorphic phantoms
• Measurements should span target volume and critical structures
Patient treatments
Portal outline visualisation, dose verification, and patient positioning are disconnected
• Inter- and intrafraction motion and uncertainty is only assessed by alignment films
• Internal organ movement and breathing artifact not ideally assessed
• Portal shape correctness assessed with poorly visualised portal images
• No fixed orientation portals available for serial rotational tomotherapy IMRT
• Fluence pattern film visualisation obscures anatomical detail, and is only qualitative
• Direct patient dosimetry limited by anatomical accessibility and steep dose gradients at body surfaces
• Methods remain under exploration for computer-enhanced exit beam dosimetry
Interpretation of sources of error in patient-based QA
• Need for reconciliation of dose differences outside acceptable tolerances
• No consensus on ideal method for multidimensional plans comparisons

For comprehensive discussion, see Ref. [52]. Note: consensus on frequency of testing yet to be completely determined. IMRT, intensity modulated radiotherapy; MU, monitor unit; QA, quality assurance.

11. Conclusions

The rationale for quality assurance in clinical trials is to ensure that eligible cases are evaluable for the trial endpoints (i.e. did the correct patients actually receive the protocol treatments?). Doubts about the precision of treatment delivered in the community, where real time audit may not be the standard of care, raises the question of generalisability of trial results. It would seem preferable that trial outcomes should be transferable to the community by improving the overall quality of treatment that is delivered rather than lowering standards for treatment delivered in research settings. This can be accomplished by applying similar methodology as has been shown to be effective in the context of clinical trials. Ultimately, this would exemplify the frequently claimed benefits of clinical research, which is to improve the care for all patients.

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