Quality Control and Quality Assurance of Radiation Oncology

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ABSTRACT

Radiotherapy (RT) has played important roles in cancer treatment for more than one century. The development of RT techniques allows high-dose irradiation to tumors while reducing the radiation doses delivered to surrounding normal tissues. However, RT is a complex process and involves understanding of the principles of medical physics, radiobiology, radiation safety, dosimetry, radiation treatment planning, simulation and interaction of radiation with other treatment modalities. Each step in the integrated process of RT needs quality control and quality assurance (QA) to prevent errors and to ensure that patients will receive the prescribed treatment correctly. The aim of this study is to help the radiotherapists in identifying a system for QA that balances patient safety and quality with available resources. Recent advances in RT focus on the need for a systematic RTQA program that balances patient safety and quality with available resources. It is necessary to develop more formal error mitigation and process analysis methods, such as failure mode and effect analysis (FMEA), to focus available QA resources optimally on the process components. External audit programs are also effective. Additionally, Clinical trial QA has a significant role in enhancing the quality of care. The International Atomic Energy Agency (IAEA) has operated both an on-site and off-site postal dosimetry audit to improve practice and to assure the dose from RT equipment. Both postal dosimetry audit and clinical trial RTQA, especially for advanced technologies, in collaboration with global networks, will serve to enhance patient safety and quality of care.

Keywords: radiation therapy, quality assurance & control, dosimetry & clinical audit, clinical trials

INTRODUCTION

Radiotherapy (RT) is one of the major options in cancer treatment. As a multimodality treatment combined with surgery and/or chemotherapy, it plays an important role in curing cancers. RT is also a very effective treatment option for palliation and symptom control in advanced or recurrent cancers (1). The process of RT is complex and involves understanding of the principles of medical physics, radiobiology, radiation safety, dosimetry, RT planning, simulation and interaction of RT with other treatment modalities. Professional teams for RT includes radiation oncologists, medical physicists, radiation technologists and radiation nurses. These professionals work through an integrated process to plan and deliver RT to cancer patients. Each step of a sequential process needs quality control (QC) and quality assurance (QA) to prevent errors and to ensure that patient will receive the prescribed treatment correctly (2). The confirmation comes from periodic and systematic audits; however, the first step towards quality in RT is good management and planning from the
beginning, through appropriately selected professionals, equipment and procedures. The likelihood of errors in radiotherapy increases with the increasing complexity of new techniques, in addition to the automation of many procedures and the demand for better local disease control with minimal toxicity through accurate targeting of tumors. Nevertheless, errors do happen even under the best circumstances, so there is a need for inspection of every step of the radiotherapy process, as can be achieved with QC, which can trigger the necessary corrective action, before errors have an impact on patient care. Finally, success of this effort as a whole needs to be re-evaluated and modified when necessary, so as to further decrease the likelihood of error in the future (quality improvement)\(^3\).

**Steps of Sequential Process of RT**

1) Assessment of patients, 2) Decision to treat, 3) Prescribing treatment protocol, 4) Immobilization and positioning, 5) Simulation, imaging and volume determination, 6) Planning, 7) Treatment information transfer, 8) Patient set-up, treatment delivery, 9) Treatment verification and monitoring \(^4\).

Because RT involves many processes from the moment at which RT is determined to be the appropriate treatment, accurate and efficient QC programs are necessary for all the individual processes. Increases in one-time doses per se mean increases in risks and this also necessitates a finer and more accurate QA. Accurate prediction and measurement of radiation doses administered to human bodies without errors is a foundation of all radiotherapies. Accurate prediction of radiation doses in minute areas is the basis of safer implementation of high-precision RT. Furthermore, the accuracy of the position of RT and the accuracy of dose prediction in organs moving due to breathing are extremely important information in actual treatment, and doctors can implement RT more confidently based on the information\(^4\).

