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FACULTY OF SCIENCE

**DEVELOPMENT OF A DOSIMETRY AUDIT
METHODOLOGY FOR ADVANCED RADIOTHERAPY.**

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Declaration

I declare that this thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

The waiver of ethics clearance was obtained on 16 October 2017 with Ref: W-CJ-171016-2 from the University of the Witwatersrand Human Research Ethics Committee (see appendix A).



(Signature of candidate)

22nd day of March of 2023 at Pretoria

Abstract

Radiotherapy treatment technologies are advancing rapidly and this necessitates the establishment of new dosimetry audit methodologies for quality improvements. The International Atomic Energy Agency / World Health Organization introduced a postal dosimetry audit service for high energy photon beams in reference conditions in 1969 using thermoluminescent dosimetry. Together with other dosimetry audit networks including Imaging and Radiation Oncology Core Houston, more complex methodologies to audit a range of radiotherapy activities have been developed over the years. Most routine audits are carried out for high energy photon reference beam output only, owing to the coverage and resources needed. End-to-end dosimetry audits include the entire radiotherapy process associated with a particular technique. This study focuses on the development of a remote end-to-end audit methodology using ionization chamber and radiophotoluminescent glass dosimeters, for complex radiotherapy treatments and requires participation of the entire radiotherapy team.

The methodology that was developed uses a head and neck phantom (with inserts for an ionization chamber or solid-state dosimeters) that was scanned, planned and treated in accordance with a given patient histology and treatment prescription based on a typical diagnosis. Five clinical teams were requested to use their local scanning protocol, delineate target volumes and other organs at risk associated with the treatment site using the local clinical and margin protocols, and then prepare a treatment plan. After treatment planning, local quality control checks and final plan approval were carried out and the phantom was then treated on a linear accelerator. During treatment, the dose at a specified point (defined in the centre of the phantom in the vicinity of the target and represented by three external markings on the phantom), was measured using a PTW 3-D pinpoint ionization chamber (Type: 31022). A second treatment delivery was then performed with a set of radiophotoluminescent dosimeters embedded at a fixed position in the phantom. In addition, small field output factors were measured for a range of selected equivalent square field sizes and compared with the onsite treatment planning

commissioning data from the centres. The data were then anonymized and centrally analyzed.

Major differences were found in the delineation of target volumes and as a result, comparative data analysis of the planning was limited, which highlighted the need for clinicians to participate in external audit teams. Differences of up to 7.5% were observed when comparing the treatment planning calculated doses to the doses obtained from the dosimeters placed in the phantom. Differences of up to 17.0% were observed in the small field output factors for equivalent square field sizes of 0.5 cm x 0.5 cm. The study also demonstrated that the end-to-end audit methodology was not sensitive to the errors in the extrapolation of small field output factors in the planning systems.

The results of this study have shown that there is a need for additional steps to be audited separately prior to performing end-to-end dosimetry audits for complex treatment techniques. In addition, differences in clinical approaches, which include clinical interpretation of a prescription, volume definitions, and the evaluation and reporting of dose objectives and constraints, need to be addressed separately. Following this, methodologies that provide pre-defined target and organ at risk volumes are likely to be more efficient for an end-to-end audit programme. On-site patient specific quality assurance alone is not sensitive to errors in the commissioning of the treatment planning systems and some treatment planning modelling parameters should be audited separately.

Dedication

This work is dedicated to my parents Mr. Munyadziwa Carlton Maselesele and Mrs Nkhangweni Sylvia Maselesele, who travelled with me throughout this long journey. To my wife and all my children, to whom I wish this to be a motivation for them.

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List of abbreviations

2-D	Two Dimensional
3-D	Three Dimensional
3-D CRT	three-dimensional conformal radiotherapy
AAPM	American Association of Physicists in Medicine
ACDS	Australian Clinical Dosimetry Services
BIPM	International Bureau of Weights and Measures
CBCT	Cone Beam Computed Tomography
CT	Computed Tomography
CRT	Conformal Radiation Therapy
CTV	Clinical Target Volume
CIRS	Computerized Imaging Reference Systems
DRR	Digitally Reconstructed Radiograph
DVH	Dose-Volume Histograms
ED	Electron Density
ESTRO	European Society for Radiotherapy and Oncology
FF	Flattening Filter
FFF	Flattering Filter Free
GTV	Gross Tumor Volume
Gy	Gray
HU	Hounsfield
kV	kilo Voltage
IAEA	International Atomic Energy Agency
ICRP	International Commission on Radiological Protection
ICRU	International Commission on Radiation Units and measurements
IMRT	Intensity-Modulated Radiotherapy (IMRT)
IROC-H	Imaging and Radiation Oncology Core Houston

LCPE	Lateral Charged Particle Equilibrium
linac	Linear Accelerator
MeV	Mega electron Volt
MLC	Multileaf collimator
MU	Monitor Unit
MV	Megavoltage
NPL	National Physical Laboratory
OAR	Organ at Risk
OSLD	Optically Stimulated Luminescence Dosimeter
PTV	Planning Target Volume
QA	Quality Assurance
QC	Quality Control
QUATRO	Quality Assurance Team for Radiation Oncology
RDS	Radiation Dosimetry Services
RPLD	Radiophotoluminescent dosimeter
SSDL	Secondary Standards Dosimetry Laboratory
TECDOC	Technical Document
TG	Task Group
TLD	Thermoluminescent dosimeters (TLD)
TPS	Treatment Planning System
TRS	Technical Report Series
SBRT	Stereotactic Body Radiotherapy
SRS	Stereotactic radiosurgery
Sv	Sievert
UV	Ultraviolet
VMAT	Volumetric Arc Therapy
WHO	World Health Organization

1. Introduction

1.1 The need for radiotherapy audits

Radiation therapy has an important role in the medical field for the treatment of cancer. In radiotherapy, patients receive high radiation doses to a well-defined target volume and where possible, less dose is delivered to surrounding healthy tissues or organs at risk (OAR). Radiation dosimetry involves the measurement or calculation of absorbed dose to a medium resulting from exposure to ionizing radiation. In radiotherapy, the outcome of treatment greatly depends on the accuracy and consistency of dose delivery to the patient (IAEA, 2016; ICRU, 2010). This in turn depends on the accuracy of the target volume localization, radiation dosimetry, treatment planning and patient positioning (Muhammad et al., 2016). According to the International Commission on Radiological Protection (ICRP, 2009), severe toxicities or even fatal consequences can emerge from variations arising from incorrect radiation beam calibrations, and lack of independent calculations of the treatment times or monitor units (MU) for treatment delivery.

Dosimetry in radiotherapy focuses on methods of quantitative determination of energy deposited in a medium by directly or indirectly ionizing radiation. Radiation measurements can be carried out using films, ionization chambers, diodes, thermoluminescent dosimeters (TLD) and other commercially available dosimeters (Podgorsak, 2006; IAEA, 2005). Mediums that can be used to facilitate beam characterization in radiotherapy include water and solid phantoms. Water as a measurement medium closely approximates muscle and other soft tissues in its radiation absorption and scattering properties. Solid phantom on the other hand can also be used, however scaling factor for close approximation to water medium are used. The choice of water as a phantom material is owing to its universal availability. Since not all radiation detectors are waterproof, solid phantoms have been developed as substitutes for water (Sibtain et al., 2012; Khan, 2014).

In radiotherapy, different techniques can be used to treat different tumors, which can be located in any part of the human body. These may include two-dimensional (2-D), three-

dimensional (3-D) and other more complex treatment planning and delivery techniques, which may require different radiation dosimetry verifications. Complex techniques such as Intensity-Modulated Radiotherapy (IMRT) and Volumetric Modulated Arc Therapy (VMAT) require more advanced radiotherapy treatment planning approaches (Khan, 2014). These techniques usually target radiation doses more precisely to the shape of the tumor aiming to reduce toxicity. They often employ the use of small, segmented fields or beamlets. The radiation treatment planning process is complex and involves multiple steps and sophisticated treatment planning calculation algorithms (Bratengeier et al., 2007). It is essential to audit processes that include the localization and segmentation of the targets and normal tissues, which could be affected by the radiation treatment. The treatment planning system (TPS) is used to calculate the dose distribution from the selected incident radiation beams (Bertelsen et al., 2010; Khan, 2007). The TPS calculations can also be verified using direct measurements in anthropomorphic phantoms. General frameworks that describe TPS commissioning procedures are also available from the International Atomic Energy Agency (IAEA), and they provide practical guidelines for medical physicists to perform end-to-end audit tests (IAEA, 2008; IAEA, 2004).

Radiation dosimetry audit measurements can involve various approaches (on-site or remote) depending on the availability of dosimetry equipment and logistics. Photon dosimetry audits for reference and non-reference conditions in conventional fields can be carried out using commercially available Farmer type ionization chambers (Khan, 2014; Podgorsak, 2006). However, it is important to note that the radiation dose output from the treatment unit is obtained by performing reference measurements in accordance with an international protocol, e.g. the IAEA Technical Report Series (TRS) No. 398 (IAEA, 2000). Other guidance may include the American Association of Physicists in Medicine Task Group 51 (AAPM, 1999) and the National Physical Laboratory Report No. 103 (NPL, 2002).

The International Atomic Energy Agency/World Health Organization (IAEA/WHO) conducts postal dosimetry audits for reference beam output and over a period of fifty

years, their services have provided approximately 13 600 dose audits for reference photon beams from about 4400 radiotherapy units in over 2300 centres in 135 countries (Izewska et al., 2020). The audits were done in low-income and middle-income countries of Africa, the eastern Mediterranean, Europe, Latin America, the Caribbean, Southeast Asia and the Western Pacific (Kaniarova et al., 2014; Izewska et al., 2006). During the period 1969 to 2018, on average 86% audit results were within the 5.0% acceptance limit. The IAEA/WHO records also showed a systematic increase in accurate beam calibrations in participating centres from approximately 50% in the early years of the service, to 70% in the early 1990's and to 97% up to the year 2018 (Izewska et al., 2020; Izewska et al., 2006). The IAEA/WHO audits previously used TLD in a powder form, however radiophotoluminescent dosimeters (RPLD) have been employed since 2017.

Routine dosimetry audits for more complex treatment planning and treatment deliveries have not been implemented extensively in radiotherapy. Auditing complex radiotherapy treatments is necessary to ensure correct interpretation of dose prescriptions and accurate patient treatment delivery processes, in order to identify systematic errors. Clark et al. (2015) examined the development of dosimetry audits performed over a period of 30 years and these included international audits. The study discussed the auditing methodologies of different external auditing bodies and suggested ways to harmonize audit methodologies and advocate for more involvement of radiotherapy centres. Regular external audits were recommended for centres to develop techniques that provide assurance that radiotherapy is planned and delivered as prescribed. The study concluded that participation in clinical trials was also an effective way for centres to access external audit services and assure accurate dose delivery (Clark et al., 2015).

The Imaging and Radiation Oncology Core Houston (IROC-H) quality assurance (QA) centre was established in 1968 as the Radiological Physics Centre (RPC) to contribute to the independent development, conduct and QA of multi-institutional cooperative group clinical trials. Centres within the same region may not necessarily deliver treatments of similar prescriptions using the same number of beams or arcs. As such these techniques may require verification through audit participation (Tol et al., 2015). The IROC-H group

have monitored about 1816 institutions and 3700 megavoltage (MV) therapy machines (Followill et al., 2017). Their dosimetry audits have implemented the use of optically simulated dosimeters (OSLD) in recent years (Musa et al., 2017; West and Kearfott, 2015). They also participate in the National Cancer Institute's (NCI's), National Clinical Trial Network (NCTN) for multi-institutional clinical trials. The major drive was to support key areas such as institution qualifications, review of clinical trial protocols, credentialing of institutions for specific protocols, transfer of radiotherapy data, clinical/technical review of the patient radiotherapy data, and management of radiotherapy data for analysis. These efforts aim to ensure that radiotherapy data outcomes analysis has minimal uncertainty (Followill et al., 2017; Taylor, et al., 2016).

Jornet et al. (2014), performed a multicentre inter-comparison of IMRT optimization, dose planning and IMRT pre-treatment verification methods. The aims were to check consistency between dose plans and validate whether pre-treatment verification results performed within the department agreed with an external audit result. The study concluded that although all plans fulfilled dosimetric constraints, plan quality depended on the local planner's expertise. External audits were also found to detect errors in IMRT implementation (Jornet et al., 2014).

Jurado-Bruggeman et al. (2017) performed a national multi-centre audit for VMAT dose planning and pre-treatment verification to analyse the dosimetric and dose delivery quality. Nine centres participated in the audit process, which also included validating whether pre-treatment verification results within the department agreed with an external audit result. Although the dosimetric goals were achieved, it was observed that plan quality and treatment delivery were heterogeneous and uncorrelated. This was attributed to differences in equipment and software as well as the local planning methodology. Differences between the external audit and measurements carried out within the department were observed. The authors also concluded that measurements carried out internal to a department for credentialing treatment processes cannot be used as a replacement for external audits (Jurado-Bruggeman et al., 2017).

Current technologies evolve rapidly and despite integrated safety mechanisms, radiation incidents continue to occur, and significant errors are being reported (Walker et al., 2014). A proper quality management system, which is important for safe radiotherapy, is always desirable. TPSs use various calculation algorithms and the accuracy of dose calculations must be verified (Bulski et al., 2015). Complex analyses have been developed to identify high-risk events associated with system failures that could lead to severe toxicity from radiotherapy as described in the report of American Association of Physicists in Medicine, Task Group 100 (AAPM, 2016). These require lengthy engagement with the entire radiotherapy team, interrogation of all radiotherapy processes and assume a solid foundation in quality management. Dosimetry audits on the other hand, offer a more focused review of a few processes in order to enhance the safety and quality of well-defined treatment processes, which can also improve the uncertainties associated with treatment delivery (Breedveld, 2005).

The role of end-to-end external audits in radiotherapy is to independently assess an institution's treatment processes. To this end, several audit methodologies have been established globally. End-to-end audit methodologies can provide an independent assessment of the overall dosimetric accuracy through measurements using a dedicated phantom and suitable detectors.

1.2 Study questions

The questions raised in this research included the following:

- How to formulate a methodology that involves the entire radiotherapy team for implementation of radiotherapy audits for complex cases in South Africa,
- How differently radiotherapy teams interpret a given histology in terms of prescription, target and OAR volumes, as well as dose constraints as part of an end-to-end audit,
- Whether the accuracy of measured and extrapolated field output factor data for small field sizes in a TPS influence the result of an end-to-end audit,

- If RPLDs can be used to verify dosimetry remotely in audits for complex radiotherapy techniques, and
- What the uncertainties associated with using RPLDs for end-to-end radiotherapy audits are?

1.3 Structure of the thesis

The thesis has 6 chapters, with chapter 1 as an introduction with section 1.1 addressing the need for radiotherapy audits and section 1.2 covers the study questions. Study objectives are outlined in section 1.4.

Chapter 2 focuses on radiotherapy dosimetry audits, presents the phantoms and detectors that have been used by different external audit groups. It also covers treatment planning as part of end-to-end audits including target definition, planning techniques, plan evaluation processes, and the concept of field output factor extrapolation on TPS.

Chapter 3 include methods and materials used for the study, while chapter 4 covers the results obtained in the study. Chapter 5 covers discussions and lastly chapter 6 is the conclusions and proposals for future work.

1.4 Study aim and objectives.

- To develop and pilot a comprehensive phantom-based end-to-end audit methodology for complex radiotherapy techniques using remotely processed RPLDs. Local protocols for target definition, treatment plan calculations and treatment delivery processes are to be employed.
- To compare the TPS field output data with measured field output factor data for small field sizes, which are used for dose delivery in complex radiotherapy techniques.

- To determine the uncertainties in the handling, reading, calibration and dosimetric use of RPLDs for remote dosimetry audits of complex radiotherapy techniques.
- To evaluate the lessons learned from the entire audit development process and the results obtained from the pilot.

2. Dosimetry audits in radiotherapy

Radiation oncology involves delivery of radiation, and its success relies in part on accurate dose measurements. Calibration of beam output and quality control (QC) on the equipment used for dose delivery is often carried out as required by the national regulatory body (Khan, 2014; AAPM, 1994). In South Africa, the regulator has adopted the national South African Standards for Quality Assurance in Radiotherapy protocol (SASQART, 2013), which requires regular verification of all mechanical and dosimetric quantities of radiation devices and an independent check by a second medical physicist is mandatory as outlined under Annexure A, items 50 (a) and (f) of Appendix B. Acceptance testing, commissioning and QA of the TPS software and hardware must always be performed, however at some institutions this has not been given priority even though it is a crucial part of quality management (AAPM, 2016). Guidelines for the QA of TPSs have been published to ensure accurate modelling and calculation of radiation dose including (IAEA, 2004; AAPM, 1998b; Van Dyk et al., 1993). As part of a comprehensive approach to QA in cancer treatment, regular independent external audit is important to ensure adequate quality of practice and delivery of treatment. Dosimetry audit methodologies can have different scopes to ensure all radiotherapy processes are covered (IAEA, 2022).

As outlined by the ICRP, QA and audits are important to disseminate knowledge and lessons learned from different types of dose delivery techniques in order to promote quality and ensure safe treatment (ICRP, 2009). This is particularly important in radiation therapy, considering that there is a rapid increase in the use of more complex treatment

techniques. Therefore, the systems and processes should be audited using a set of tests described by different protocols or other audit methodologies (IAEA, 2008; IAEA, 2004). There have been extensive debates on the range of the dosimetry procedures that should undergo external audits. In 2008, the European Society for Radiotherapy and Oncology (ESTRO, 2008) summarized a small dataset of IMRT audits and concluded that more information was urgently needed about the accuracy of IMRT treatment delivery in Europe through independent audits. In the United Kingdom (UK), Budgell et al. (2011) performed national dosimetry audits to independently check the safe implementation of IMRT and identify problems related to treatment delivery in order to implement corrective measures.

The different aspects of QA programmes in radiotherapy include regular equipment checks, beam dosimetry, and treatment planning aspects. External or independent checks can be coordinated by a national or international organization and in some cases, a peer review by qualified medical radiation physicists can be requested locally (Shiau et al., 2021). Both on-site audit systems and postal dosimetry programmes can exist in parallel. Izewska et al. (2008) has reiterated that there has been an extensive debate on the range of the dosimetry procedures that should undergo an external audit to enhance the confidence that clinical dosimetry is accurate and QA procedures are adequate.

2.1 Dosimetry audits for reference fields

The IAEA/WHO postal programme for external dosimetry audits on the calibration of high-energy photon beams used in radiotherapy has been in operation since 1969. These audits can be an effective tool for identifying problems at participating centres and be brought to the attention of medical physicists. The process also involves support in finding the source of the problems and suggesting ways of rectifying them. Audits also ensure good quality practices and accuracy of dosimetry in the entire radiotherapy sphere with results improving over time (IAEA, 2016). Through repeated participation and regular follow-up of poor TLD results, dosimetry audits have shown reduced uncertainties as well as increased precision and consistency as shown in figure 2.1(a).

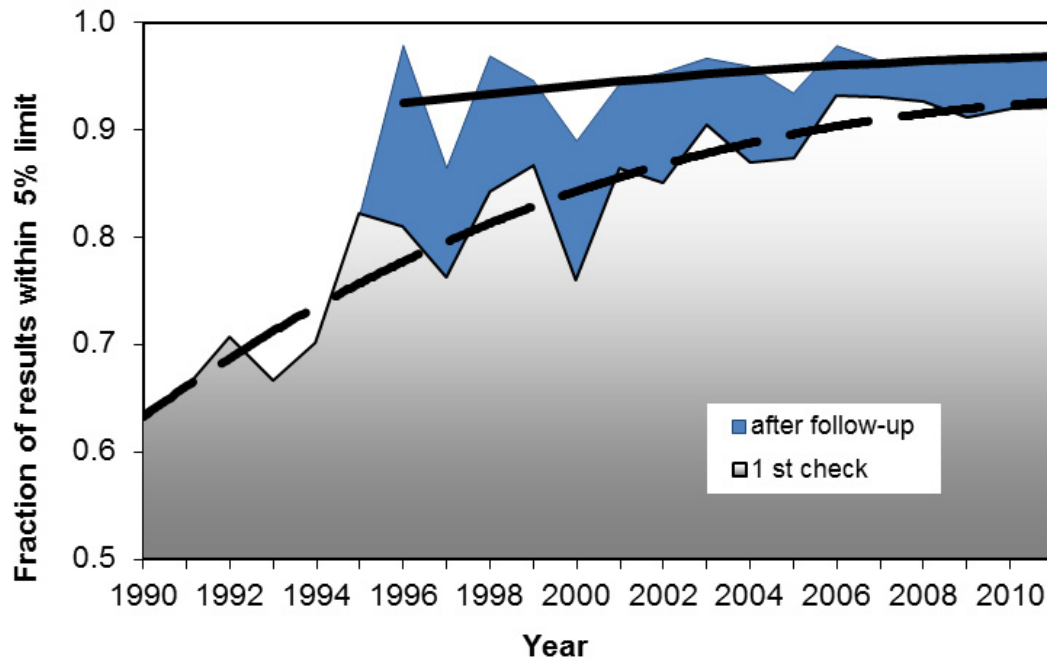


Figure 2.1(a) IAEA/WHO TLD postal dosimetry results within 5.0% acceptable limit showing reduced uncertainties with time (grey) and the improvement in results when regular follow up of poor results (blue) is conducted. The fraction of results within the 5.0% tolerance are shown before follow-up (dashed black line) and after follow-up (solid black line) since 1996 and this illustrates the importance of doing follow-ups on audit results (Izewska et al., 2020). <https://pubmed.ncbi.nlm.nih.gov/32036736/>.

Figure 2.1(a) shows the fraction of the dosimetry audit results within the 5.0% acceptance limit of radiotherapy centres from 1990 to 2010. From the dosimetry audits performed between 1969 to 2018, 86% of the overall results were within 5.0% (Izewska et al., 2020). Data records from the IAEA showed an overall increase in acceptable results with time. The increase was from approximately 50% in the first years of the audit programme, which went to about 65% to 70% in early 1990's, and 97% from 2016 to 2018 (Izewska et al., 2020). Follow-up of poor results was initiated in 1996 and have since been conducted regularly and the fraction of acceptable results increased further to approximately 99%. This was mainly attributed to centres showing increased interest in QA and regular participation in audits (Izewska et al., 2019).

The dosimetry audit programme aims at improving the accuracy and consistency of clinical dosimetry in radiotherapy centres worldwide. Since its inception, the TLD audit services were offered globally, but recently it is mainly focused on low-and-middle income countries (Izewska et al., 2003; Izewska et al., 2002; Izewska et al., 2001), owing to the establishment of audit programmes in some Member States. The IAEA/WHO results for reference beam audits carried out over the period 1969 to 2018 are given in figure 2.1(b). In addition, radiotherapy dosimetry audits are also offered to the Secondary Standards Dosimetry Laboratories (SSDLs) that disseminate traceability to end-user institutions by calibrating their local reference dosimeters for use in radiotherapy. Bulski et al. (2020) has investigated the role of SSDLs in dosimetry audits and concluded that continuous collaboration with the IAEA is crucial in testing the capabilities and methodology in order to include new audits in the routine services, especially when looking beyond reference dosimetry.

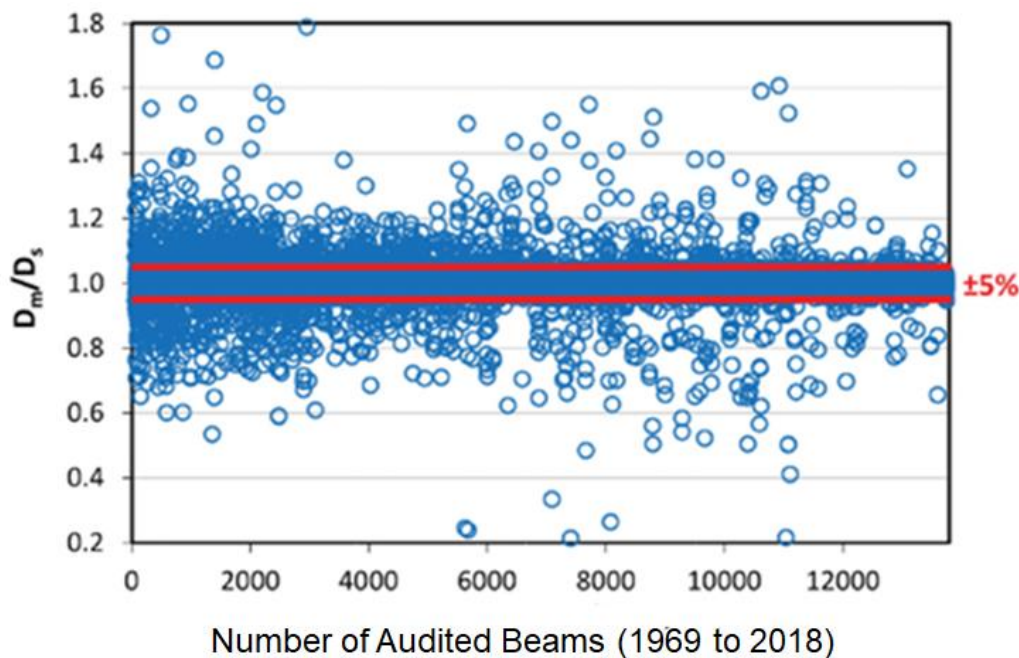


Figure 2.1(b) Results of the IAEA/WHO postal dose audits of radiotherapy centres showing ratios D_m/D_s of the IAEA's measured dose (D_m) to the dose stated by the centre (D_s). The data were collected over the period 1969 - 2018 (Izewska et al., 2020). <https://pubmed.ncbi.nlm.nih.gov/32036736/>.

In over fifty years, the IAEA/WHO has provided 13,600 audits to 136 countries in six geographical regions (Izewska et al., 2020). Centres voluntarily participate in the audits. From the data acquired over these years it was observed that 30% of all audits were done in Latin America and 28% in Europe (Kaniarova et al., 2014; Izewska et al., 2006). Only 6% audits were performed in Africa and this was attributed to the lower number of radiotherapy centres as compared to other regions. From all the participating centres 86% were within 5.0% tolerance before follow-up and more than 95% were within 5.0% tolerance after follow-ups (Izewska et al., 2020).

Various methodologies are used by different audit networks operating dosimetry audits at national or international levels. For instance, the IAEA developed simple tubular holders made out of polymethyl methacrylate (PMMA), with openings for RPLDs as shown in figure 2.2. The holder design facilitates postage, assembly and use. It is light and suitable for a mailed audit system at low shipment cost, which is particularly advantageous when considering a wide geographical distribution of audit participants. Such a holder can be setup for irradiation in any suitable water container, a dosimetry phantom or if not available, a plastic bucket (Izewska et al., 2007)

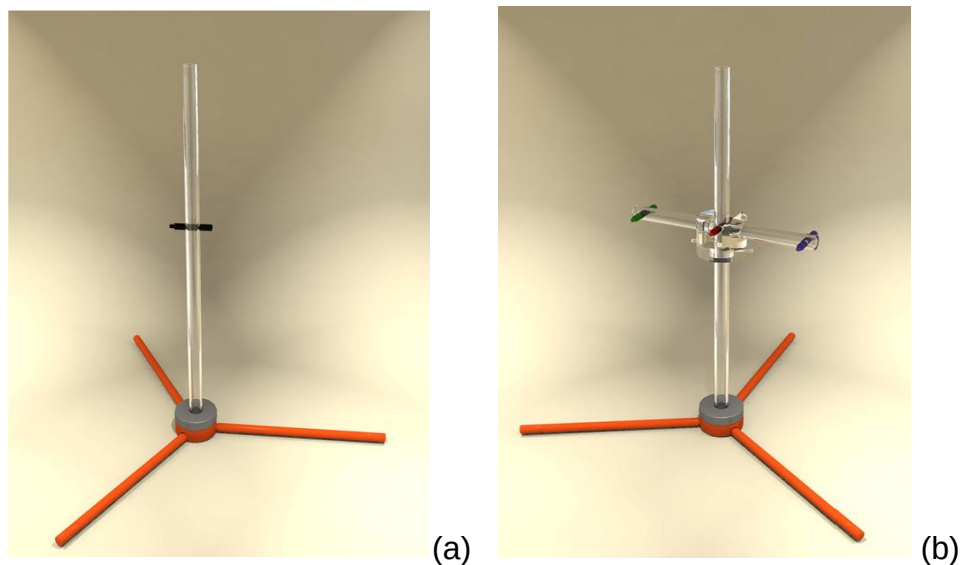


Figure 2.2 Two IAEA holders for (a) central axis and (b) off-axis measurements (Izewska et al., 2007). <https://pubmed.ncbi.nlm.nih.gov/32036736/>.

The results of an IAEA pilot study for dosimetry in reference and non-reference conditions are given in figure 2.3 and illustrates dose ratios of the IAEA measured dose to those stated by the participants (Izewska et al., 2007). In total, 203 measurement points were taken for Cobalt-60, and high energy X-ray beams between 6 MV and 23 MV. The mean ratio of measured dose to the participant stated dose was 0.999 ± 0.013 . Statistical distributions of the various groups of measurements had a spread of results with the standard deviation varying between 0.011 for open fields and 0.015 for wedged fields (IAEA, 2016; Izewska et al., 2007).

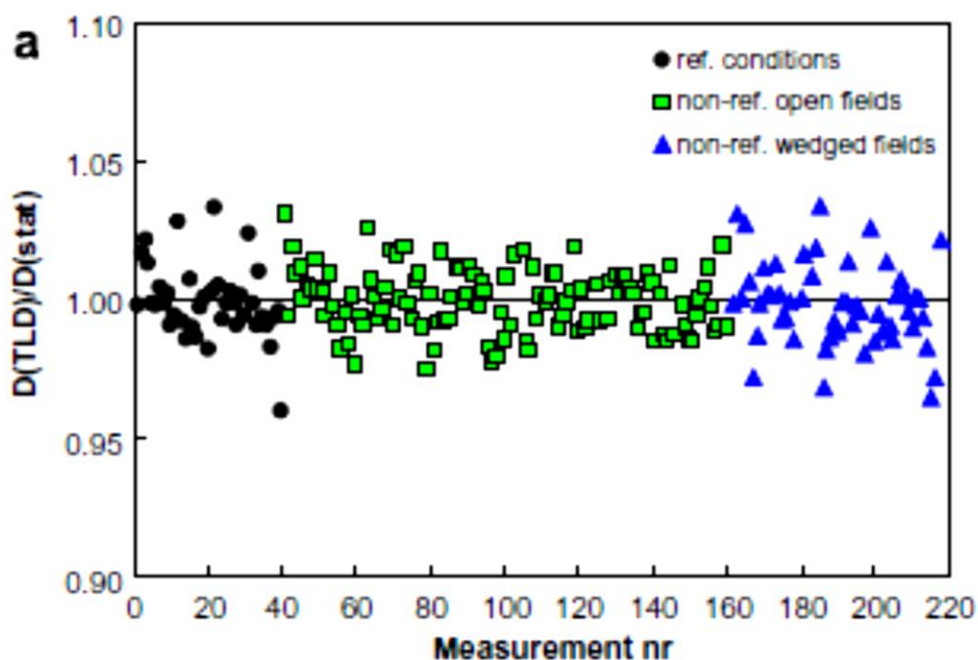


Figure 2.3 Multinational audit results for a pilot study for reference and non-reference conditions). $D(TLD)/D(stat)$ is the ratio of the TLD reading measured by the IAEA which is indicated as $D(TLD)$, to the dose stated by the participant which is indicated as $D(stat)$. Measurement nr is a number assigned to each of the different measurement points provided by the study participants. “Ref. conditions” refer to measurements of reference output at the beam central axis in a 10 cm x 10 cm field size. “Non-ref. open fields” are off axis measurements in a 10 cm x 10 cm field size. “Non-ref. wedged fields” are for measurements in wedged 10 cm x 10 cm field sizes (Izewska et al., 2007). <https://pubmed.ncbi.nlm.nih.gov/17628209/>.

Simple non-reference beam dose audits have a limited scope since they are only capable of providing verification of a few selected beam parameters, which does not cover the whole radiotherapy process. However, dose audits for photon beams in reference conditions are recommended to be scheduled before launching other subsequent levels of audits (IAEA, 2016). It is also important to audit parameters that are related to treatment planning and actual dose delivery. Therefore, it is crucial to perform dosimetry audit measurements for both three-dimensional conformal radiotherapy (3-D CRT) and more complex radiotherapy techniques.

Most external audit systems for beam output verification are relatively simple. For IROC-H, each year participating institutions receive a package containing a lightweight platform and acrylic mini-phantoms containing several OSLDs for irradiation with each reference beam as shown in figure 2.4 (Alvarez et al., 2017). Instructions supplied, explain the irradiation procedure, and the institution is requested to describe their calibration procedure. The blocks and other equipment are returned to the IROC-H where the OSLDs are analyzed (IROC-H, 2020; Pradhan et al., 2008). Consistently each year, up to 6% of the United State (US) photon beams audited have fallen outside of the $\pm 5.0\%$ dose tolerance. From the analysis it was indicated that the incorrectly calibrated beams were distributed among approximately 10% to 20% of the institutions monitored by the IROC-H, which was significantly above the 5.0% dose tolerance. The outliers were identified, and their results corrected through an on-site visit, with audit measurements repeated using an ionization chamber. Other follow-up included the Radiological Physics Centre (RPC) which conducts annual mailed audits of machine calibration. One of the recommendations was to make follow up and investigate factors that contributed to such high discrepancies and identify events that have the worst consequence and estimate the frequency of their occurrence, in order to prioritize dosimetry audits activities that should be repeated or revisited (Ibbott, 2010).

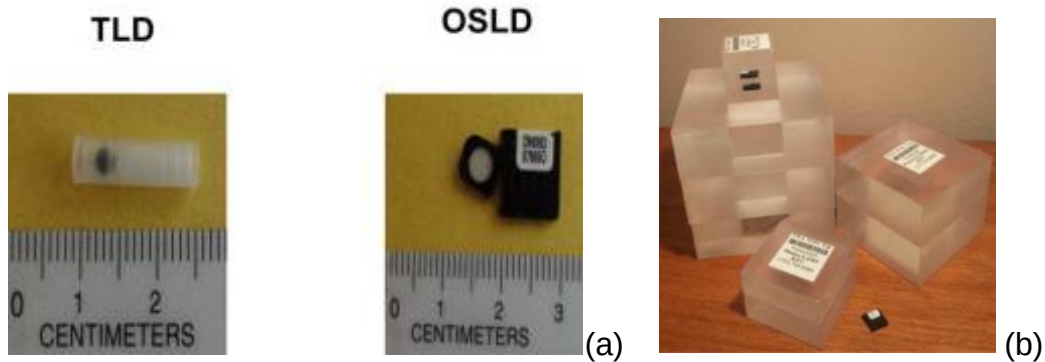


Figure 2.4 Sample image of the (a) TLD as compared to OSLD (b) the dosimeters placed inside the acrylic block (Alvarez et al., 2017).

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5722458/>.

Clark et al. (2015) examined the development of dosimetry audits in the UK for the past 30 years and these included the involvement of the UK in international audits. In their findings they concluded that the significance of dosimetry audits must always be highlighted to each radiotherapy centre. Audits promote best practice and high-quality treatment, as tight consistency of the dose delivered to individual patients across different centres can be verified. Audits for more complex treatment techniques can be used to support implementation, and facilitate awareness and understanding of issues, which may exist during treatment deliveries. This can be made more effective by benchmarking centres with similar equipment and encouraging collaboration among different audit groups.

From the UK audits, all the reference dosimetry audits using the local code of practice were within the 2.5% tolerance, with 95% beams within 1.5% as in figure 2.5. Photon beam reference dosimetry audits conducted in departments within different regions in the UK, provided basic assurances of the accuracy in dosimetry of radiotherapy treatments and showed a significant improvement with time as indicated in figure 2.5 (Palmer et al., 2011). The results have shown significant improvements amongst participating centres over time as the audits were repeated within the period 1993 to 2008. This also supports the belief that dosimetry audits should be a continuous process to ensure improved quality in radiotherapy treatment processes.

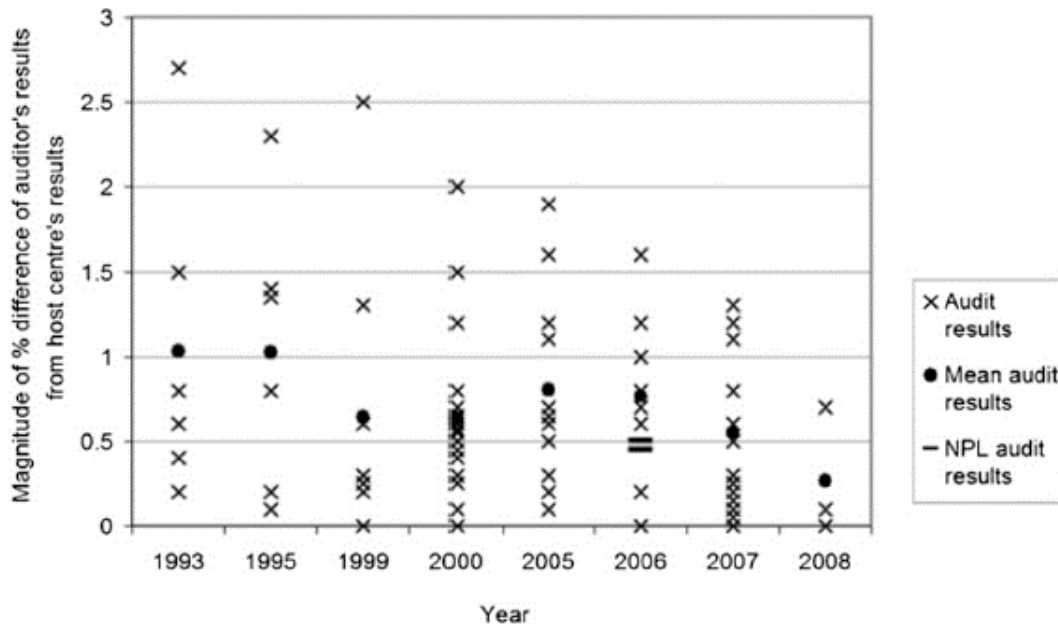


Figure 2.5. The improvement in the results of the UK radiation dosimetry audit over time (Palmer et al., 2011). <https://pubmed.ncbi.nlm.nih.gov/21159805/>.

Kry et al. (2018) also reviewed the results and trends of the audits performed by several audit organizations across several geographical regions. Beam output audit results from the Australian Clinical Dosimetry Services (ACDS), IAEA, IROC-H and Radiation Dosimetry Services (RDS) were evaluated from 2010 to 2018. The methodologies for conducting remote beam output audits, including details of the dosimetry audit procedures, were reviewed. A total of 210,167 remote beam output audit results were included in the study, including 114,124 results from IROC-H, 90,024 results from RDS, 4,240 results from the IAEA, and 1,779 results from the ACDS. This included 87,780 photon beam results and 122,387 electron beam results. A total of 1,323 results, which was about 0.63%, were found to be outside $\pm 5.0\%$ tolerance, as shown in figure 2.6 for each QA group.