**Development of QA Techniques and Programs**

RT for cancer patients is a complicated process that involves many stages. Quality assurance (QA) aims to check the entire process carefully, preventing or minimizing errors that may occur, and effectively improving treatments. When a patient has decided to receive RT, therapy is planned according to the doctor’s prescriptions to obtain optimum RT dose distributions. Immediately before the RT and during the RT, there are processes to check whether the RT is implemented properly. In particular, with the development of RT techniques, normal tissues are exposed to relatively less radiation so that gradually higher-dose radiation can be delivered to tumors. This can be to the extent that a one-time dose prescribed for tumors exceeds 20 Gy in some cases. Increases in one-time doses per se mean increases in risks and this also necessitates of finer and more accurate QA. If not supported by strict controls, RT cannot be implemented safely and accurately no matter how much it is technologically developed \(^4\). It has been suggested in several studies and reviews that the systematic implementation of a QA program in radiotherapy contributes to the prevention of systematic errors and the reduction of the frequency and severity of random errors. The first QA programs focused on dosimetry and the validation of the proper function of the mechanical and electrical parameters of the equipment. Then, they gradually expanded to include treatment planning processes, patient set-up immobilization and treatment implementation. Lately, the scope of a QA program in radiotherapy has expanded to include the radiotherapy process as a whole, from the decision to treat a patient, to follow up. Moreover, parameters such as staffing and organizing a radiotherapy department, including the necessary expertise and continuous training of the personnel, can be determined by a QA program in radiotherapy \(^3\).

The goal of an RTQA program is to deliver the best and safest RT to each patient to achieve cure or palliation. The quality of RT has been defined as the totality of features or characteristics of the RT service that bear on its ability to satisfy the stated or implied goal of effective patient care. The integrated nature of QA in RT makes it impossible to consider QA as limited to simply checking
machine output or calibrating brachytherapy sources. QA activities cover a very broad range of areas in which the actions of radiation oncologists, radiation technologists, dosimetrists, accelerator engineers and medical physicists are important. With the increase of the complexity of the equipment and processes required to deliver modern RT, the activities required to maintain and enhance quality are consuming even more resources, and we need to re-examine the amount and distribution of resources committed to QA. In particular, we need to link QA activities to the expected benefit to the patient. In addition to re-examining current practice, the rapid introduction of new advanced technologies poses other challenges. The current process of developing consensus recommendations for prescriptive QA activities remains valid for many of the devices and software systems used in modern RT; however, for some technologies, QA guidance is incomplete or out of date. The formulation of QA guidance lags far behind the penetration of IMRT and IGRT into the community, leaving physicists and radiation oncologists without a clear strategy to maintain the quality and safety of treatment. In addition to leaving practitioners and patients at greater risk of catastrophic delivery errors, data from phantom testing have suggested that the quality of IMRT delivery has been much poorer than that expected\(^5\). In such situations, physicists will be best served by guidance on how to approach the development of a QM system. Even before the availability of advanced technologies such as IMRT and IGRT, it was clear that the treatment preparation and the delivery equipment had such a wide range of possible configurations that both commissioning and routine QA activities could do no more than sampling the performance of the equipment under selected conditions. There is a need to re-examine objectively those selected conditions and confirm that they are the most critical for modern RT\(^6\).\(^7\).

RT QA is basically divided into periodic QA and patient-specific QA. Periodic QA consists of machine QA, dose QA, and image QA for treatment equipment. This includes QA for the therapy planning system that establishes RT plans, treatment information systems, treatment equipment, and measuring instruments. There is also QA for the process through which individual devices are combined to actually deliver radiation. For such complicated QA, many recognized institutions such as the American Association of Physicists in Medicine (AAPM), the American Society of Radiation Oncology (ASRO), the International Commission of Radiation Units & Measurements (ICRU), the International Atomic Energy Agency (IAEA), the American College of Radiology (ACR), and the European Society of Therapeutic Radiation Oncology (ESTRO) provide efficient and safe quality control protocols\(^8\)\(^-\)\(^12\).