There were significant differences in the percentage of audit results outside of tolerance between the QA groups. Significant differences were found between all groups except for two groups ACDS/IROC-H and ACDS/RDS for photon beams and ACDS/RDS for

electrons. The most pronounced difference was for the IAEA, which reported a relatively high number of results outside of the 5.0% tolerance (1.6%), as shown in figure 2.6. This was attributed to the fact that the IAEA audits are the most global and include countries that struggle to sustain radiotherapy resources. The ACDS had the lowest percentage of results outside of 5.0% tolerance with no noticeable difference between IROC-H and RDS as in figure 2.6 (Kry et al., 2018). In summary, local or national dosimetry audits are usually within the tolerances whereas regional audits are more often outside tolerance. This may be attributed to the differences in available resources and expertise when conducting these audits.

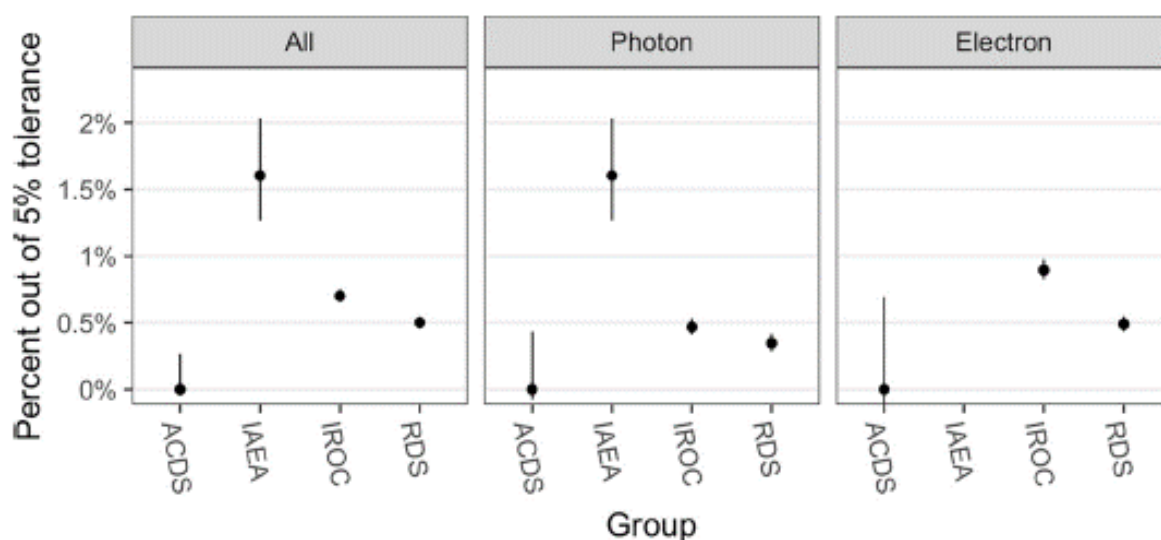


Figure 2.6 Percentage of remote beam output audit results outside the $\pm 5.0\%$ tolerance (Kry et al., 2018).

<https://www.sciencedirect.com/science/article/pii/S2405631617300891>.

Furthermore, a comparison of IROC-H and ACDS on-site audits of reference and non-reference dosimetry was carried out by Lye et al. (2019). The tests performed in this comparison were a subset of each group's on-site dosimetry review visits. The two audit approaches gave similar results when errors were deliberately introduced into the TPS. They both picked up incorrect percentage depth dose (PDD) and wedge data, but both approaches were unable to pick up a 2.0% change to small field output factors. The IROC-

H group conducted a more thorough review of the procedures, documentation, treatment records and assessment of capability such as multileaf collimator (MLC) calibrations (AAPM, 2001). On the other hand, the ACDS on-site visits were focused on dosimetry measurements, but were not focused on fundamental beam modelling and conformality in delivery. This comparison between different audit group methodologies and results are important for groups planning to establish dosimetry audits for the first time in their centres or countries.

2.2 Audits in radiotherapy treatments

During on-site audits reviews of QA programmes, different checks can be carried out. Medical physics checks could include dosimetric, electrical, mechanical and safety parameters of the radiotherapy equipment (Mayles, 1999). These can also include tests of the TPS commissioning and a review of the clinical dosimetry records (IAEA, 2022). The basic type of on-site dosimetry audit is however limited to reference beam calibration verification using ionization chamber measurements conducted in water phantoms. If the result is outside tolerance, further checks may be performed to resolve the source of observed discrepancy.

Radiotherapy plays a pivotal role in the curative treatment of head and neck carcinomas, especially for locally advanced disease. An estimation of about 476,125 people were diagnosed with oral and oropharyngeal cancer in 2020 worldwide (Cancer.net, 2022). According to the National Cancer Register (NCR) report of 2019, in South Africa about 83,000 cancer diagnoses were registered and close to 5,000 were head and neck cases (NCR, 2019). Manufacturers such as Computerized Imaging Reference Systems (CIRS) (Model: 136500) have developed head and neck phantoms as shown in figure 2.7(a) that can be used for the purpose of real time verification of treatment dose deliveries. These also provide the opportunity to perform geometric and radiation alignment QC, with system checks that are as challenging as a real patient scenario. Another type of phantom such as the IROC-H in figure 2.7(b), can also be used for dose verifications and dosimetry audits (Ibbott and Thwaites, 2015).

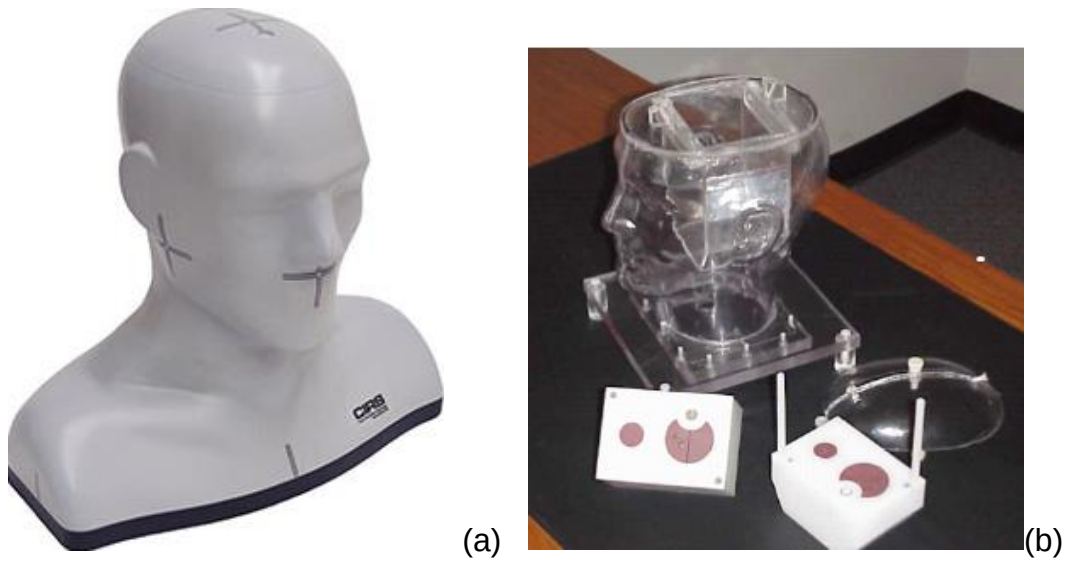


Figure 2.7 (a) CIRS phantom Model:136500 (CIRS, 2020) and (b) the IROC-H phantom Model:002LFC with inserts, (IROC-H, 2020).

By using phantoms, it is possible to simulate different techniques used in actual patient treatment planning and delivery. Anthropomorphic and tissue-equivalent designs provide opportunities to account for the challenging effects of tissue heterogeneity. Geometric, dosimetric and target inserts allow for comprehensive image QA, geometric machine and TPS QA to evaluate system performance. Phantoms usually accommodate a multitude of dosimeter inserts for dose verification. When used with various imaging inserts, they provide a tool for comprehensive end-to-end testing and QA of complex radiotherapy treatments (IAEA, 2008; CIRS, 2020).

Scans of these phantoms, as in figure 2.8, can be obtained from computed tomography (CT) scanners in order to perform the entire treatment planning processes on-site. These scans are used to create 3-D volumes in the TPS for planning and perform plan verifications during audits.



Figure 2.8 Transverse CT image of the CIRS Head and Neck phantom, Model:136500 (CIRS, 2020).

CT scanning is the preferred method of imaging for photon beam treatment planning. The treatment planning software allows for contouring of patient body outline, treatment targets and OARs. In addition, the 3-D attenuation data can be obtained from the CT numbers or Hounsfield units (HU), which is a key component for dose calculations in inhomogeneous media (Nakao et al., 2020; Nakao et al., 2019).

The IAEA TECDOC-1583 (IAEA, 2008) describes 3-D CRT methodologies for on-site end-to-end audits, simulating the essential parts of the radiotherapy workflow where anthropomorphic phantoms are treated in a clinical manner and independent auditors can verify the doses. This on-site audit methodology reviews the dosimetry, treatment planning and radiotherapy delivery processes using an end-to-end approach. The test cases covered a wide range of typical clinical situations, including checks for single beams, standard multiple field techniques and complex multi field arrangements. After performing the dosimetry for a set of test cases within the phantom, the measured and planned doses are compared. The result of these comparisons provides the assurance that the beam parameters in the TPS algorithms are correct if the calculated doses agree with the measurements. As such the methodology can be a useful tool for verifying TPS data modelling and treatment delivery to ensure that correct doses are planned and delivered.

Using guidelines for implementation and verifications of IMRT delivery, multicentre studies have analyzed patient specific dosimetry QA (Merlotti et al., 2014; ESTRO, 2008). This was achieved by comparing measured versus TPS dose through parameters such as mean difference and standard deviation. Amols et al. (2014), reported mean differences between -1.8% to 1.5%, and standard deviations between 0.8% to 3.7%, from audits of ten different centres.

Lehmann et al. (2018) reported on the design and findings of 3-D CRT audits. The audit results were considered to pass at an optimal level when deviations were within 3.3%, and to pass at an action level when deviations were greater than 3.3% but within 5.0%. Out of tolerance was reported for deviations beyond 5.0%. The audit was conducted on-site using the CIRS Model 002LFC (Norfolk, VA, USA) anthropomorphic phantom. Absolute dose point measurements were performed with a Farmer-type ionization chamber (Attix, 2004; Cherry and Angela, 2009) and the treatment plans included open and half blocked fields, wedges and lung inhomogeneities. The results showed that of the 94 audits performed, 50 (53.0%) scored a pass at optimal level, 32 (34.0%) scored a pass with an action level and 12 (13.0%) scored out of tolerance results. Beam modelling of low-density inhomogeneities, photon calibration, wedges and off axis, were found to contribute to the discrepancies. The 3-D CRT audits illustrated dosimetric problems in clinically used dose calculation algorithms especially at low density inhomogeneities such as lung and also when using wedges. This showed that 3-D CRT dosimetry audits remain relevant and can identify fundamental global and local problems that can also affect all treatments techniques. Despite the expansion of the 3-D CRT audit into more complex treatment techniques, the 3-D CRT audits remain a fundamental part of auditing in order to identify flaws in individual implementation of beam models.

For IMRT and VMAT audit methodologies, a portable phantom can also be considered. Clark et al. (2009; 2014) performed dosimetry audits on different types of IMRT techniques for various treatment disease sites. The study concluded that a 3.0% tolerance could be applied to planning target volume (PTV) point doses. For gamma tolerances, the 3.0%/3.0mm on individual fields and 4.0%/3.0mm for combined fields

were proposed for multi-centre head and neck IMRT trials. The gamma index is a standard technique method for planar dose verification, in both IMRT and VMAT QA. The planar dose is obtained using a film, a 2-D array detector or the electronic portal dosimetry detector (EPID). It uses preselected dose difference (DD) and distance to agreement (DTA) criteria, which returns a gamma value that is used to determine the outcome of the QA plan, i.e. if it passes or fails (Li et al., 2011). In clinical practice the gamma index acceptance criteria have been based largely on experience, without any underlying statistical analysis. In the study conducted by Ceberg (2013) it was proposed that the gamma-evaluation method could be reinterpreted such that the DD and DTA criteria are replaced by the standard deviations of the associated uncertainties, which can be used to evaluate pass and fail gamma index levels (Ceberg, 2013). Park et al. (2018), investigated the reliability of the gamma index analysis for verification of VMAT plans and concluded that correlations between the global and local gamma passing rates varied according to the dosimeter type, linac type, and gamma criteria. Therefore, to utilize the gamma index analysis, it was proposed that each institution should carefully establish their own gamma analysis protocol (Park et al., 2018).

Adolfsson et al. (2014) conducted a pilot study at four clinics on dosimetry audits of 3-D CRT and IMRT or VMAT, based on lithium-formate dosimetry using a semi-anthropomorphic head and neck phantom. In the study the dosimeters were loaded into the rods in the phantom and then sent with instructions by mail to the audit sites. Dose values measured in the audit agreed with TPS calculated doses in the PTV to within $\pm 5.0\%$ for 3-D CRT and $\pm 7.0\%$ for IMRT/VMAT for all participating clinics. It was concluded that some deviations were attributed to the TPS algorithm and the CT calibration curve that was used. As a result, auditing should be conducted for each of the different steps to ensure accurate commissioning.

Other dosimetry studies conducted by Jornet et al. (2014) focused on multicentre validation of IMRT pre-treatment verification by comparing results of the audits amongst the participating departments. The conclusion was that although all plans fulfilled dosimetric constraints, plan quality was highly dependent on the planner expertise.

External audits were found to be an excellent tool to detect errors in IMRT implementation and could not be replaced by inter-comparisons obtained locally. Dosimetric audits were also successfully carried out for IMRT implementation in over 90% of UK radiotherapy departments as reported by Budgell et al. (2011). Modelling and delivery of IMRT achieved over 95% pixels, passing a gamma criterion of 3.0%/3.0mm within the 20% isodose, suggesting that the implementation of IMRT had been carried out safely. Dosimetry audits for more complex treatments like IMRT and VMAT still required further investigations and as such, further participation from different centres offering these kinds of treatments were encouraged (Eaton et al., 2015).

IROC-H uses anthropomorphic QA phantoms to credential sites that are using advanced technologies to deliver complex treatment plans, like IMRT and VMAT. The audits have also shown potential benefits for 3-D CRT treatment techniques. The failure rate for the IROC-H IMRT head and neck phantom was reported to be around 10% to 15% by Followill et al. (2017) for audits conducted during a period of 15 years. According to IROC-H nearly 70% of all US radiation therapy centres participate to some degree in cooperative group clinical trials (Ibbott and Thwaites, 2015). Complex techniques such as IMRT and VMAT require a substantial physics effort to qualify the institution to enter into patient clinical audits. IROC-H also has anthropomorphic lung, liver, head and neck, prostate, stereotactic radiosurgery (SRS) and spine phantoms that are used for credentialing and QA purposes. The phantoms include structures that closely simulate targets and OAR, and are made from tissue equivalent materials, high impact polystyrene, solid water, cork and acrylic as shown in figure 2.9 (Mehrens et al., 2016). Motion on the treatment table is used to mimic breathing patterns for some lung and liver phantoms. Doses were measured with TLDs and radiochromic films in various planes within the target of the phantoms as part of audit methodology (Ulya, 2017; AAPM, 1998a).

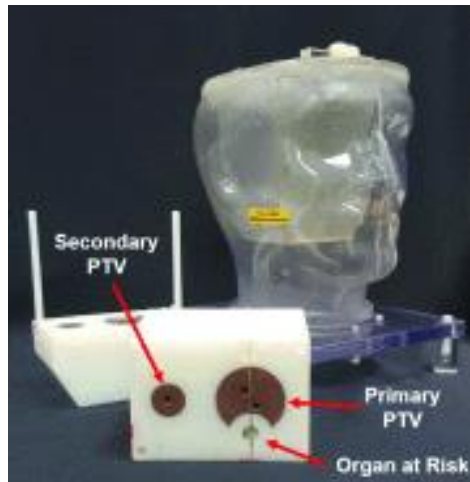


Figure 2.9 IROC-H head and neck phantom with inserts (Mehrens et al., 2016).
https://www.researchgate.net/figure/IROC-H-H-N-phantom-with-block-dosimetry-insert_fig1_309960128.

Carson et al. (2016) examined credentialing criteria from the IROC-H's anthropomorphic head and neck phantom and observed that 90% of institutions treatment plans agreed within $\pm 5.0\%$ of the measured dosimetry audit doses. The study concluded that most phantom failures were resulting from systematic dosimetric differences between the TPS calculated doses and the measured dose, which were attributed to noise-induced failure from the use of films and TLDs. Further work was needed to diagnose and resolve the observed dosimetric inaccuracies even though it was found that 5.0% TLD and 5.0%/4.0 mm gamma criteria was practically achievable, which also motivated this study.

Followill (2016) addressed lessons learned from the IROC-H audits including lack of proper radiation beam characterization in TPSs, which leads to poor quality treatment that can then be linked to inferior patient survival. The study also concluded that a negative impact was observed when comparing different dosimetry audit protocols without significant variation to those with a noticeable variation. One of the findings was that QA in radiation oncology was largely driven by technological advances. On the other hand, safety improvements for more complex treatments were driven by reactive responses to past system failures. Another observation was that prescriptive approaches

to quality and safety alone often do not address the huge variety of processes and techniques used in radiation oncology. Risk-based assessments of radiotherapy processes provided a mechanism to enhance quality and safety, both for new and for established techniques (Lin, 2014). As such it is important to investigate the observed shifts especially when expectations from the patient are high, but quality and resources are lacking.

Thwaites (2019) observed that since radiotherapy is a safe and critical use of high-dose radiation, it requires that clear and consistent methods are applied so that individual treatments can be delivered safely and accurately. The overall accuracy in the radiation dose delivered to the patient dose specification point is generally recommended to be within $\pm 5.0\%$ of prescription at the 95% confidence level (IAEA, 2016). Audits were directly effective in identifying problems and providing support to reduce them. This improved practice and the accuracy of dosimetry in a wide range of centres. Different literatures (Izewska et al., 2020; Ibbott and Thwaites, 2015) has shown that audits also improve practice over time, help to maintain systems and ensure better overall performance at later audits. The IAEA/WHO and IROC-H fifty-year-old programmes have improved consistency in radiotherapy dosimetry. There should also be a global increase in coverage of audits and advocacy for more centres to participate. As the complexity of radiotherapy continues to develop, the scope of what can be included in dosimetry and quality audits also needs to continue to increase. Considerable increase in complexity brings opportunities for new types of human and system errors and problems with treatment delivery equipment. Therefore, with advanced technologies, the need for both regular QA and audit increases. Radiotherapy dosimetry audits allow for the independent testing of procedures and identification of errors. Dissemination of information on these errors or mistakes as soon as they become available is crucial to the radiation therapy community especially with new technologies (Hussein et al., 2013). Information on circumstances that almost resulted in serious consequences is also important, as the same type of events may occur elsewhere. The QC procedures required for participation in clinical trials establishes a baseline for institutions and can include external audits for dosimetry, planning and delivery systems (Ibbott and Thwaites, 2015).

2.3 Radiophotoluminescent dosimeters (RPLD)

There are different types of detectors that have been used to perform dosimetry audit measurements. These may include film, ionization chamber, TLD, OSLD and RPLD (Izewska et al., 2020). Farmer type ionization chambers are used worldwide as a detector of choice for output measurements in conventional fields under reference conditions (Knoll, 2000). In this case, the dose delivered to a given point in the medium is determined by measuring the amount of charge produced in the small air cavity (Khan, 2014; Attix, 2004). In radiotherapy treatment, one of the approaches used to verify a treatment plan is by delivering a plan on an anthropomorphic phantom and comparing dose distributions calculated by the TPS with those measured by radiochromic films or suitable detectors.

There are different types of passive dosimeters, including film and TLD that have also been extensively used for dosimetry measurements in radiotherapy. Different types of films including radiographic or gafchromic types have traditionally been used in measurements of dose in radiotherapy as passive dosimeters (Borca et al., 2013; Girard et al., 2012). Radiochromic films, EBT3, can also be used to measure the dose from small fields which are commonly used to deliver treatment in complex radiotherapy. As mentioned by Mathot et al. (2014), EBT3 films have high spatial resolution and offer the benefit of being self-developing. The most important EBT3 characteristics include responses at high-dose levels, sensitivity to scanner orientation and post-irradiation coloration, energy and dose rate dependence as well as orientation dependence with respect to the film side. Major advantages of EBT3 include tissue equivalence, high spatial resolution, large dynamic range from 10^{-2} to 10^6 Gray (Gy), relatively low spectral sensitivity variation, insensitivity to visible light, and no need for chemical processing. One of the EBT3 film drawbacks when performing dosimetry is non-linear dose-response. This implies that for relative dose measurements using film, a calibration process is required and then convert film response into absolute dose distribution that can finally be normalized to a selected point (Girard et al., 2012). Film dosimetry also requires delicate handling to avoid results being affected by contamination due to fingerprints, improper storage and scanning time, which affect the dose accuracy.

More recently passive dosimeters, like RPLD and OSLD are being used in many parts of the world with the advantage that these dosimeters can be read repeatedly (Mizuno et al., 2008). The RPLD (Model: GD-302M) was considered a dosimeter of choice for this study and its characteristics will be discussed in this section. The RPLD is an accumulation type solid-state dosimeter, based on the radiophoto luminescence of silver activated phosphate glass (Son et al., 2011; AGC TECHNO GLASS CO, 2008). Typical RLPDs and holders are shown in figure 2.10.

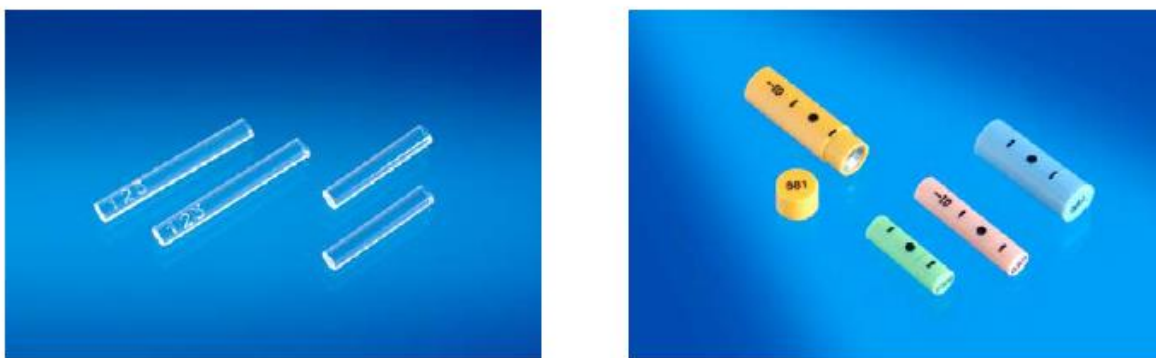


Figure 2.10 (a) RPLDs (Model: GD-302M) with engraved identification numbers and (b) different coloured plastic holders showing the sensitive length of the dosimeter as indicated by the dashed lines on either side of the central dot (AGC TECHNO GLASS CO, 2008). <https://www.c-technol.co.jp/eng/e-small>.

The dimension of each dosimeter is 1.5 mm in diameter and 12 mm length, while the plastic holder used in this study had a 2.8 mm outer diameter and was 13 mm in length. The sensitive length of each dosimeter is 6.0 mm, and the sensitive volume is 10.6 mm³. The RPLD fits snugly into the holder.

The radiophotoluminescent centres caused by the irradiation on the glass do not disappear by the readout operation and can be read out repeatedly. The pulsed ultraviolet (UV) laser excitation method is used to obtain the signal from RPLD (Rah et al., 2009; Araki et al., 2004). When the glass is exposed to ionizing radiation, stable luminescent centres appear in it, and when it is excited by UV-ray, the glass emits an orange

luminescence, resulting in the phenomenon called radiophoto luminescence (RPL). The signal is detected by a photomultiplier tube, and the luminescence amount is proportional to the radiation dose the glass was exposed to (Miyamoto et al., 2011). Figure 2.11 is a schematic illustration of the pulsed UV activation after irradiation.

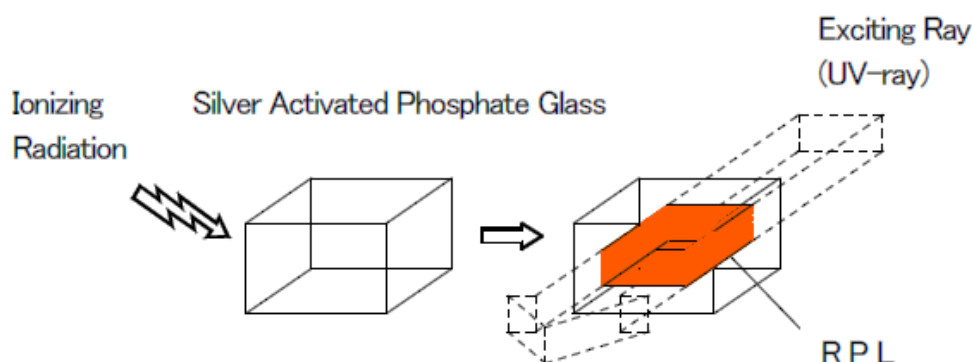


Figure 2.11 Illustration of the pulsed ultraviolet activation process (AGC TECHNO GLASS CO, 2008). <https://www.c-technol.co.jp/eng/e-small>.

RPLDs have a wide dose measurement range from a minimum of 0.01 mGray (mGy) to a maximum of 10 Gy (AGC TECHNO GLASS CO, 2008; ICRU, 1980). They can therefore be used for a wide range of applications such as personal monitoring systems for beta, gamma and x-rays measurement. Environmental monitoring systems for natural radiation, gamma and x-rays, as well as higher dose measurements that are typical in the medical exposure environment can also be carried out (Knezevi, 2011; Miyamoto et al., 2011). The chemical process can be illustrated as in figure 2.12, which illustrates that when Phosphate tetrahedron (PO_4) in glass is exposed to radiation there by losing its electrons and traps positive holes (hPO_4). Simultaneously, the Silver ion (Ag^+) in glass traps a single electron and changes to the Ag^0 ion. Then hPO_4 is assumed to move to the Ag^+ ion and generates Ag^{++} ion. The Ag^0 and Ag^{++} can function as the stable luminescent centre (Hsu et al., 2007), as shown in figure 2.12.

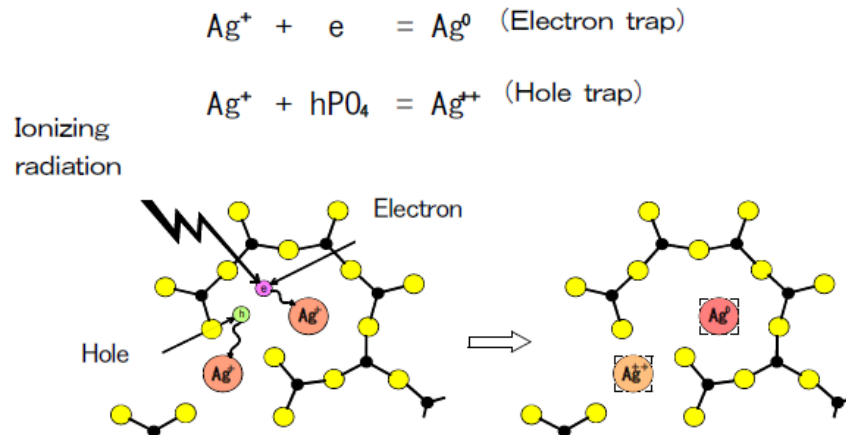


Figure 2.12 Illustration of chemical process when RPLD is exposed to radiation (AGC TECHNO GLASS CO, 2008). <https://www.c-technol.co.jp/eng/e-small>.

Mizuno et al. (2008) carried out a feasibility study on the use of RPLDs for postal dosimetry audits on high-energy radiotherapy photon beams (Mizuno et al., 2008). The study focused on characterization of both the RPLDs and TLDs by assessing and comparing different parameters like reproducibility, field size, and energy dependence. The standard deviation in the reproducibility was 0.8% for the RPLD, compared to 0.7% for TLD. The outputs of the RPLD showed a slight decrease from 1.7% to 2.7%, for a 5.0 cm × 5.0 cm field compared to 10.0 cm × 10.0 cm and 20.0 cm × 20.0 cm fields. The energy dependence correction factor was within the uncertainty of 1.6%. Postal dosimetry audit pilot trials at 106 facilities returned a central value of 0.3% and the standard deviation for 182 beams (95% of those audited) was within ±3.0%.

The application of RPLDs to non-reference conditions was also studied by Mizuno et al. (2014) by obtaining correction factors for the RPLD output for field sizes ranging from 5.0 cm × 5.0 cm to 25.0 cm × 25.0 cm and different wedge angles ranging from 15° to 60°. The mean difference between the measured and stated doses were within 0.5% for field size and wedge angles. The uncertainties for field sizes and wedge angles were 1.4% and 1.6%, respectively. This also supported the premise that RPLDs could be used in

place of TLDs (Rah, et al., 2011). Compared to TLDs, RPLDs also have the advantage that they can be readout repeatedly without loss of signal.

Dosimetric properties of RPLDs were also evaluated for high energy photon beams on a linear accelerator (linac) (Khan, 2014). In the studies conducted by Sona et al. (2011) and Araki et al. (2004) other factors included, were dose-response linearity and angular dependence. For each dose point obtained from an average of four dosimeter readings and for one standard deviation of each, the dose point measurements agreed within 1.0%. The energy dependence from 4 MV to 18 MV was found to be within 2.0%, and the response for 4 MV and 10 MV x-ray beams were within 0.6%. The angular dependence was within 1.5% for the angle ranging from 0° to 120°. This also demonstrated that RPLDs can be used for in vivo dosimetry. These studies show that there is a very close comparison in terms of characterization of RPLDs with other well-established dosimeters like the TLDs, and RPLDs can be considered a good alternative for passive dosimetry (Sona et al., 2011; Araki et al., 2004).

2.4 Radiotherapy treatment planning processes.

The TPS is used to calculate dose distributions based on variable beam arrangements, energies, field sizes, fluence patterns and modifiers. The accuracy of the TPS dose calculations is very important to the delivery of the correct dose (Barrett et al., 2009). In a TPS, data such as output factors, percentage depth doses and beam profiles are measured in a 3-D water tank, to characterize the treatment unit. Commissioning of a TPS entails that radiation beam parameters are adequately modelled in the system and are properly validated. When a new TPS has been purchased, initial testing is crucial in ensuring that the linac can deliver the calculated dose. IAEA TRS 430 (IAEA, 2004) outlines all the parameters that must be verified for commissioning and QA on the TPS. A TPS is generally capable of calculating planned doses for single fields, 2-D, 3-D CRT, and complex plans including IMRT and VMAT. The TPS is at the heart of radiation therapy, so it is very important that the parameters and data from the treatment unit are measured and entered correctly (Khan, 2014; Khan, 2011).

2.4.1 Target and Organs at risk delineation

During treatment planning, localization and delineation of the gross tumor volume (GTV), clinical target volume (CTV) and PTV is carried out using given margins. The definition of target volumes for radiotherapy is vital to its successful treatment dose delivery (Steenbakkers, 2007). The size, shape and location of the target must be properly described (Bertelsen, 2007; ICRU, 1999). This requires the best possible characterization of the location and extent of the tumor (Burnet et al., 2004). According to the International Commission on Radiation Units and Measurements report (ICRU, 2010), OAR or normal critical structures are tissues that, if irradiated, could suffer radiation damage. In principle, all non-target tissues might be considered organs/tissues at risk with the aim of delivering maximum dose to the tumor volume while sparing healthy tissues (Lin, 2014; Njeh, 2008).

2.4.2 Plan Evaluation

In radiotherapy, a prescription dose to be delivered to the target should be defined, and radiation dose constraints to the OAR must also be defined. After modelling and dose calculation is completed, dose volume histograms (DVHs) for the targets and each OAR are evaluated (Oinam et al., 2011). The choice of the treatment plan is then usually made, regardless of further physical and radiobiological considerations, by inspection of the DVHs and isodose coverage for each tentative plan that is considered (ICRU, 2010).

2.5 Impact of small field size output factors on TPS dosimetry audits.

The developments in automated collimation systems for radiotherapy treatments have also increased the use of smaller field sizes. In the case of IMRT, the MLC mode can deliver the dose by step and shoot or dynamic MLC mode. Step and shoot mode is delivered with small segments while dynamic mode is delivered with the MLC continuously moving as the dose is delivered (Khan, 2014; AAPM, 2001). On the other hand, VMAT treatment is delivered with dynamic movements of the MLC and gantry rotating simultaneously with varying dose rate. In all the cases mentioned above, the dose is delivered with very small field aperture sizes. Small field beam dosimetry requires more

investigations and field output measurements (Azangwe et al., 2014). The general formalism for small field dosimetry defined by Alfonso et al. (2008) consists of an approach to determine the absorbed dose to water using machine specific reference fields. The IAEA in collaboration with the AAPM, has published a code of practice, protocol that addresses small-field dosimetry, known as IAEA TRS 483 (IAEA, 2017), in which small fields are defined by at least one of three physical conditions: loss of lateral charged particle equilibrium (LCPE), partial occlusion of the primary photon beam and the size of the detector relative to the field (Alfonso et al., 2008).

The field output factor data that are collected for commissioning of a commercial TPS are defined by the vendor. The missing data are interpolated or extrapolated using the TPS algorithms like Monte Carlo, Collapsed Cone and Pencil beam. It is therefore very important to perform measurements of small field output factors with a detector suitable for small fields measurements to ensure that TPS commissioning data is accurate (Wuerfel, 2013; Followill et al., 2012). The measured field output factors are then corrected for detector response, which can be determined from a direct measured value, an experimental generic value or a Monte Carlo calculated generic value (IAEA, 2017).

The output correction factors are determined for each small field size defined by full width half maximum (FWHM) at the detector measurement depth for both the in-plane and cross-plane beam profiles. For a small rectangular field with uneven in-plane and cross-plane FWHMs, the equivalent square small field size (S_{clin}) is given by equation 2.1.

$$S_{clin} = \sqrt{AB} \quad 2.1$$

where A and B are the in-plane and cross-plane dosimetric field widths obtained from FWHM of the measured profiles, during measurement of profiles (IAEA, 2017). It is important to align the detector in the proper orientation as in figure 2.13 to minimize the effect of extra cameral current due to stem or cable signals.

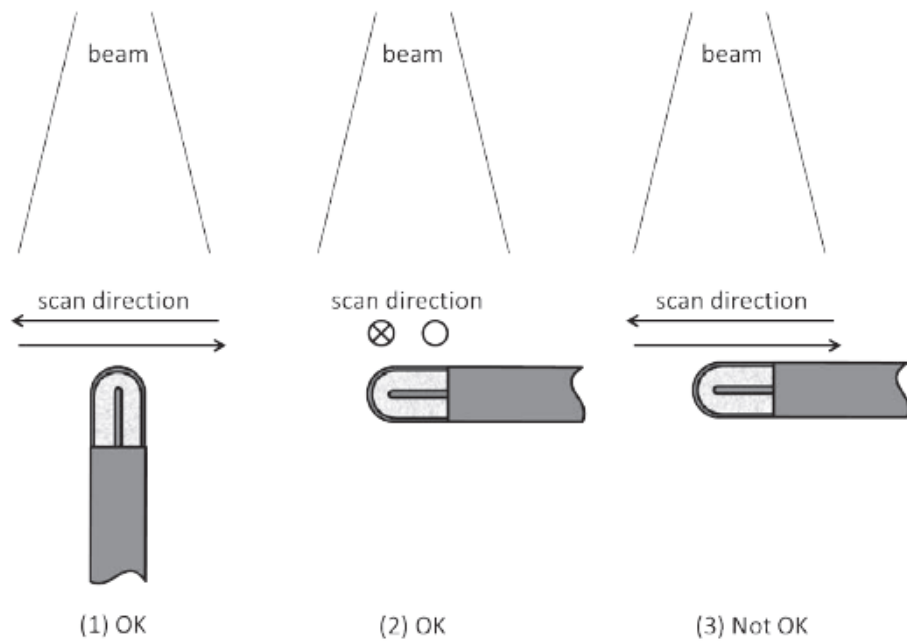


Figure 2.13 Detector orientation for measurements of lateral beam profile with arrows indicates scanning directions in the paper plane while circle and crossed circle symbols refer to scanning directions perpendicular to the paper plane (IAEA, 2017).

The centre of the radiation field must be determined at different positions when scanning the profiles, and this need to accurately be aligned or corrected with the central beam axis (CAX correction).

Different types of detectors can be used for the measurement of output factors for small fields, however, there is no ideal detector for performing these kinds of measurements. For the determination of both field output factors and lateral beam profiles, it is recommended by the IAEA TRS 483 (2017) that two or more different types of suitable detectors should be used so that redundancy in the results can provide more confidence and assurance that no significant dosimetry errors are being made. The field output factor ($\Omega_{Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$) is given by equation 2.2.

$$\Omega_{Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}} = \frac{M_{Q_{clin}}^{f_{clin}}}{M_{Q_{msr}}^{f_{msr}}} k_{Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}} \quad 2.2$$

where $k_{Q_{clin}, Q_{msr}}^{f_{clin}, f_{msr}}$ is the output correction factor, which can be determined as a direct measured value, an experimental generic value or a Monte Carlo calculated generic value.

The readings $M_{Q_{clin}}^{f_{clin}}$ and $M_{Q_{msr}}^{f_{msr}}$ are obtained from detector measurement corrected for influence quantities in the clinical field and the machine specific reference (msr) field. The values of the output correction factor for a range of detectors are given in Tables 26 and 27 for 6 MV and 10 MV flattened beams in the IAEA TRS 483 (IAEA, 2017). Recommendations for other technologies capable of producing small fields are also listed in the code of practice. When auditing these technologies, the accuracy of the TPS small field data may need to be audited separately in order to establish whether there is a systematic error in all small field applications.

2.6 Dosimetry audits in South Africa

According to the South African Health Products Regulatory Authority (SAHPRA), part of the licensing requirements that are stipulated in an Annexure A of the license for the use of electronic products in radiotherapy (see Appendix B), is that a comprehensive quality management system for radiation safety must be compiled. This should include policies, procedures, protocols, tests and evaluations as well as roles and responsibilities of respective members of radiation oncology team. The requirements also include independent verification of the results of QC tests, which form an essential part of QA programme (Shapiro, 2002; Mayles, 1999). During the process of dosimetry audits, it was assumed that all centres were compliant with licensing requirements as they held valid licenses issued by the authority, and that their QC procedures were in accordance with SASQART (SASQART, 2013) since their units were operational clinically. As a result, no proof of compliance was requested.

Radiotherapy centres in South African are historically invited to participate in the IAEA/WHO reference beam dosimetry audits. The efforts to create a routine, national reference dose audit through the National Metrology Institute of South Africa (NMISA) was initiated 20 years ago. Anonymized results were presented at the South African Association of Physicist in Medicine and Biology (SAAPMB) annual congresses. These audits utilized a dosimetry kit, which was sent to centres to verify their photon reference beam output based on IAEA TRS 398 (IAEA, 2000). Furthermore in 2017, NMISA piloted an on-site photon reference beam dosimetry audit using an independently calibrated ionization chamber and the results from five participating centres were within 3.0% (Maselesele et al., 2017).

Subsequently, as part of establishing national dosimetry audits in South Africa, a pilot 3-D CRT audit based on IAEA TECDOC-1583 (IAEA, 2008) was carried out at four different centres. An ionization chamber and the CIRS phantom were used, and the dose verification measurements were carried out at the isocentre represented by the three-point markers on the phantom surface. The comparison between TPS calculated dose and measured dose inside the phantom was within 7.5%. (Maselesele et al., 2019). The highest difference was attributed to one of the dose measurement points positioned in the low-density lung area, close to the edge of the field and the use of an ionization chamber volume of 0.6 cc. Recommendations included the need for follow-up methodologies to be developed, wider participation from centres, and a treatment plan with dose verification points such that the detector is not positioned where low Hounsfield number tissues are adjacent to much higher Hounsfield number tissues (Maselesele et al., 2019). Similar observations were made by Adolfsson et al. (2014) following a pilot study that was conducted at four centres for dosimetry audits in 3-D CRT.