Periodic QA can be generally divided into daily, monthly, and yearly QA. Daily QA mainly consists of tests of elements that seriously affect patients’ setups and individual beam ports’ aiming, equipment doses, and basic safety devices. This QA is intended to prevent serious errors from occurring in patients due to wrong treatment procedures. Monthly QA measures detailed areas that may become problems through gradual accumulations of errors over approximately one month, based on the premise that daily QA of equipment is implemented properly and controls for factors that cause systematic errors in many patients, although not revealed easily such as beam uniformity. Yearly QA conducts measurements comparable to receiving inspections conducted when equipment is introduced, and careful inspections of equipment to check conformity with the therapy planning system. According to the results, there may be a need to implement maintenance of modeling in the QA or therapy planning system. Ideally, all measurements should be conducted at the level of yearly QA, but this will cause problems in time and labor power due to precise measurement. Accordingly, combinations of the most ideal frequencies for the maintenance of treatment equipment and measuring methods that fit the frequencies are recommended in the form of QA at different frequencies to enable finding the balance between costs and efficiency\(^13\). Patient-specific QA means the process to check whether the actual radiation delivered is the same as the treatment plan for each patient, through therapy planning and radiation processes that are the same as those for the actual patient but implemented on a human body model phantom before treating the patient. In the newest cutting-edge treatment methods in which the operation of mechanical devices for radiation, irradiation is
complicated and exquisite, target volumes and normal tissues are close to each other, changes in doses are large in boundaries, or one-time delivery doses are larger than normal fractional doses. To implement these processes in all patients, numerous manpower resources and time are necessary and investments in this manpower, equipment, and time leads to patients’ safety and accurate RT. In the case of high-precision treatments such as intensity modulated RT and stereotactic body radiation surgery, patient-specific QA needs to be implemented in all patients. Recently, surpassing the basic QA in RT processes, individual QA has been implemented for the safety of treatments of individual patients. This QA can be divided into pre-treatment QA that is implemented as end-to-end tests of treatment processes before patient specific treatment, and in-vivo measurements to evaluate accuracy in the process of actual treatment. This QA is intended to secure the safety of treatments of individual patients, recognizing the limitations of the hardware and software that predict doses actually delivered to patients, and considering human factors that may occur.

ISO 9001 in Radiotherapy

Both ESTRO and EORTC have published papers and guidelines for quality assurance in radiotherapy and in clinical trials, involving dosimetry, treatment planning evaluation, treatment volumes delineation, infrastructure, staffing and organization standards for radiotherapy departments. In order to evaluate the organization and the services provided by a radiotherapy department, the PACE Foundation criteria can be used, which are based on ISO 9001 standards and adjusted for use in health services. Both PACE criteria and ISO 9001 describe what needs to be assessed rather than suggesting ways of organization, they tend to be less detailed and more flexible. PACE criteria refer to the processes within a department as a whole and in relation to other departments. Input for PACE model are the patients referred to radiotherapy and output are considered to be the patients discharged having completed treatment. The output, which is the result of the processes within the system, can be considered successful or of good quality if the following prerequisites are met:

1) Departmental policy: it is the responsibility of the Head of the department to describe the vision and the aim for the implementation of a QA program and to ensure that the procedures run smoothly. All the hierarchical connections and the links between the processes must be clearly defined.
2. Equipment: detailed records of the processes involving equipment commissioning and maintenance must be kept.
3. Knowledge, experience, specialization: continuing professional development of personnel (skills and qualifications) is the responsibility of the Head of the department.
4. Control of processes: protocols that describe all the processes from patient referral to discharge and follow up are particularly useful.
5. Quality control: an internal process of quality control needs to be designed in order to ensure continuous evaluation of the QA effectiveness, so as to be updated when needed.

Fig. (1): Quality assurance model based on PACE criteria.
Quality Control and Continuous Improvement

Through systematic evaluation, a radiotherapy department can examine to which extent the processes meet both the internal and external demands for quality and ensure continuous improvement. Internal evaluation of processes and quality control of the department’s suppliers enable the management:

a) To perceive emerging problems before they become urgent. b) To pinpoint errors, bottlenecks that hinder the flow of a process, so as to be dealt with instantly. c) To assess the effectiveness of quality controls \(^{1}(3)\).

**Quality control of suppliers:** ensures that the internal processes of the department’s suppliers meet predefined quality standards. They are usually yearly and when deviations are noted, compliance can be requested. **Internal audit:** refers to both preventive and corrective actions. It is a snapshot of the departments’ performance and can detect deviations from the targets so as to trigger corrective actions to eliminate problems\(^{1}(3)\). Elements that need to be addressed are:

a) Clear definition of processes and evaluation criteria. b) Record keeping of progress in time by registering prior inspections, interventions and their results. c) Ways of early error detection, effectiveness of quality control (percentage of errors detected), responsiveness (how soon they are corrected). d) Defining the type of feedback that the personnel needs.

Success of a QA program is based on the automation of the following steps, which are considered to be key elements of successful internal and external quality control and form the cycle of continuous improvement, through re-evaluation and feedback (Figures 2 & 3). Moreover, Table (1) illustrates the 7 basic quality measurement tools in summary\(^{3}\).

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[Fig. (2): The cycle of continuous improvement \(^{3}\)](image)

[Fig. (3): The quality Management circle \(^{19}\)](image)
Table (1): Seven basic quality measurement tools.

<table>
<thead>
<tr>
<th>Tool</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause-and-effect diagram (fishbone diagram/Ishikawa diagram)</td>
<td>Identifies many possible causes of a problem</td>
</tr>
<tr>
<td>Check sheet</td>
<td>Data collection form for the frequency of certain events</td>
</tr>
<tr>
<td>Control chart (process behavior chart)</td>
<td>To quantify and predict the outcome of a process</td>
</tr>
<tr>
<td>Histogram</td>
<td>Recording and schematic depiction of the distribution of data</td>
</tr>
<tr>
<td>Pareto chart</td>
<td>Data analysis to illustrate the most important events</td>
</tr>
<tr>
<td>Scatter chart</td>
<td>Schematic method for determining the correlation between two variables</td>
</tr>
<tr>
<td>Stratification</td>
<td>Categorizes data in order to highlight the situation of a substrate (alternatively used flowchart)</td>
</tr>
</tbody>
</table>

New Paradigm for RTQA

It is important to evaluate more formal error mitigation and process analysis methods of industrial engineering, such as aircraft accident analysis \(^{(20)}\), to focus available QA resources more optimally on process components that have a significant likelihood of compromising patient safety or treatment outcomes. The new possible approach is based on designing a framework for QM activities with the maximal impact being achieved when resource allocation reflects both the probability of an event and the severity should it occur. This requires quantitative knowledge of both probability and severity. To understand the new approach, new concepts, failure mode and effect analysis (FMEA) need to be understood \(^{(21)}\). This is a systematic method for documenting potential failure modes, determining effects, identifying causes of failures, developing plans, team concurrence and taking action.

For each potential cause of failure, values are assigned in three categories:

- O, the probability that a specific cause will result in a failure mode;
- S, the severity of the effects resulting from a specific failure mode should it go undetected throughout the treatment; and
- D, the probability that the failure mode resulting from the specific cause will go undetected.

Convention uses numbers between 1 and 10. The product of these three indices forms the risk probability number (RPN \(= O \times S \times D\)). When designing a QM program based on the RPN values, resources should be allocated to failure modes with higher RPN values. TG 100 of the AAPM is now working to develop a consistent set of values for O, S and D, and a consistent set of terminology for describing the potential causes of failure and potential effects of failure. TG 100 also suggests that this approach could be a useful framework for the objective analysis of myriad emerging technologies. Adoption of a standard approach to QM would have clear advantages in developing new recommendations efficiently \(^{(1)}\).

Additionally, the WHO program "World Alliance for Patient Safety" has taken an initiative to address high-risk areas in the RT process of care, complementary to the International Atomic Energy Agency (IAEA)-developed safety measures and other previously developed standards, to address non-equipment, non-system faults associated with RT delivery. An expert group facilitated by the World Alliance for Patient Safety is in the process of developing a guide to identify high-risk practices in RT and to suggest specifically targeted interventions to improve patient safety. A literature review showed that, in the last three decades (1976–2007), .1700 patients were affected and ~2% of patients were
reported to have died due to radiation overdose toxicity in middle- and high-income countries, in the USA, Latin America, Europe and Asia. Most incidents (~98%) were reported to have occurred in the planning stage during the introduction of new systems and/or equipment. Of all incidents without any known adverse events to patients, 7% were related to the planning stage; 39% were related to information transfer and 19% to the treatment delivery stage. The remaining 35% of incidents occurred in the categories of prescription, simulation, patient positioning or in a combination of multiple stages (personal communication). The report will be published in the near future and will be useful to develop process-oriented RTQA programs(1).