There is no existing end-to-end national dosimetry audit program for more complex treatment techniques in South Africa. As a result, this study was initiated to develop and pilot an end-to-end methodology for complex techniques to expand the audit scope and to address challenges that may arise when the audits are established at the national level.

It is important to clarify that clinical audits, as outlined by the European Commission (EURATOM, 1997) and in a similar way by IAEA/WHO QUATRO (IAEA, 2022), are not applicable to regulatory inspections and as such they should not be for regulatory compliance or used as an enforcement tool. There should be a national approach that highlights the need for participation in national audits and encourages voluntary participation to ensure quality in radiotherapy processes. The department quality manuals should include all elements and information that should be made available to an audit team (IAEA, 2022; IAEA, 2016).

There are different types of audits that can be performed based on the availability of the resources. Quality audits such as QUATRO can be arranged through coordination of the IAEA with the aim of strengthening radiotherapy human resources, infrastructure and improving treatment delivery. These include a team of radiotherapy experts who visit the centre for a planned period to perform on-site review, evaluation and measurements. Dosimetry audits have been performed worldwide using different methodologies with the aim of achieving uncertainties that are comparable to those provided by the major dosimetry audit groups (IAEA, 2016; Rosenblatt et al., 2015; Koniarova et al., 2014; Izewska et al., 2007).

Table 2.1 list different types of audits, the dosimetry equipment used, responsible persons and the uncertainty used during the comparison of doses between the audit group and the participating centres. Audits can be fielded as on-site audits (an individual or team visits the centre) or as remote audits (detectors or equipment is mailed together with audit instructions for the resident team).

Table 2.1 Different types of dosimetry audits with detectors and phantom, their uncertainty and responsible professionals.

Dosimetry audit	Detectors	Phantoms	Uncertainty	Responsibility
Reference beam	Ionization chamber, TLDs, RPLDs, OSLDs	Water and Perspex	5.0%	Medical Physicists
IROC-H credentialing	Ionization chamber, TLDs, OSLD	IROC-H Phantom (Inc., Norfolk, VA, USA)	5.0%	Medical Physicists
IAEA coordinated research projects	Ionization chamber, TLDs and RPLDs	Defined during the design of the project	5.0%	Medical Physicists
QUATRO	Ionization chambers	Hospital Equipment including a 3D automatic beam scanner	5.0%	Medical Physicists, radiation oncologists and radiation therapists
IAEA end-to-end 3-D CRT	Ionization chamber	CIRS (Model: 002LFC)	5.0%	Medical Physicists
IMRT/ VMAT audits	Ionization chamber and film	SHANE, CIRS (Inc., Norfolk, VA, USA)	5.0%	Medical Physicists, radiation oncologists and radiation therapists

Dosimetry for reference beams is performed worldwide primarily through the two major dosimetry audit networks, which are the IAEA and IROC-H. These are performed with a customized detector holder, which is irradiated under predetermined irradiation conditions (Alvarez et al., 2017; Izewska et al., 2007).

Dosimetry audits for complex treatment that involves treatment planning processes, have been performed using phantoms like the CIRS head and neck (Shane) as well as the IROC-H phantoms (Kazantsev, et al., 2020; Mehrens et al., 2016;). For CIRS head and neck phantoms, the targets can be drawn or imported via DICOM, whereas IROC-H phantoms are often manufactured with clearly visible targets and OARs as shown in figure 2.9, which makes treatment planning less variable. Dosimetry audits for advanced technology in radiotherapy have also been performed with a simple cube phantom with predefined targets and OARs (Izewska et al., 2016). The advantage of this approach is that the end-to-end results can be predicted, and the audits can be carried out by the medical physicist alone. However, the biggest disadvantage is that the audit does not then involve the entire radiotherapy team, which should be the main goal of the audit as it is a tool aimed at improving treatment delivery.

The CIRS thorax phantom (Model: 002LFC) has been used by the IAEA for commissioning and auditing of the TPS. In South Africa a pilot study for establishing dosimetry audits for 3-D CRT was carried out in 2017. The results of this study were published, and this also formed the precursor to this research study (Maselesele et al., 2019). This study focuses on establishing dosimetry audits for advanced radiotherapy techniques. The concept of an end-to-end dosimetry audits that involves CT scanning of a phantom, delineation of target and OAR based on a given histology and prescription followed by generation of an approved treatment plan as well as treatment delivery while measuring dose with RPLDs, has not been fully interrogated. This study seeks to develop the end-to-end dosimetry audit methodology for complex radiotherapy treatment techniques which will involve the entire radiotherapy team and to investigate the challenges involved in establishing this methodology.

3. Materials and Methodologies

In 2017, a survey was fielded to 54 radiotherapy centres in South Africa requesting information about their equipment and treatment techniques. This included an invitation to participate in a pilot study for the development of a national end-to-end methodology for auditing complex radiotherapy treatments. The survey was followed by film dosimetry audits for small fields. A remote TPS process was initiated as part of developing and piloting an on-site end-to-end dosimetry audit methodology using a head and neck anthropomorphic phantom. Then dose verification was performed at five participating centres, using an ionization chamber and RPLDs as the detectors of choice. The pilot process revealed deficiencies in the methodology and additional data needed to be requested from the centres in order to arrive at meaningful audit findings.

3.1 Radiotherapy survey

A survey of radiotherapy centres was conducted as part of a feasibility study. This involved sending out a questionnaire (see Form 4.1, section 4.1) requesting information on the equipment and treatment techniques (2-D, 3-D, IMRT or VMAT) in use. Information about the type of beam energies {flattering filter (FF) and flattening filter free (FFF)}, radiotherapy patient setup imaging technologies, TPS models and dosimetry equipment (used for pre-treatment plan verification) were requested. The radiation regulator, through NMISA, was requested to assist with the contacts of responsible person at each centre. The centres were also asked to state the last time they participated in the IAEA/WHO or NMISA reference beam dosimetry audit, or any other equivalent.

A letter was also forwarded to each centre inviting participation in the proposed development of the end-to-end dosimetry audit for complex radiotherapy treatment techniques and requesting access to the radiotherapy equipment, for this purpose. The centres were also requested to confirm availability of the radiotherapy team (radiation oncologists, medical physicist and radiation therapists) to assist in carrying out the audit. More detailed information about the equipment and other relevant parameters (e.g. TPS

algorithm used), was to be obtained on-site once a formal agreement to participate in an audit was obtained.

The expectation was that the Oncologists would review the CT scans, interpret the given histology and prescription, and then perform delineation of target(s) and OAR(s). The oncologist would approve the final plan prepared by the therapists and medical physicist(s). The radiation therapist's tasks included performing the treatment planning in accordance with their local protocols, and then performing the setup of the phantom for the treatment delivery. The medical physicist's responsibilities during the audit included ensuring that all the imaging and treatment equipment were calibrated and that the appropriate planning and delivery QA had been performed. Also, the medical physicists were responsible for performing the dose measurements and placing the detectors in the phantom during the treatment delivery sessions.

3.2 Film dosimetry measurements

A preliminary accelerated dosimetry audit check on a chosen field size was carried out using Gafchromic film. Film calibration was conducted at one centre using film strips of 5.0 cm x 25.4 cm, cut from the same batch of EBT3 film. The films were handled with care to avoid introducing fingerprints and other impurities which may affect the dose. To generate the dose calibration curve, the MU was calculated to deliver doses of 0.5, 1.0, 2.0, 3.0 and 4.0 Gy at a depth of 10.0 cm in Perspex, for a field size of 10.0 cm x 10.0 cm at 90.0 cm SSD in a 6 MV beam. The doses were confirmed prior to film measurement using a PTW farmer ionization chamber inside the Perspex with MU calculated using the correct scaling factor. The film strips were then scanned, more than 12 hours after irradiation using an EPSON (Expression 11000XL) film scanner. The film processing was done using film Pro QA 2014 software (Ashland Inc., Wayne, NJ, USA) from which a dose calibration curve was generated.

From all the centres surveyed, only four centres agreed to participate in the film dosimetry audit. Three Gafchromic EBT3 film strips from the same batch were sent to each centre;

one for background and the other two for irradiation. The centres were requested to deliver a dose of 4.0 Gy at a depth of 10.0 cm and 90.0 cm SSD for a field size of 4.0 cm x 4.0 cm using a 6 MV beam in a Perspex water phantom. The centres were also requested to use their TPS commissioning data to calculate the MU. The choice of a 4.0 cm x 4.0 cm set field was based on the fact that most beam data collection guides require TPS data for this as the minimum field size. The dose obtained with the calculated MU was also verified by performing ionization chamber measurements in the same setup conditions as the film irradiation.

The EBT3 films strips from the participating centres were scanned and analyzed, more than twelve hours post irradiation using the same EPSON film scanner. The dose was computed by calculating the average response obtained at the central area of the scanned film strip using the previously obtained calibration curve and the percentage difference was calculated when comparing with 4.0 Gy stated dose.

3.3 CT scanning for audit Phantom

For this part of the research, an accelerated feasibility study was conducted at one centre, in order to decide on the most practical approach. The initial stage involved acquiring a CT scan image set of the head and neck anthropomorphic CIRS phantom using a Philips Brilliance big bore CT scanner. The phantom consists of anatomical structures that are very close to that of a human being. It can be separated into two parts coronally and one in the axial direction. The posterior and anterior sections are shown in figure 3.1 below with a third small axial section that connects superiorly and is used to hold the two major coronal sections together.



Figure 3.1 Different sections of the dismantled CIRS phantom (Model: 136500) showing the posterior, anterior and third small axial section. The base plate holder (black) is used to hold the sections together.

A film can be positioned between the two major coronal sections of the phantom. The phantom can also accommodate different types of detectors. When detectors are not used, a solid insert of the same material as the phantom is used. During CT scanning, the phantom was positioned using the anterior, left lateral and right lateral markers. These markers were aligned to the centre of rotation of the CT and this position was considered the zero-scan position. No immobilization was used, and the radiation therapists performed the phantom setup. CT scans of the phantom were to be acquired using the imaging protocol of the participating centres and it was assumed that local routine imaging tests had been performed. The entire CIRS head and neck phantom was scanned including the supraclavicular area.

Another set of CT scans was acquired to determine the dose using five RPLDs in the central detector slot. This test was mainly to quantify the dose contribution from the CT scan. These same points of interest were to be used ultimately in the TPS as dose points in the end-to-end audit.

Histology and dose prescription for a head and Neck case (***Cancer of the oral cavity, Stage 2 with positive nodes. Target volume treated to 70 Gy in 35 fractions***) was discussed with five radiation oncologists. It was agreed that during the TPS processes each participating centre would delineate their own target volume(s) on-site, based on the proposed histology and prescription. It was assumed that all relevant ICRU guidelines and recommendations would be used (ICRU, 2010; ICRU, 1999; UCRU, 1993).

3.4 Treatment planning processes

Five centres agreed to participate in the dosimetry audit of the treatment planning processes. To compare the differences in the TPS inhomogeneity corrections, data for CT number (HU) to electron density (ED) calibration curves were requested from each centre. This data was used to evaluate the differences that may arise from TPS calculations when inhomogeneity corrections are applied.

The TPS audit data collection form, as given in appendix C, was sent to each participating centre outlining the processes that should be followed. CT scans of the CIRS phantom were expected to be acquired using the imaging protocol of the participating centres. The instruction also required that the radiotherapy team contour the body outline, treatment target volumes and all OARs using the departmental protocols. All constraints and objectives were to be applied as per the local treatment planning protocol, when preparing and approving the treatment plan. The radiation oncology team was responsible for delineating target volumes, OAR and suggesting the possible treatment technique to be used, in order to contribute their experience to the development of this methodology. The treatment planning team then commenced with the treatment planning processes. On completion of the treatment planning, the plans were presented to the oncologist for evaluation and approval.

The team was requested to report their reasons for choosing a particular treatment delivery technique and to report on the time spent on delineating the volumes. All information relating to the target volume borders on Anterior, Posterior, Superior and

Inferior was also requested. Details including the volumes (in cm³) of the delineated target and OARs were requested on the reporting TPS audit form. As part of treatment planning reports the TPS type, algorithm, calculation grid, smallest field segment allowed in the TPS, MLC type and leaf width were also requested. Plan evaluation parameters including the DVH, and the minimum, mean and maximum doses for all volumes were also requested.

Finally, the participating centres were requested to provide information relating to the treatment setup imaging protocol used (if applicable). TPS screen shots for specified CT slices with the relevant dose information, were also requested. The resources and services for requesting data in the form of DICOM files were not available, and therefore screen shots and printouts were considered the most viable options for data collection. Using screen shots limits assessment capabilities since there is lack of image adjustment. DICOM files would have provided more data and an automated platform to view, adjust, select or process information.

For each treatment plan, five specified-dose points of interest were requested. The length of each RPLD holder is 9.5 mm, so the five positions covered a length of 47.5 mm. The central RPLD (number 3) was positioned at the centre of the CIRS phantom, which was coincident with the zero-scan position as defined by the external markers on the phantom, as shown in figure 3.2.

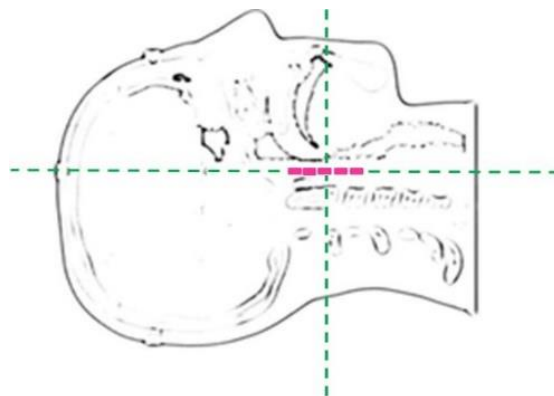


Figure 3.2 Sagittal section of the phantom showing five RPLDs positions, where RPLD 3 is centred at the zero-scan position.

The information received back from the data collection forms from the participating centres was analyzed by computing the correlation coefficient (CV) given by equation 3.1.

$$CV = \frac{\sigma}{\bar{X}} \quad (3.1)$$

Where,

σ is the standard deviation of the data set obtained from participating centres which is calculated using equation (3.2) and, $\bar{X}$ is the average of the data set (BIPM, 2008).

$$\sigma = \sqrt{\frac{\sum (X_i - \bar{X})^2}{N}} \quad (3.2)$$

Where X_i is the individual data received from participating centres and, N is the number of data set received from participating centres. All the parameters used for analysis were calculated using Microsoft Excel.

3.5 On-site treatment delivery processes

After the treatment planning processes were completed, an on-site visit for treatment delivery and dose measurements was arranged. The predefined dose points of interest where the different detectors or dosimeters (the ionization chamber and RPLDs) would be positioned inside the CIRS head and neck phantom slots, were used for on-site dose measurements. For ionization chamber measurements, the dose was measured at the zero-slice at the position of the central RPLD (number 3).

3.5.1 Dose measurements using an ionization chamber.

A PTW 3-D pinpoint ionization chamber (Type: 31022) with sensitive volume of 0.016 cm³, calibrated at the PTW laboratory for absorbed dose to water at Co-60, was used to measure the dose. The choice of this ionization chamber was based on the treatment delivery techniques, which were sliding IMRT and VMAT where small beamlets or

segments are delivered to the target volume and as such a calibrated chamber with small volume was considered suitable. The energy dependent correction factors (k_Q) were determined from methods described by other authors (Maphumulo, 2020). The ionization chamber was inserted into a fixed position, which corresponded to a predefined dose point as shown in figure 3.3. The perturbation caused by the presence of the ionization chamber itself was not considered to be significant (owing to its small volume) and was not accounted for in the dosimetry.

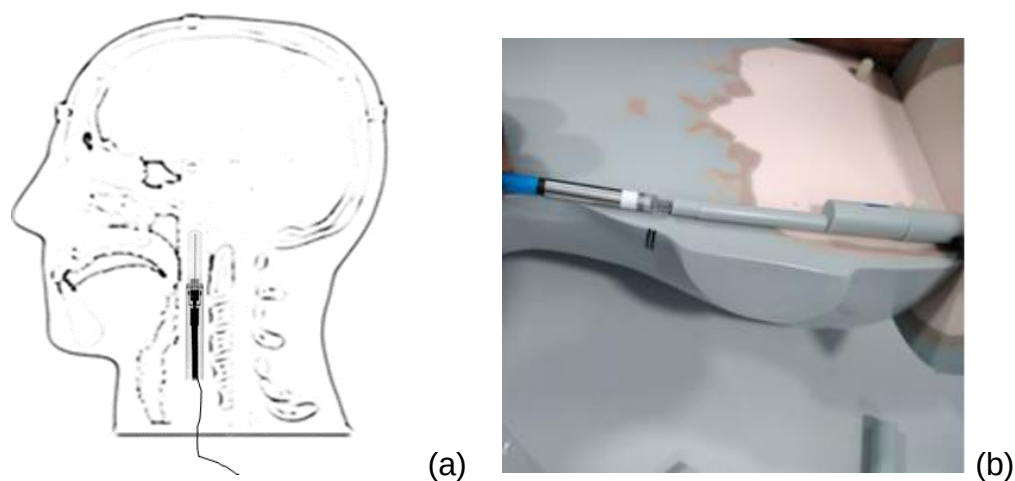


Figure 3.3 (a) Sagittal section of the CIRS phantom indicating the position of the ionization chamber when inserted (b) Illustration of the chamber position, which is aligned to the lateral marker on the phantom.

The ionization chamber was positioned inside the CIRS head and neck phantom such that it was also at the centre of the phantom indicated by the markers on the anterior and lateral sides of the phantom. Films were not used in this dosimetry audit based on the consideration that they need special handling and the generation of calibration curves for dose computations. Also, the allocated time and resources at the participating centres were very limited to carry out these procedures.

The CIRS head and neck phantom was positioned on the treatment couch of the linac using the three-point markers aligned to the lasers, as indicated in figure 3.4 (b).

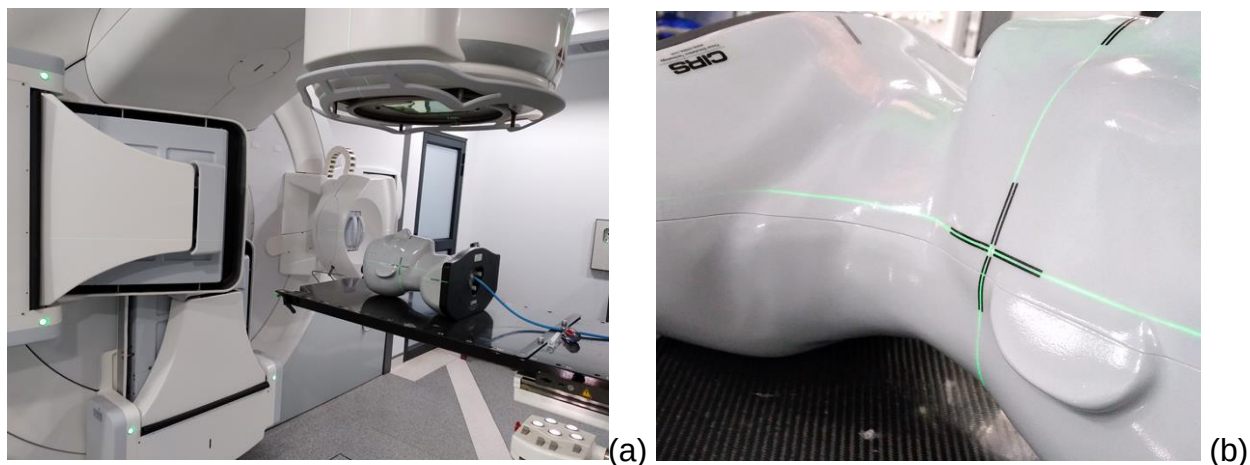


Figure 3.4 (a) Linac setup with ionization chamber inside the CIRS head and neck phantom (b) CIRS phantom showing the lasers projected on the phantom marker.