External Peer Review Audit

External audit programs for RTQA can serve to improve patient safety and quality of care. The international basic safety standards(21) require radiation centers to establish comprehensive QA programs for medical exposure, including external auditing for RT. Both regulatory authorities and professional societies have responded, producing similar end products. The Council Directive of the European Community 97/43/European Atomic Energy Community strengthened the need for clinical auditing in Europe. The regulatory authority of Finland(23-24) is pursuing a program to implement the European Union directive in all areas of radiation medicine. Norway’s Radiation Protection Authority(25) has reported that 'Clinical audit/review involves mutual learning wherein colleagues evaluate completed work from the perspective of good clinical practice. This is essentially different from an authority’s regulatory inspection where practice/activities are evaluated against laws and regulations. The ESTRO has initiated a process to define comprehensive auditing(26). In all cases, the auditing team is composed of professionals; physician, medical physicist and radiation technologist. The IAEA also introduced its QA Team for Radiation Oncology (QUATRO)(27). The objective of QUATRO auditing is to review and evaluate the quality of the practice of RT at a cancer center to define how to improve the practice to the best. A guideline document(28) has defined how to conduct the audit. The IAEA has organized several workshops to train QUATRO auditors, and 17 missions were completed as of November 2006 in Europe and Asia. Individual RT centers received recommendations on quality improvement. In eastern European countries, most audited centers operate at a level requiring only minor improvements, except for the general shortage of well-qualified radiation technologists. Two centers were identified as operating at an internationally accepted level(29). Some countries, such as the Czech Republic(30), have adapted the QUATRO approach for national clinical auditing. In Asia, existing structural inadequacies were addressed. In addition to an on-site audit, an off-site audit, such as a postal dosimetry audit program, is necessary to assure the dose from RT equipment. For more than three decades, the IAEA has operated a postal thermoluminescent dosimetry (TLD) dose-auditing program(31) for more than 1600 RT institutions in 120 countries. A global and steady improvement in the performance of dosimetry audits has been occurring so that ~95% of the participating institutions are within the 5% acceptance limit for beam calibration. Several countries have adopted the IAEA’s method to establish their own national auditing networks(32-34). In Japan, a similar postal dosimetry audit program using a glass dosimeter was started on November 2007(35-36). Further development is being considered to check not only the reference condition, i.e. beam calibration, but also non-reference conditions, such as irregularly shaped and wedged beams(1).

Recently, RT has undergone great development mechanically and systematically as compared to the past, leading to an improvement in the accuracy of RT and decreasing in the frequency of mechanical or human mistakes or errors. The newest RT equipment has been changed to be excellent in stability and accurate in the delivery of prescribed radiation doses. However, although the stability of the equipment has become excellent as such, and system errors are decreasing, ironically, RT QA is becoming more complicated, more time-consuming, and more difficult. This is because, although the overall stability improved with the introduction of computer systems, highly severe errors appear in forms that cannot be easily detected in complicated detailed processes(4). In 2010, some studies
reported intensity modulated RT and other RT related accidents. These articles comprehensively addressed human mistakes, machine failure, and software problems that lead to so-called catastrophic failure and mentioning the risk of RT that is not properly controlled. As a result, changes in the paradigm of advanced cutting-edge RT QA were needed. Accordingly, surpassing the existing quality control of related hardware and software, recent QA programs require the construction of QA systems based on actual risks in treatment through analysis of failure modes in the entire process. Major methods include Failure Mode Effectiveness Analysis (FMEA). FMEA analyzes the processes of RT, defining possible “Risks” by stage, and analyzing the probability for the risks to lead to failure modes (Occurrences), the severity of the failure modes, and the ease of detecting the risks through quantitative methods to configure radiation treatment safety.

Systematic RTQA programs have been coming to the fore recently. These programs are intended to adjust the efficiency and safety of RT to achieve balance through treatment process analysis methods such as FMEA, using resources available in each process of treatment. It also, intended to control failure modes occurring in complicated processes most effectively, even with the restrictions on funds and resources, through systematic and appropriate approaches designed by expert groups. RT and quality control will undergo processes to be continuously developed so that accurate radiation doses prescribed can be delivered to tumors and less radiation can be delivered to surrounding normal tissues. Recently, various clinical studies have been actively conducted as domestic multicenter studies or through participation in international clinical studies. In these cases, if RT is included in the clinical study protocols, the RT should be managed by each institution that conducts the study using domestically/internationally unified protocols and quality control programs. In international clinical studies, in the USA, RT quality control is conducted by an institution named Imaging and Radiation Oncology Core (IROC, formerly the Radiation Physics Center (RPC)). General verification procedures are implemented up to 3D-CRT and in the case of IMRT, Site Specific QA under a concept similar to Patient Specific QA is added. In Europe, RT quality control is managed by an institution named Equal Estro, and in Korea, the Korea Food and Drugs Administration is in charge of RT quality control.

Clinical Trial QA

In the USA, RTQA programs have been developed mainly through clinical trial QA. The Radiological Physics Center (RPC) has been funded by the National Cancer Institute (NCI) continually since 1968 to provide quality auditing of dosimetry practices at institutions participating in NCI cooperative clinical trials. The primary responsibility of the RPC is to assure the NCI and the cooperative clinical trial groups that all participating institutions have the equipment, personnel and procedures necessary to administer radiation doses that are clinically comparable and consistent. The monitoring tools used include on-site dosimetry reviews; remote auditing tools, including TLD and anthropomorphic phantoms; and reviews of both benchmark and actual protocol patient treatments. As of 2007, the RPC monitors nearly 1500 RT institutions. Discrepancies detected by the RPC are investigated to help the institution to resolve them. The RPC overall RTQA program has an impact not only on the treatment received by patients enrolled in clinical trials, but also on the quality of treatment administered to all patients treated at the institution. The NCI-sponsored Advanced Technology QA Consortium (ATC), which consists of the Image-Guided Therapy QA Center (ITC), Radiation Therapy Oncology Group (RTOG), RPC, QA Review Center (QARC) and Resource Center for Emerging Technologies, has pioneered the development of an infrastructure and QA method for advanced technology clinical trials that requires volumetric digital data submission of a protocol patient’s treatment plan and verification data. In particular, the ITC has nearly 15 years’ experience in facilitating the QA review for RTOG advanced technology clinical trials. This QA process includes: (i) a data integrity review for completeness of protocol-required elements, the format of data, and possible data corruption, and recalculation of dose–volume histograms, (ii) a review of compliance with target volume and organ-at-risk contours by study chairs and (iii) a review of dose
prescription and dose heterogeneity compliance by the RTOG Headquarters Dosimetry Group. They also require institutions to obtain credentials before participating in clinical trials. The concepts pioneered by the ITC and RTOG include:

(i) a facility questionnaire that documents the institution’s technical capabilities and identifies the critical treatment team individuals and (ii) a series of tests that are protocol modality-specific, including an electronic data submission test and a dry-run test, to demonstrate understanding of the protocol planning and data submission requirements. New modalities such as IMRT and Stereotactic Body Radiation Therapy (SBRT) require additional credential tests. The RPC developed a postal anthropomorphic phantom (Fig. 4) that contains dosimeters to test the delivery capabilities of the institutions’ IMRT systems\(^{(41)}\) and a localization credential test has been implemented for SBRT protocols to test the reproducibility of the patient setup\(^{(42)}\).

![Fig(4): The Radiological Physics Center postal anthropomorphic phantom.](image)

The primary goal of credentials is to reduce the deviation rate for data submitted to clinical trials. Cooperative groups have experienced deviation rates that sometimes amount to as much as 17% of the cases submitted, according to a study conducted by the RPC\(^{(43)}\). An elevated number of deviations reduces the quality of the study, and increased rates of major deviations may limit accrual to the trial. Credentialing evaluations result in feedback to the institution, to explain the results of the procedure and to give suggestions to improve those results in the future. Three protocols for which credentialing was required from all participants had rates of deviation between 0 and 4%, whereas two protocols that had limited credential requirements had rates of deviation of the order of 7–17%\(^{(43,44)}\). These activities have also been adopted in Europe and Japan. As early as in 1982, the European Organization for Research and Treatment of Cancer RT Group (EORTC) established RTQA programs. In the course of 25 years, QA procedures have become a vast and important part of the activities of the group. The radiation dosimetry QA program demonstrated the disappearance of large deviations of photon and electron beam calibrations after two successive audits\(^{(45)}\). This methodology has now become a standard procedure in RT routine practice in Europe. In Japan, following the results of a phase III trial that revealed poor protocol compliance (40%), the Japan Clinical Oncology Group(JCOG) started clinical trial RTQA programs in 2002\(^{(46,47)}\). The QA scores of the first trial (JCOG 0202) that required on-going RTQA have been reported recently and showed good protocol compliance\(^{(48)}\). The JCOG is also collaborating with the ATC and EORTC to establish a global standard in advanced technology clinical trial QA. A phase II SBRT trial for stage I non-small cell lung cancer (JCOG0403) is supported by the ATC\(^{(49)}\) and individual case reviews are being performed using a web-based remote review tool (Fig. 5).
Quality Assurance Review

For initial QA review, copies of pre-treatment diagnostic chest X-ray and CT, simulation and portal films, worksheets for monitor unit calculation of the prescribed dose, and RT charts with the record of the irradiated time were collected. Information on the initial RT plan was required to be sent to the QA review center within 7 days after the start of RT. Information on the total course of RT, including the boost treatment plan, was required to be sent within 30 days after completion of RT. These were reviewed periodically at least twice a month by the RT principal investigator (S.I.), and also by an independent radiation oncologist (N.S.) after patient accrual. RT QA for prophylactic cranial irradiation was not performed. After the review of the initial RT plan, the RT principal investigator sent each institution a letter reporting whether they had complied with the treatment protocol as well as an inquiry about QA documentation when necessary (Figure 6). Progress remarks and problems were reported at periodical meetings for investigators.