The linac gantry, collimator and couch were positioned at zero degree. Setup tools like distance indicators and crosshairs were also used. The approved plan was delivered, and the dose measured by the ionization chamber was compared with the TPS dose and calculated as a percentage difference.

3.5.2 Dose measurements using RPLDs.

The CIRS head and neck phantom is usually customized with different inserts for ionization chambers or solid-state detectors depending on the measurements to be done. Films were not used for this part of audit using the CIRS phantom after considering the challenges mentioned in section 2.3 and only RPLDs were used. For this study, there were no customized inserts for the RPLD holders. A Polylactide (PLA), which is a thermoplastic polyester with backbone equivalent material of density 1.2 g/cm^3 , was used to create a customized RPLD holder insert. The insert, shown in figure 3.5, was designed and manufactured using a milling machine that employs 3-D printing technology. The inner and outer diameter of the holder was 3.0 mm and 13.0 mm irrespectively, and to accommodate a minimum of 5 RPLDs, the length of the insert was 115 mm.

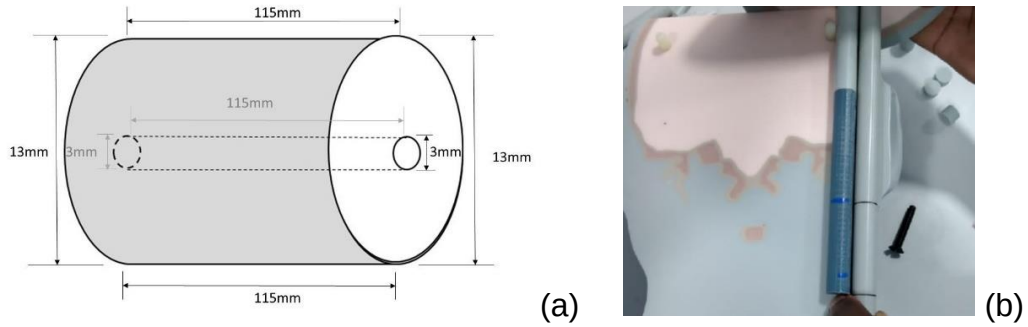


Figure 3.5 (a) Schematic Illustration of RPLD insert showing the dimensions, and (b) the customized RPLD insert (blue) used for positioning the RPLDs, placed next to the insert for the ionization chamber that was provided by CIRS (light grey).

The five RPLDs were positioned inside the holder shown in figure 3.6(a) and inserted in the phantom. The length of the cavity was such that the central position of the third RPLD corresponded to the blue mark on the RPLD holder, as indicated in figure 3.5 (b) or 3.6 (b) which is the zero-scan position inside the phantom (when the three external markers are aligned). All the positions and the identity of each RPLD were also noted. Figure 3.6 (b) shows the holder next to the RPLDs before they are inserted inside the phantom in accordance with the locations shown in 3.6 (a).

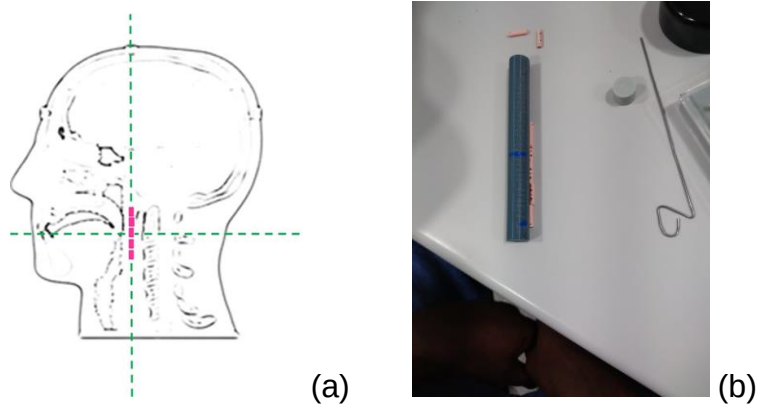


Figure 3.6 (a) Schematic illustration of RPLDs position (b) 3-D printed insert next to two RPLDs showing the relative dimensions as well as the pin that is used to remove them from the insert.

The approved plan was delivered again with the five RPLDs inside the phantom. All the RPLDs (including the ones irradiated with the CT and the three reserved for the background) were returned to NMISA for remote analysis.

3.5.3 RPLD dose computation.

When the irradiated RPLDs were prepared for readout, three reference calibration RPLDs are added to the same reading magazine. These reference calibration RPLDs were prepared at NMISA before transporting the RPLD sets to the participating centres. The reference RPLDs were irradiated to 2.0 Gy in a Co-60 beam at NMISA. After reading the RPLDs a calibration factor was calculated using equation 3.3, which was used to determine the dose to the RPLDs received from the participating centres.

$$N_{krpld} = \frac{GD}{D_{rpld}} \quad (3.3)$$

Where,

N_{krpld} is the individual RPLD calibration factor.

GD is the given dose.

D_{rpld} is the raw counts/reading from the RPLD.

Each reading was corrected for the reading magazine correction factor (f_{mag}), sensitivity factor (f_{scf}) and beam quality correction factor (f_{energy}). The factors were obtained from the RPLD commissioning data (Maselesele et al., 2017).

The measured doses were compared with the doses from the TPS dose points obtained from participating centres. The percentage errors and the RPLDs uncertainties of these measurements were calculated.

3.5.4 Measurement of field output factors.

Each participating centre was also requested to provide the field output factors calculated by their TPS based on their commissioning data. The data was requested for set field sizes of 0.5 cm x 0.5 cm, 1.0 cm x 1.0 cm, 2.0 cm x 2.0 cm, 3.0 cm x 3.0 cm, 4.0 cm x 4.0 cm, 5.0 cm x 5.0 cm and 6.0 cm x 6.0 cm for a setup of 90.0 cm SSD and 10.0 cm depth in water.

Field output factors were then also independently measured at one centre (centre 1) for the same set field sizes and setup, and three measurements were taken for each field size for uncertainty calculation. The measurements were carried out in a PTW BEAMSCAN 3-D scanning water tank. Three different types of PTW detectors, 3-D pinpoint (Type: 31022 of volume 0.016 cm³), 3-D semiflex (Type: 31021 of volume 0.07 cm³) and a synthetic microdiamond (Type: 60019 of volume of 0.004 mm³) were used. The field size limitations used for the detectors are given in table 3.1 (Maphumulo, 2020; IAEA, 2017). The field size limitation is defined by identifying the field size at which the field output correction factor exceeds 5.0% (IAEA, 2017).

Table 3.1 The field size limitations of the detectors that were used as a function of their orientation in the beam (Maphumulo, 2020; IAEA, 2017).

Selected detectors	Field size limitation (perpendicular orientation)	Field size limitation (parallel orientation)
PTW 3-D PinPoint (31022)	1.0 cm x 1.0 cm	1.0 cm x 1.0 cm
PTW 3-D Semiflex (31021)	1.2 cm x 1.2 cm	1.2 cm x 1.2 cm
PTW Microdiamond (60019)	-----	0.4 cm x 0.4 cm

Profiles in both in-plane and cross-plane were scanned in order to confirm the field sizes, which were determined from the FWHM after determining the central axis (CAX) correction, which was adjusted to be within 0.5 mm. The measured field output factors were repeated three times for each field size and then corrected using field output factor

correction factors for a 6 MV beam for each detector and then compared with the TPS values. The field output factor correction factors and the uncertainties that were used for the different detectors and different field sizes for a flattened 6 MV beam with MLC, are given in table 3.2 and were obtained from published data (Casar et al., 2020; IAEA, 2017). The measurements carried out at centre 1 were used to compare the field output factors obtained from the three detectors. The calculated TPS field output factors obtained from the participating centres were then compared to the data from centre 1. An assumption was made that the equivalent square field sizes for the TPS data received from all centres were the same as the set field size. In addition, it was assumed that the 6 MV flattened beams collimated with MLC that were used at all the centres would have very similar field output factors because no distinction between machine type is made in the field output factor correction factors published in the IAEA TRS 483 (IAEA, 2017).

Table 3.2 The field output factor correction factors that were used for the different detectors for selected equivalent square field sizes in a 6 MV beam (Casar et al., 2020; IAEA, 2017).

	Output factor correction factors for detectors and their standard uncertainties (U_x)					
Equivalent Square Field Size (cm ²)	PTW 3-D Pinpoint (31022)	U_x (Casar et al., 2020)	PTW micro diamond (60019)	U_x (IAEA, 2017)	PTW 3-D Semiflex (31021)	U_x (Casar et al., 2020)
0.5	---	---	0.962	0.8%	---	---
1	1.039	0.3%	0.984	0.5%	---	---
2	1.004	0.2%	0.977	0.4%	1.007	0.2%
3	1.004	0.2%	1.000	0.4%	1.003	0.2%
4	1.000	0.2%	1.000	0.3%	0.994	0.2%
5	1.000	0.2%	1.000	0.3%	0.996	0.2%
6	1.000	0.2%	1.000	0.3%	0.997	0.2%

4. Results and analysis

4.1 Radiotherapy survey

Nine of the 54 centres responded to the survey of radiotherapy equipment. Form 4.1 shows the information requested from the centres during the initial equipment survey questionnaire. Only five centres agreed to the invite to participate in national radiation dosimetry audit research activities. No other selection criteria were used. Additional information that included pretreatment setup verifications, MLC types etc were requested using the data collection form used to provide the audit instructions as provided in appendix C. In cases where more data were needed such as the smallest segment in the TPS, calculation grid etc, these were requested separately.

Form 4.1 Initial questionnaire form used to collect radiotherapy information from centres.

National Radiotherapy Dosimetry Audit Programme, Hospital Questionnaire													
NB: Only complete spaces with white background													
Hospital/Institution:				Contacts:									
Responsible Person:				email:									
Radiotherapy equipment and technique													
No.	Treatment Unit			Technique in Use					Treatment Planning Sys		Calibrations, QC & Verification equipment		
	Type	Brand	MV energies	1	2	3	4	5	1	2	TRS 398	QC	IMRT/VMAT
1													
2													
3													
4													
5													
Completed by:				Date									
Position in the Institution				Signature									
SF- Single field, PP-Parallel Opposing Fields, 3D-CRT- 3D Conformal Planning, IMRT- Intensity modulated Radiotherapy, VMAT- Volumetric Arc therapy/RapidArc, IGRT-Image guided RPM-Real Time Patient Management/Respiratory Gating, SRS - Stereotactic Radiotherapy and Others													
NB: Will your center be willing to participate in National radiation dosimetry audit research activities													
NB: This information will be treated with highest degree of confidentiality.													
Comments from the End user:													

The information from the radiotherapy survey feedback received from the nine centres is summarized and given in table 4.1.

Table 4.1 Summary of questionnaire data from different centres.

Centres	Linacs type	Beam type	Technique	Setup imaging technique	Pretreatment QA equipment	Last IAEA Audits
1	Agility	A, and C*	1, 2, 3, 4 and 5**	MV and CBCT	PTW	2017
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV and CBCT	PTW	
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV and CBCT	PTW	
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV and CBCT	PTW	
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV and CBCT	PTW	
2	2100C	A and C*	1, 2,3 and 4**	MV	iba	2017
	TrueBeam	A, B, and C*	1, 2, 3,4 and 5**	MV & CBCT	iba	
3	Unique	A*	1, 2, 3, 4 and 5**	MV	PTW	-
4	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV & CBCT	PTW	2020
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV & CBCT	PTW	
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV & CBCT	PTW	
	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV & CBCT	PTW	
5	Versa HD	A, B, and C*	1, 2, 3, 4 and 5**	MV	SNI	2018
6	2100C	A, and C*	1, 2 and 3**	MV	iba	2017
	TrueBeam	A, B, and C*	1, 2 and 3**	MV & CBCT	iba	
7	Agility	A, B, and C*	1, 2, 3 and 4**	MV & CBCT	PTW	-
8	TrueBeam ST	A, B, and C*	1, 2, 3, 4 and 5**	MV & CBCT	iba	2019
9	Triology	A, B, and C*	1, 2, 3,4 and 5**	MV & CBCT	iba	2019

*: A-MVFF, B-MVFFF and C-MeV

**: 1 – 2-D, 2 – 3-D CRT, 4 – IMRT and 5 – VMAT

From the above table it shows that four centres had more than one linac. Centre 3 did not have FFF beams but performs all four techniques, whereas centre 6 has linacs with FFF

capabilities but only performs 2-D and 3-D treatment techniques. Of all the nine centres, eight of them were treating IMRT and seven were treating both IMRT and VMAT techniques. Out of the seven centres treating both IMRT and VMAT, only one did not have FFF beams. None of the centres provided any reasons for any preference between using FF or FFF beams on both IMRT and VMAT other than dose rate considerations. The MLC used on the linacs were either 120 or 160 leaves. Data provided by the centres indicating the treatment delivery techniques and patient setup imaging techniques are plotted in figure 4.1 below.

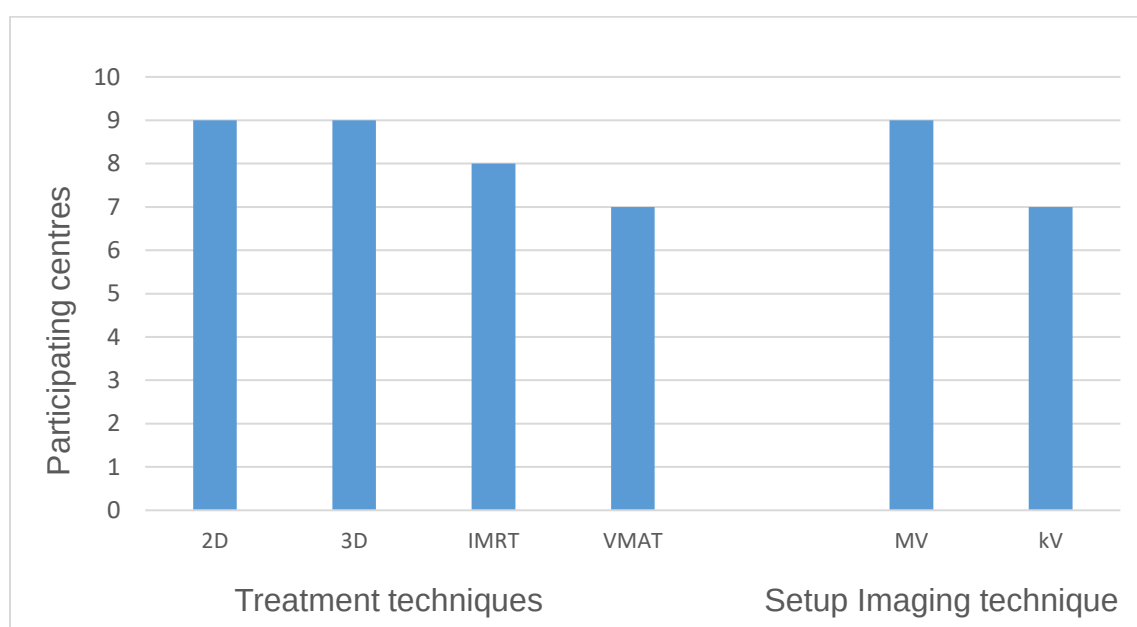


Figure 4.1 Data received showing treatment delivery techniques and radiotherapy patient setup imaging technology from participating centres.

All centres claimed to have QA equipment capable of performing pre-treatment TPS plan verifications on IMRT/VMAT techniques. Most of the centres reported participation in the IAEA/WHO reference dosimetry audits.

The centres who participated in the audits reported that their IAEA/WHO reference beam dosimetry audit results were within the $\pm 5.0\%$ tolerance. Only two centres did not participate in the IAEA/WHO reference beam dosimetry audits and no reasons were provided.

4.2 Gafchromic film dosimetry from participating centres

The film calibration results obtained from the irradiated film strips from one centre are shown in Figure 4.2(a). These were used to generate the film calibration curves as shown in figure 4.2(b).

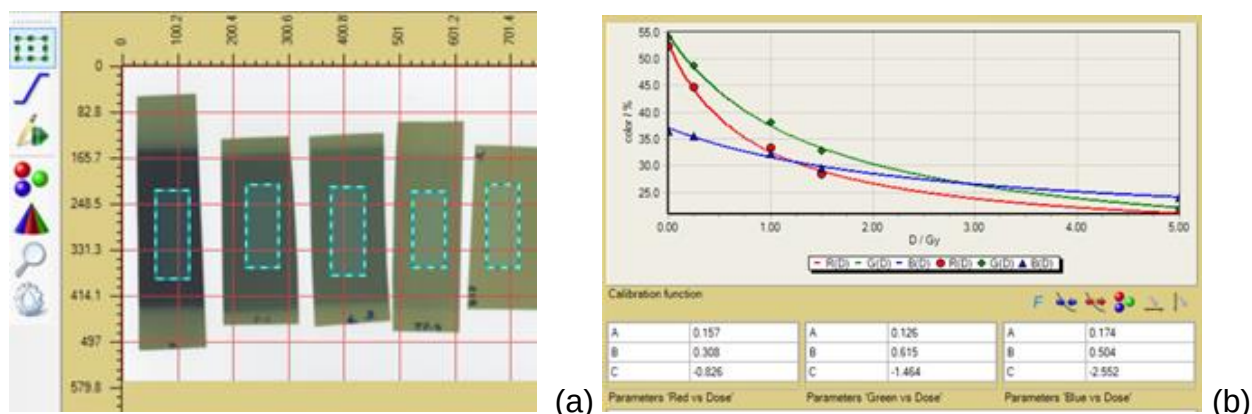


Figure 4.2 (a) Scanned EBT3 film strips and (b) The film calibration curves generated for dose calibration in the different colour range.

Figure 4.3 shows an example of an irradiated film received from one of the participating centres, which were used to verify the dose in the 4.0 cm x 4.0 cm field.

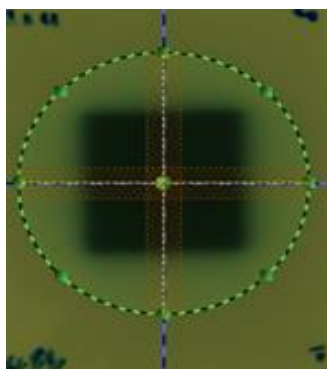


Figure 4.3 An example of the irradiated film from a participating centre.

Table 4.2 provides the stated dose, the absolute dose as measured with an ionization chamber for the calculated MU and the dose obtained from the film dosimetry for the four participating centres. All centres performed ionization chamber dosimetry in accordance with IAEA TRS 398 (IAEA, 2000).

Table 4.2 Comparisons of stated dose with dose measurements carried out using a PTW farmer type chamber (Type: 30013) ionization chamber (% Difference 1) and dose calculated from the film dosimetry (% Difference 2) for the four centres that participated in the small field dosimetry audit.

(4 cm x 4 cm field, depth 10 cm, 6 MV flattened beam)	TPS Calculated MU	Stated dose (Gy)	Locally measured ionization chamber dose (Gy)	% Difference 1 (Stated to measured dose)	Measured film dose (Gy)	% Difference 2 (Stated to measured dose)
Centre 1	486	4.00	4.01	-0.2%	4.11	2.8%
Centre 2	496	4.00	4.01	-0.2%	4.25	6.3%
Centre 3	514	4.00	4.05	-1.3%	4.26	6.5%
Centre 4	488	4.00	4.03	-0.8%	4.18	4.5%

The maximum percentage difference observed between stated and doses measured with the film was 6.5%. The overall uncertainty of the film dosimetry measurements was estimated to be 5.0% as stated by Marroquin et al. (2016). The maximum percentage difference when comparing the stated dose to the ionization chamber locally measured doses was less than $\pm 1.5\%$, which is typical of a daily linac output fluctuation which should be within $\pm 2.0\%$, (AAPM, 2009).

4.3 Treatment planning process for end-to-end audit

4.3.1 CT data analysis

The five centres provided data on CT number (HU) versus relative electron density for -1000 HU, 0 HU and 1000 HU and these are presented in figure 4.4.

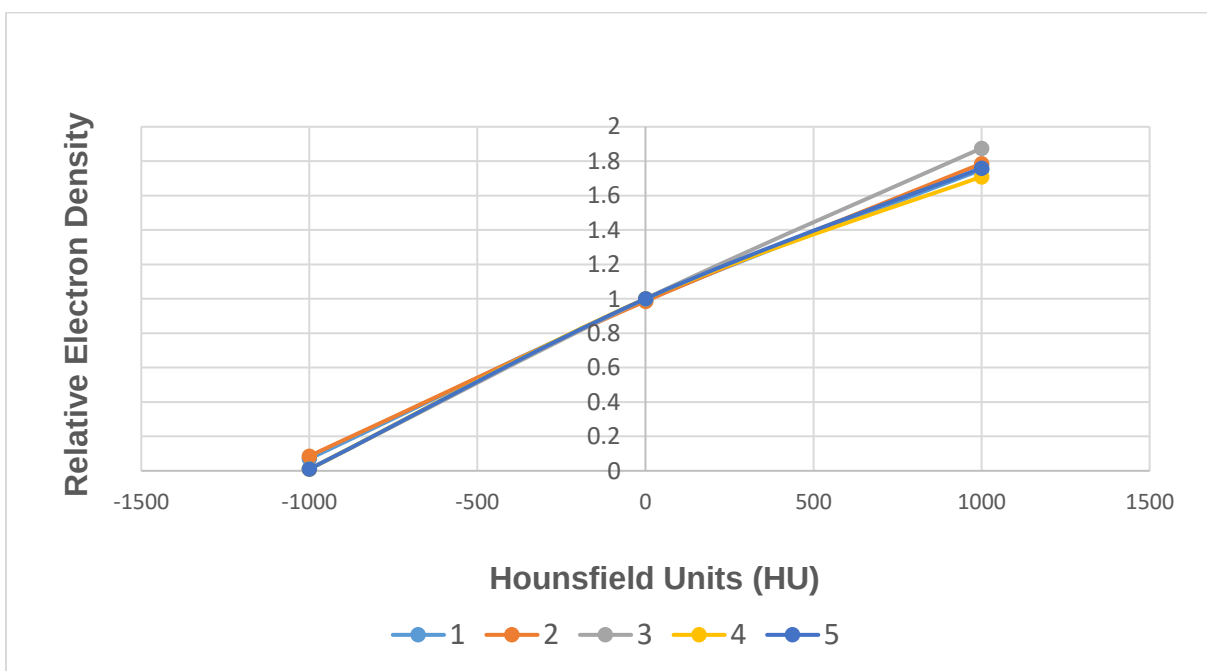


Figure 4.4 Comparison of the CT relative electron density calibration curves for the five participating centres (each represented by a different colour).

The maximum deviation was 3.0% for +1000 HU (representing bony structures) and 1.2% for -1000 HU (representing lung structures) from the five participating centres. The difference that would be obtained from treatment planning inhomogeneity corrections if the audit program was to use the same set of the CT scans at different centres was not considered to contribute significantly to the TPS dose calculation (Cozzi et al.,1998).

The CT dose contribution to the RPLDs from the scanning process are presented in Figure 4.5 below.

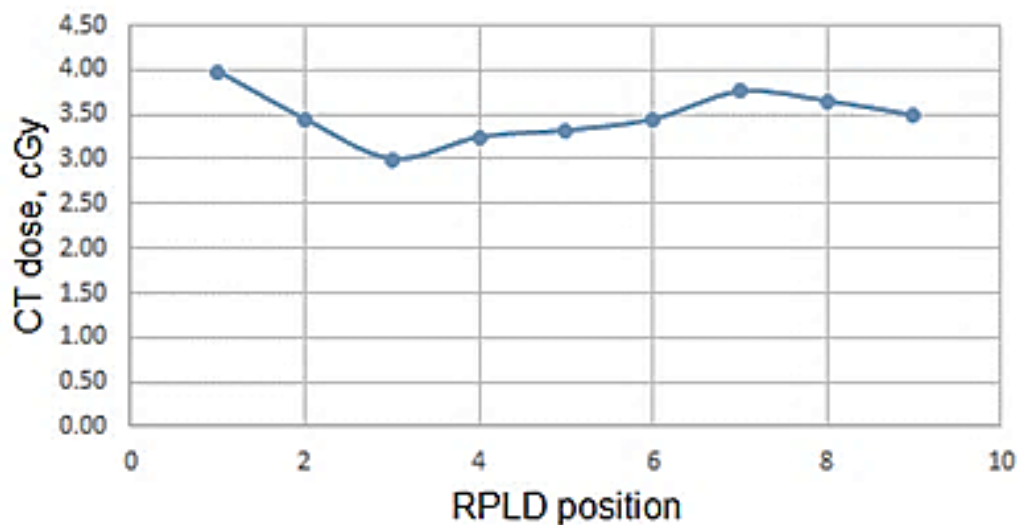


Figure 4.5 CT dose results measured with the RPLDs coincident with the centre of rotation of the CT.

The above result shows that the CT dose contribution to the RPLDs was less than or equal to 0.04 Gy. This dose is significantly lower than the dose prescription of 2.0 Gy per fraction. The calculated CT dose contribution to the RPLD readings was 2.0% when compared to a single fraction dose of 2.0 Gy. This could be considered negligible since the phantom is only scanned once and when comparing CT dose to the total prescription dose of 70.0 Gy the contribution was 0.06%, which is well within the dosimetric uncertainty of 1.0% (Mahur et al., 2017; Cozzi et al., 1998).

4.3.2 TPS processes from participating centres

The phantom was scanned on-site using the external alignment markers as described in Section 3.3. On-site delineation of target volume(s) and OARs was then performed as part of this study. Five centres provided data from the TPS processes, and the results are presented below. Figure 4.6 shows a treatment planning screenshot from one of the participating centres. The figure shows dose coverage on a transverse, sagittal and coronal view as well as the plan reporting statistics. Similar screenshots were received from the other four participating centres.

Figure 4.6 shows that a VMAT plan was produced. The target volumes and OAR (spinal cord, brain, mandible and brain stem) that were delineated, are shown.

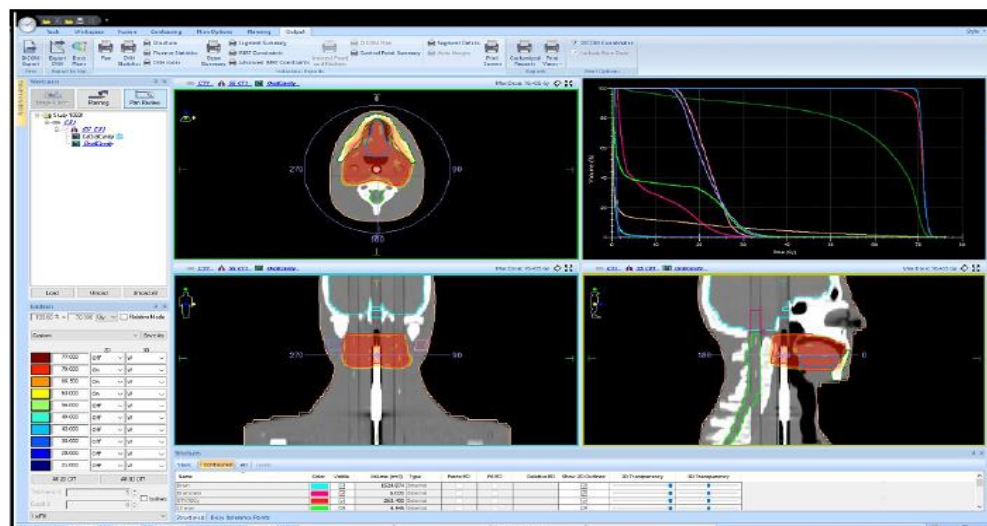


Figure 4.6 Sample TPS report from one centre showing dose coverage in different views.

To compare the target dose coverage, a transversal slice obtain within 3 mm superior to the zero slice was requested from the five centres and the results are shown in figure 4.7. The slice is located at the reference markers on the phantom (see Figure 3.4) and represents the zero slice and is also the measurement position of the ionization chamber and the central RPLD 3 (see Figure 3.6).

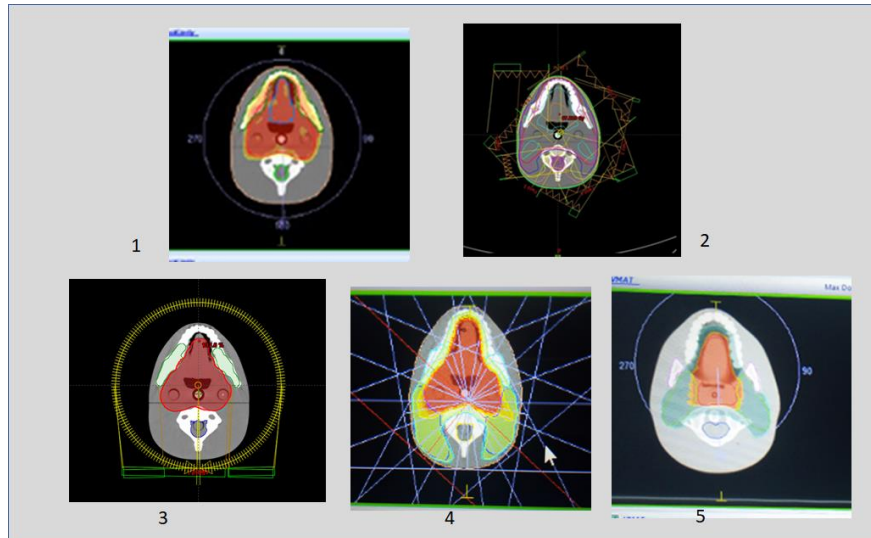


Figure 4.7 Comparison of target and dose coverage on the same transversal slice from the five participating centres.

It is evident that some Oncologists preferred to delineate a single target including the nodal volumes, whereas others delineated separate volumes. Assumptions were made that each centre will use appropriate guidelines and recommendations from ICRU (ICRU, 2010; ICRU, 1999; ICRU, 1993). Similarly, the dose coverage of the central sagittal view is shown in figure 4.8.

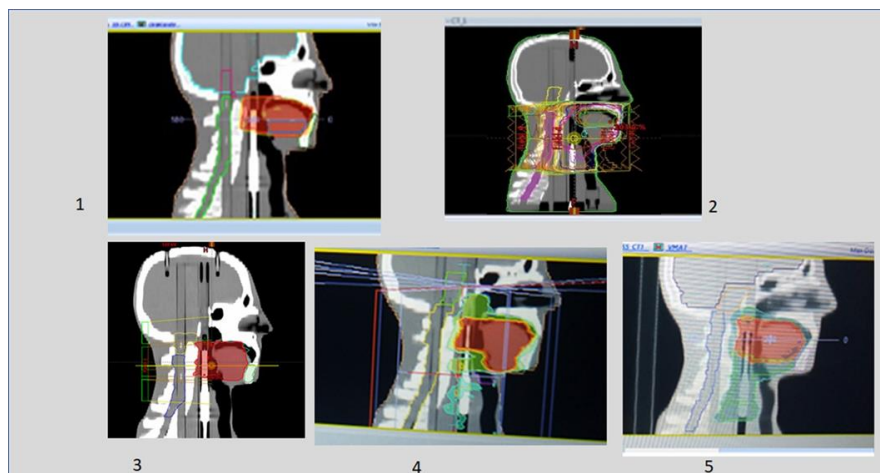


Figure 4.8 Comparison of target and dose coverage on the central sagittal slice from the five participating centres.

Differences can be seen in the anterior, posterior, superior and inferior borders that were delineated at each centre. From figure 4.8, both the superior and anterior borders of the delineated targets showed small variation when assessed visually. The posterior border, which was along the spinal cord, also did not show major differences. The results are also summarized in Table 4.3A, indicating the extent of anatomical levels for the superior, inferior, anterior and posterior borders of the target volume.

Table 4.3A A comparison of the anatomical levels used for the borders of the target volume as described by the five different radiotherapy teams.

Centre	Superior	Inferior	Anterior	Posterior
1	Below the base of the skull	C7/T1	Mentum	The anterior aspect of vertebral bodies
2	Zygomatic arch (TM joint)	SSN	Clear Lips	Post Spinal Process
3	Base of skull	Insertion of Clavicle	Mandible	Vertebral body
4	1cm above the hard palate	Usually, to thyroid the match SFC	Mandible	To involve posterior neck nodes
5	Inf border of mandible	Ant of spinal cord	Beginning of hard palate	The base of the oral cavity

Table 4.3B shows the TPS type, software version, algorithm and the number of leaves for the MLC of the treatment delivery system, that was used for the treatment planning at each centre.

Table 4.3B The TPS type, software version, algorithm and the number of leaves of the MLC that was modelled in the TPS that was used at each centre.

Centre	TPS type	Version	Algorithm used	Number of leaves for the MLC modelled in the TPS
1	Monaco	5.11.02	Monte Carlo	160
2	Eclipse	15.5	Acuros XB	120
3	Eclipse	15.5	Acuros XB	120
4	Monaco	5.11.03	Monte Carlo	160
5	Monaco	5.11.03	Monte Carlo	160

Table 4.3B shows the TPS type, version, algorithm and MLC type that was modelled and then used for the complex treatment planning calculations carried out at each participating centre.

The time spent delineating the target volume(s) is shown in table 4.3C. Centres were not requested to provide times spent in delineation of OAR.

Table 4.3C Time (minutes) spent at each of the five participating centres to draw the target volume(s).

Centres	Time (Min)
1	22
2	20
3	15
4	30
5	15

From the TPS plan samples that were received, the selected technique and MU to deliver the plan is summarized in table 4.3D for the IMRT and 4.3E for the VMAT plans.

Table 4.3D Summary of IMRT MU calculated by the TPS at centres 2 and 4.

IMRT Fields	Field 1	Field 2	Field 3	Field 4	Field 5	Field 6	Field 7	Field 8	Field 9	Total MU
Centre 2 (MU)	176	152	89	124	134	87	133	---	---	895
Centre 4 (MU)	194	166	161	123	159	169	220	225	299	1716

The comparison between the two centres, which use two different types of TPS, showed that centre 4 calculated MU that is almost twice that of centre 2. Centre 2 has 120 MLC leaves while centre 4 has 160 MLC leaves and, this suggests that centre 4 used an increased number of levels of intensity and/or a higher proportion of small field size segments since the same energy (6 MV) was used for both centres.

Table 4.3E Summary of VMAT MU calculated by the TPS at centres 1, 3 and 5.

Centre	Technique	Arc 1 (MU)	Arc 2 (MU)	Total MU
Centre 1	VMAT	390	513	903
Centre 3	VMAT	444	---	444
Centre 5	VMAT	877	---	877

There was a significant difference observed in the total MUs calculated by the TPSs when comparing centre 3 to centres 1 and 5, which were almost double. Centre 3 has 120 MLC leaves while centres 1 and 5 have 160 MLC leaves. VMAT is dependent on the design of the treatment unit and the treatment delivered is based on a combination of dose rate, gantry position and speed, and MLC leaf speed.

Table 4.3F shows data on the techniques, target volumes, TPS calculated minimum, mean and maximum doses for the respective approved plans. Data for the variation, e.g.

standard deviation, conformity index, etc. on the target dose were also requested from each centre. The centres did not use these metrics consistently to evaluate plans and the calculated metrics were different for each TPS type, hence these results were not considered useful to this study. In addition, there was no well-defined tumour and nodal GTVs, CTVs and PTVs from the centres. As a result, the calculation of these metrics was not considered relevant, and it was therefore not possible to assess and compare target dose variation in terms of these metrics.

Table 4.3F The techniques, target volumes, and minimum, mean and maximum doses to the targets as reported from each centre.

Centre	Technique	Target volume (cc)	Minimum Dose (Gy)	Mean Dose (Gy)	Maximum Dose (Gy)
1	VMAT	195.80	61.6	71.47	76.51
2	IMRT	175.10	63.7	70.07	73.43
3	VMAT	234.70	67.9	71.54	76.65
4	IMRT	216.83	40.6	72.35	77.70
5	VMAT	263.40	55.3	72.10	76.72

There was fair correlation amongst all centres for both the mean and the maximum dose, which was within 2.2%. It is however clear that only Centre 2 appears to be closest in complying with the ICRU report 83 prescription recommendations (ICRU, 2010).

All the centres reported that the tolerances used for each critical organ were obtained from Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC), (Emami, 2013) and these are tabulated in table 4.3G with the full table presented in appendix D.

Table 4.3G Dose tolerances to critical organs obtained from QUANTEC (Emami, 2013).

OAR	Structure type	Tolerance doses
Spinal Cord	Serial	45 Gy (Max Dose)
Brain	Serial	60 Gy (Max Dose)
Brainstem	Serial	55 Gy (Max Dose)
Parotid (Unilateral/Bilateral)	Parallel	20/25 Gy (Mean dose)
Mandible	Serial	70 Gy (Max Dose)

The tolerance doses for each OAR were also reported (see Appendix D). More detailed dose-volume and spatial dose data was not requested, and DICOM-dose files were not available in this study. Figure 4.9 shows the comparison of the parotid OAR volumes.

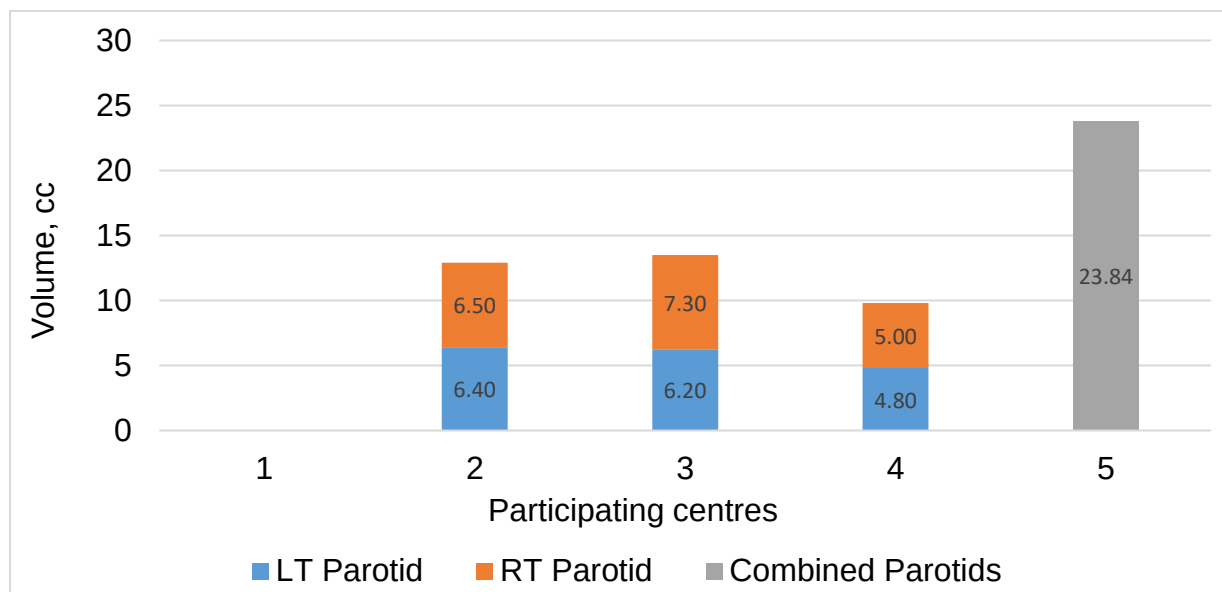


Figure 4.9 Comparison of parotid OAR volumes (cc) obtained from the participating centres (using a different colour for each OAR).