Fig. (6): Flow of QA review. After the QA review, feedback was given to the institutions. Treatment planning was modified when possible.

To assess protocol compliance for RT, the following parameters were reviewed: the dose and field border placement for PTV (adequacy of margins for GTV and ENI), doses to organs at risk, such as the spinal cord and the normal lung, overall treatment time, inter-fraction interval, and dose calculation without heterogeneity correction. The QA assessment was given as per protocol (PP), deviation acceptable (DA), violation unacceptable (VU), and incomplete/not evaluable (I/NE). The criteria were set for each parameter as follows. For the dose and field coverage of GTV, VU was defined as a dose less than 40.5 Gy, more than 49.5 Gy, or the distance between the field edge of the blocks or multi-leaf collimators and the rim of GTV less than 1 cm or more than 3.5 cm. For the dose and field coverage of ENI, a dose less than 27 Gy, more than 36 Gy or inclusion of the contralateral hilum was judged as VU. If heterogeneity correction was used for dose calculation and the recalculated uncorrected dose deviated more than 10%, it was judged as VU. Other criteria for the QA assessment are listed in Table 2. These criteria were arbitrary rather than based on the literature. We set these criteria based on the patterns of practice in Japan at the start of this trial. After parameter compliance was assessed, overall RT compliance was determined as PP overall, no DA or VU in any parameter; VU overall, at least one VU in any parameter; or DA overall, neither PP nor VU. The proportion of 2-D X-ray simulation vs. 3-D CT simulation was analyzed, and a comparison was also made between compliance in the first half vs. the second.
Table (2): Criteria for QA Scores\(^{(48)}\).

<table>
<thead>
<tr>
<th></th>
<th>PP</th>
<th>DA</th>
<th>VU</th>
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<tbody>
<tr>
<td><strong>GTV</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>distance to field</td>
<td>1 – 3.5 cm</td>
<td>NA</td>
<td>&lt; 1 cm or &gt; 3.5 cm</td>
</tr>
<tr>
<td>borders</td>
<td></td>
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<td></td>
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<tr>
<td>prescribed dose</td>
<td>45 Gy</td>
<td>Neither PP nor VU</td>
<td>&lt; 40.5 Gy or &gt; 49.5 Gy</td>
</tr>
<tr>
<td><strong>ENI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>distance to field</td>
<td>1 – 3.5 cm</td>
<td>Neither PP nor VU</td>
<td>contralateral hilum included</td>
</tr>
<tr>
<td>borders</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>prescribed dose</td>
<td>27 – 36 Gy</td>
<td>NA</td>
<td>&lt; 27 Gy or &gt; 36 Gy</td>
</tr>
<tr>
<td>Overall treatment</td>
<td>21 – 42 days</td>
<td>NA</td>
<td>&gt; 42 days</td>
</tr>
<tr>
<td>time</td>
<td></td>
<td></td>
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<tr>
<td>Interfraction interval</td>
<td>≥ 5.5 hrs</td>
<td>4 – 5.5 hrs or &lt; 4 hrs (once)</td>
<td>&lt; 4 hrs more than once</td>
</tr>
<tr>
<td><strong>Organs at risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal cord</td>
<td>≤ 36 Gy</td>
<td>Neither PP nor VU</td>
<td>&gt; 39 Gy</td>
</tr>
<tr>
<td>Lung</td>
<td>- ≤ 1/2 ipsilateral hemithorax</td>
<td>Neither PP nor VU</td>
<td>-&gt; 1/2 ipsilateral hemithorax</td>
</tr>
<tr>
<td></td>
<td>-(≤ 2/3, upper lobe tumor) or V(_{20}) ≤ 35%</td>
<td></td>
<td>- (&gt; 2/3, upper lobe tumor) or V(_{20}) &gt; 40%</td>
</tr>
<tr>
<td>Heterogeneity</td>
<td>No</td>
<td>Yes (≤ 10% total dose difference)</td>
<td>Yes (&gt; 10% total dose difference)</td>
</tr>
<tr>
<td>correction</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: PP, per protocol; DA, deviation acceptable; VU, violation unacceptable; GTV, gross tumor volume; ENI, elective nodal irradiation; NA, not applicable; hrs, hours; V\(_{20}\), percentage of the total lung minus PTV receiving ≥ 20 Gy

Management Commitment

The head of the NMS expresses commitment to the development, implementation and improvement of the QM system by:

- Establishing a quality policy;
- Ensuring that quality objectives are defined;
- Communicating with NMS staff members on the importance of meeting customer needs as well as statutory and regulatory requirements;
- Planning and properly managing resources;
- Conducting management reviews\(^{(50)}\).

Quality Management Systems in Nuclear Medicine

The adoption of a quality management system (QMS) should be a strategic decision of an NMS. The design and implementation of an NM QMS is influenced by various needs and constraints, particular objectives, the nature of services provided, the processes employed and the size and structure of the NMS. An NMS should implement, document and maintain a QMS. Its effectiveness should be continuously improved in accordance with the requirements of professional, regulatory, standardization or accrediting bodies. A QMS aims to enable the NMS to achieve the expectations set forth in its quality policy and to satisfy its customers\(^{(50)}\).

The QMS documentation of an NMS typically includes:

- Documentation of a quality policy and quality objectives;
- A quality manual;
• Written standard operating procedures (SOPs) for primary (diagnosis and therapy) management and supporting processes (see Fig. 7);
• External/reference documents;
• Records of indicators and parameters.

The QMS standardizes the processes to guarantee consistency in providing high level services to patients, referring physicians and other stakeholders in a safe environment. The NMS management ensures the availability of necessary resources and information to support the operation and for monitoring of processes. The management also ensures the effectiveness of the QMS through self-assessments, data analysis, verification of activities and management reviews.

Fig. (7): Example of a process map for a nuclear medicine service, showing the primary, management and support processes (adapted with permission from the Committee for Accreditation of Nuclear Medicine Department of the European Association of Nuclear Medicine). PAC: picture archiving and communication.

Objective of the Quality Management Audit and Composition of the Audit Team

The objective of audits is to review and evaluate the quality of all elements involved in the different processes, such as staff and their professional competence, equipment and procedures, patient protection and safety, and the overall performance of the NMS as well as its interaction with external services. Audits assist NMSs in maintaining and improving the quality of service for patients, referring physicians and other stakeholders. A multidisciplinary team, including experienced NM physicians, medical physicists, radiopharmacists and NM technologists / radiographers, should carry out internal and external audits. If appropriate, other professionals such as quality experts, administrators or nurses might join the team. In some instances, a laboratory service specialist in radioimmunoassay may be needed to provide additional support. The final composition of the audit team should be communicated to the staff before the actual audit. A similar team may also be required for follow-up. The IAEA recommends using the present publication as a tool to carry out self-assessments (internal audits) with the intention of applying good clinical practice and to identify opportunities for improvement.

CONCLUSION

RT has played important roles in cancer treatment for more than one century. The development of RT has allowed for irradiating tumors with higher doses while continuously reducing the radiation doses delivered to surrounding normal tissues. As RT has become more complicated and finer, precise QA is necessary in all procedures from the beginning to the end of RT for accurate
aiming and the administration of accurate radiation doses. Although errors were maximally reduced through periodic QA of equipment or systems in the past, recently, an age has come in which RT is implemented while verifying doses according to therapy plans for individual patients. Recent advances in RT focus on the need for a systematic RTQA program that balances patient safety and quality with available resources. It is necessary to develop more formal error mitigation and process analysis methods such as FMEA to focus available QA resources more optimally on process components to avoid catastrophic delivery errors. External audit programs for RTQA are also effective. The Advanced Technology Consortium has pioneered the development of an infrastructure and QA method for advanced technology clinical trials, including credentialing and individual case review. These activities have an impact not only on the treatment received by patients enrolled in clinical trials, but also on the quality of treatment administered to all patients treated in each institution.

REFERENCE


(36) Cancer Control and Information Services, National Cancer Center. Remote and on-site radiotherapy audit program.(2008) Available at: http://www.ncc.go.jp/jp/cis/divisions/01clinical/cclinicaltest05_en.html.