Three centres chose to draw both left and right parotid separately while one centre drew it as one structure. One centre did not draw parotid structures at all and on follow up it was mentioned that there was insufficient anatomical detail in the phantom to localize the

parotid structure. Phantoms would not easily show the proper anatomic details as compared to the actual patient scans since they are designed differently. The mean dose to the parotid is shown in figure 4.10.

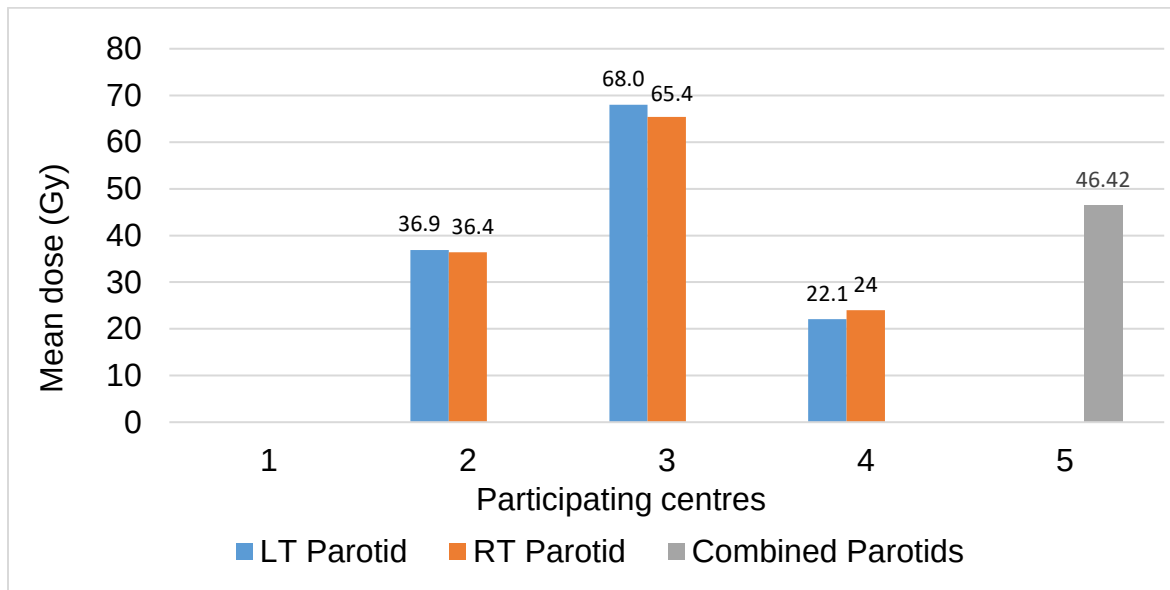


Figure 4.10 Comparison of the mean dose to the parotid OARs obtained from the participating centres (using a different colour for each OAR).

Analysis of the mean dose shows that a minimum of 22.0 Gy and a maximum of 68.0 Gy on the bilateral parotids was achieved. The mean doses for the parotids were therefore above the stated mean dose constraints for all the centres (25 Gy for bilateral parotids and 20.0 Gy for unilateral parotid). One of the main reasons cited for not reaching or forcing this constraint was the difficulty to delineate the parotid on the phantom since the structure was not visible.

Similar analyses were made for the serial structures (brain, brainstem, spinal cord and mandible). The inconsistency in OAR delineation is an indication that treatment plan approval across centres can be based on different information, which can lead to different dose evaluation and reporting. This leads to an inconsistency in the dosimetry audit results when comparing between centres.

Figure 4.11 shows the comparison of OAR volumes for the brainstem, spinal cord and mandible.

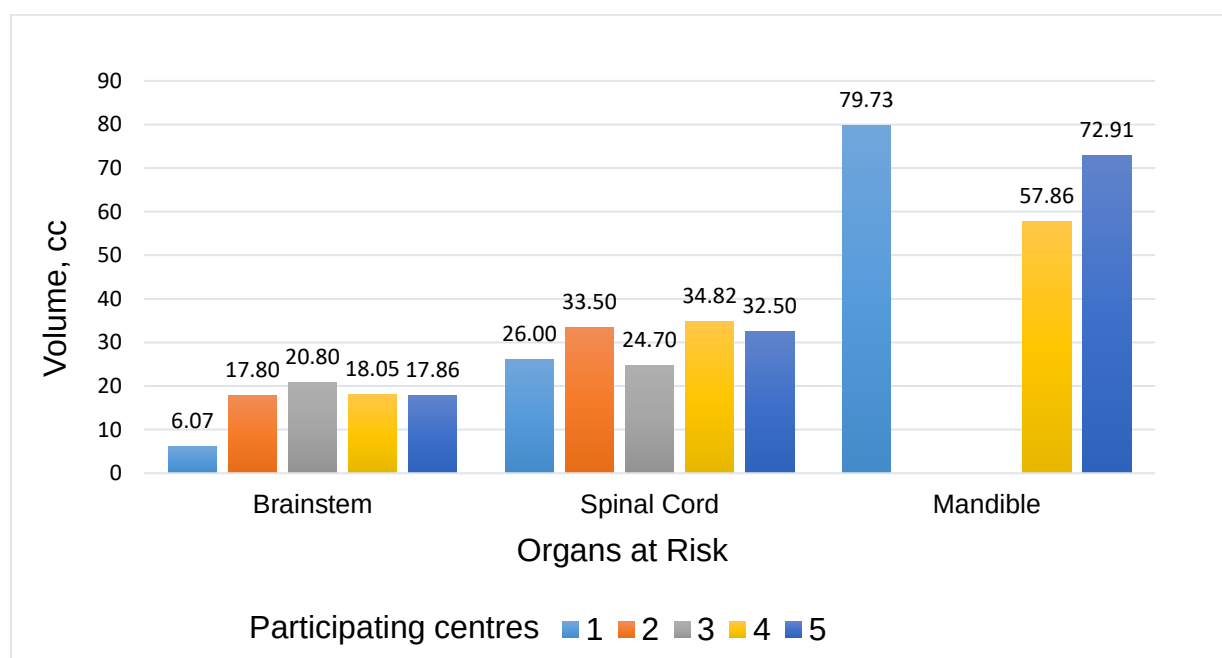


Figure 4.11 Comparison of brainstem, spinal cord and mandible serial organ volumes obtained from each of the five participating centres (using a different colour for each centre).

For the brain stem, the volumes were compared and it was observed that centre 1 did not delineate the entire brainstem claiming that there was not clear enough anatomical structures in the phantom and as such, the volume (figure 4.11 in green) appears to be an outlier. When excluding centre 1, the maximum deviation in the brainstem volumes was 7.8%.

The CT slices where the spinal cord was delineated as a serial organ were also analyzed. The maximum deviation for the spinal cord volumes was 15.2%. It was observed that some centres only delineated part of the spinal cord while others delineated on the entire

CT image set and this contributed to a significant variation. Three centres delineated the mandible and the maximum difference in the OAR volume was 15.9%.

Figure 4.12 below shows the maximum dose to the serial OARs from the centres.

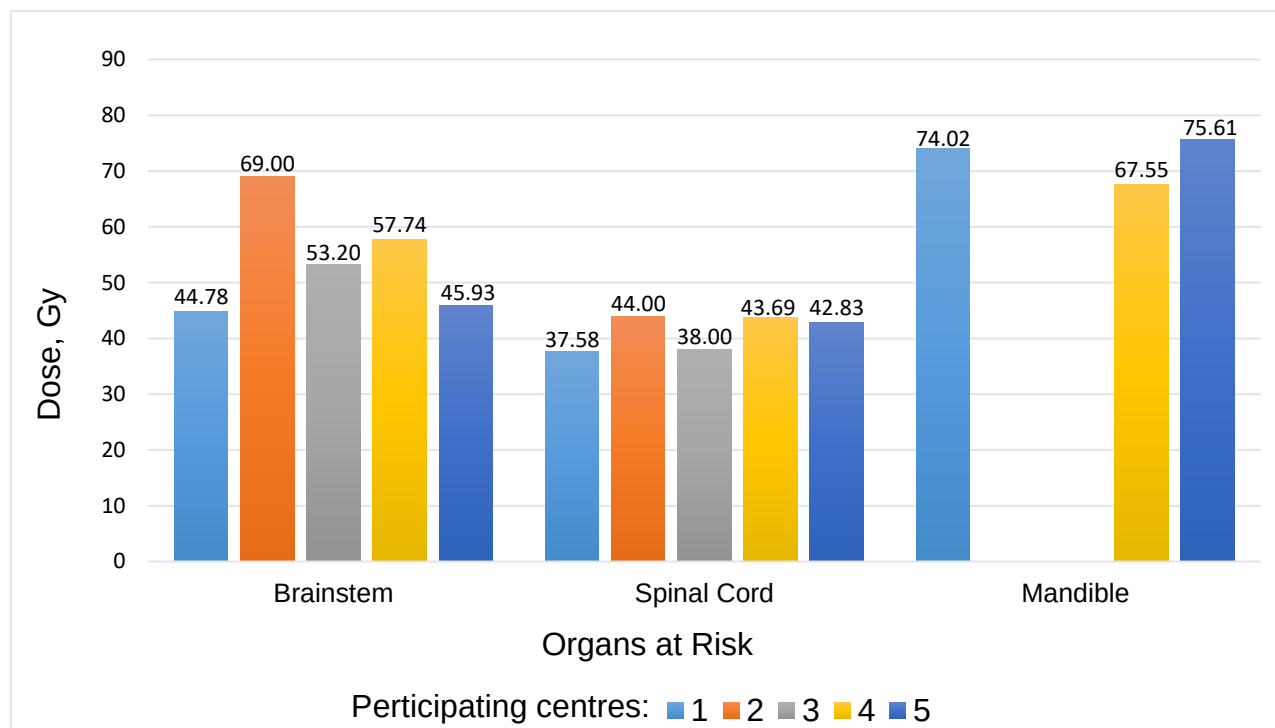


Figure 4.12. Comparison of brainstem, spinal cord and mandible serial organs in terms of the maximum doses obtained from each of the five participating centres (using a different colour for each centre).

When comparing doses, the deviation on the brainstem maximum doses was 18.2% and centre 2 and 4 exceeded the 55.0 Gy dose limit. This shows that centres did not pay attention to the dose constraints of the OAR.

The analysis of maximum dose to the spinal cord volumes showed a deviation of 7.6%. The spinal cord dose tolerance of 45.0 Gy was met by all participating centres.

The deviation when comparing the maximum doses to the mandible volumes for the three centres was 6.9%. Two centres exceeded the maximum dose of 70.0 Gy as per the QUANTEC (Emami, 2013).

The brain OAR volume results are shown in figure 4.13 below.

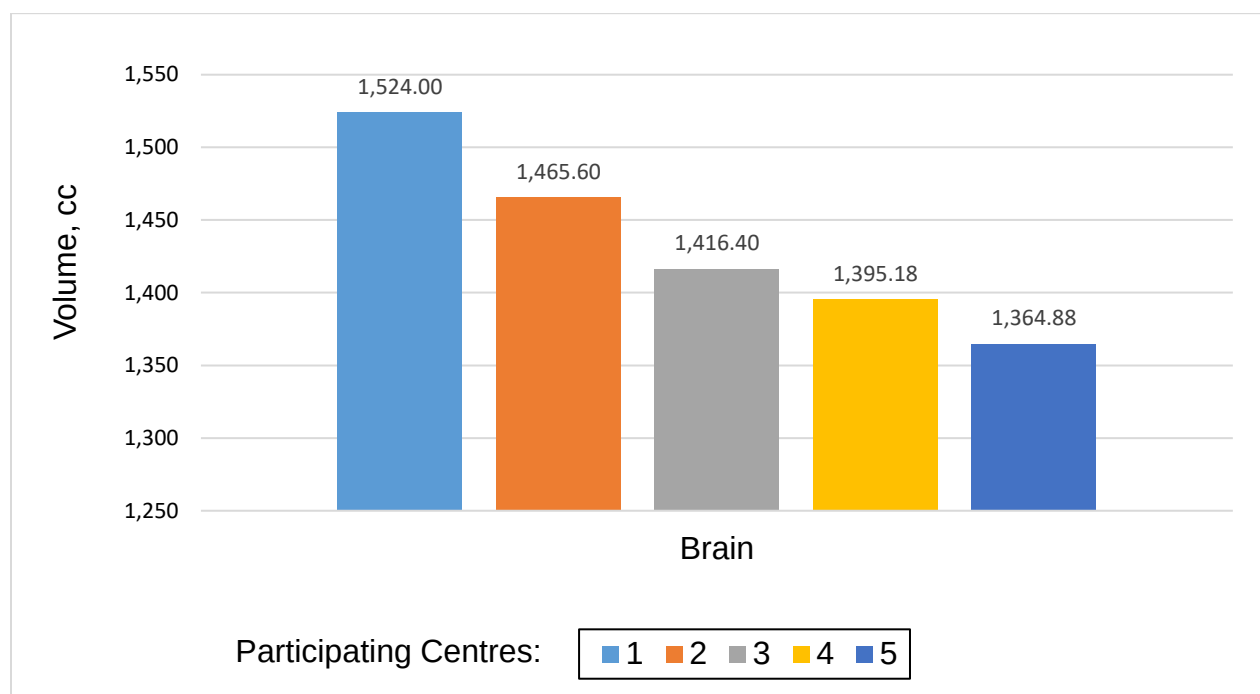


Figure 4.13 Comparison of brain serial OAR organ volume obtained from each of the five participating centres (using a different colour for each centre).

The difference between the maximum and the minimum brain volume was 159 cc (4.4%). This agreement was likely to be due to the fact that the brain is clearly visible on the CT scans of the CIRS head and neck phantom. Centre 1 delineated a higher volume and from figures 4.7 it is evident that part of the brainstem was delineated as the brain structure whereas centres 2 - 5 separated the brain structure from the brainstem.

Figure 4.14 shows the results for the maximum dose to the brain OAR for the different participating centres.

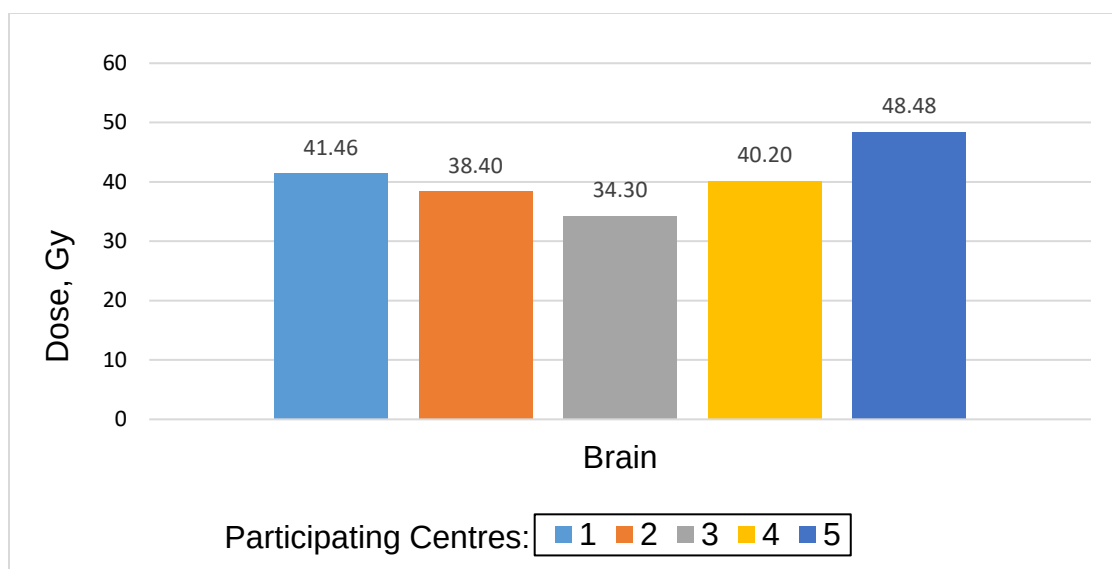


Figure 4.14 Comparison of brain serial OAR maximum dose obtained from each of the five participating centres (using a different colour for each centre).

The standard deviation in the maximum dose to the brain OAR for the four participating centres was 12.5%. The doses to the brain for all the centres were within the 60.0 Gy limit. Overall, dose constraints were not consistently or strictly applied, which can potentially lead to clinical toxicity.

4.4 On-site audit results with ionization chamber measurements and RPLDs.

Following volume delineation, Centre 2 revised their target volume after a follow up was made requesting additional information from the oncologist on the interpretation of the given histology and prescription. As a result, the centre was not able to participate in the onsite dosimetry verification process. On-site ionization chamber measurements were therefore carried out at four of the centres (1, 3 - 5) at the fixed point in the phantom. The percentage difference between the dose measurements and the TPS calculated dose points is given in table 4.4A. On-site independent measurements with the ionization chamber and RPLDs were only performed once. The results for ionization chamber measurements from the four centres are presented in table 4.4A.

Table 4.4A Comparison between the dose measured with an ionization chamber and the TPS calculated dose at the measurement point.

Centres	TPS dose (Gy)	Ionization chamber dose (Gy)	% Difference
1	2.00	2.09	4.5%
3	2.00	1.92	-4.0%
4	2.00	1.96	-2.0%
5	2.00	2.13	6.5%

Table 4.4A shows the percentage difference calculated from the TPS stated dose with ionization chamber measurement. The negative sign indicates measured doses that were less than TPS calculated dose.

Table 4.4B shows the RPLDs readings or counts (uncorrected) for each of the five dose points from the four participating centres.

Table 4.4B RPLD readings/counts (uncorrected) from participating centres 1, 3 - 5.

RPLD	Centre 1 (Counts)	Centre 3 (Counts)	Centre 4 (Counts)	Centre 5 (Counts)
1	2233800	2237000	2253000	2217800
2	2261400	2241000	2256000	2156400
3	2237400	2244000	2252000	2237000
4	2247000	2236000	2278000	2229000
5	2206600	2264000	2275000	2157000

Table 4.4C shows the parameters and values that were used for calculating the dose from the RPLD readings (each with a unique ID) at centre 1. The calibration factor N_{krpld} (mGy/counts) obtained with reference field size of 10 cm x 10 cm was used to convert the RPLD counts to dose (Gy). Appendix E describes all the correction factors used for the dose calculation from the RPLDs. This procedure was repeated for all the RPLD readings from the participating centres. Data from centre 1 was used to illustrate all the parameters and correction factors used for RPLD dose calculation (Appendix E), and the results of other centres are reported as a summary.

Table 4.4C The parameters and the correction factors that were used for calculating the dose from the five RPLDs irradiated at centre 1.

Centre 1									
				N_{krpld}	8.94E-07				
Magazine Position	RPLD ID	RPLD Counts	U_x (%)	f_{scf}	F_{mag}	f_{energy}	TPS point Dose (Gy)	Calculated RPLD dose, (Gy)	% Error
1	0441	2233800	1.03	1.025	1.00	1.04	2.00	2.13	6.5%
2	0442	2261400	1.00	1.001	1.00	1.04	2.00	2.09	4.4%
3	0443	2237400	1.00	1.003	1.00	1.04	2.00	2.08	3.9%
4	0444	2247000	1.00	1.002	1.00	1.04	2.00	2.08	4.1%
5	0445	2206600	1.00	1.007	1.00	1.04	2.00	2.05	2.5%

N_{krpld} is the calibration factor in mGy/Counts.

U_x is the RPLD reader uncertainty obtained from five repeated measurements of each dosimeter.

F_{scf} is the RPLD sensitivity factor for the batch calibrated under the same condition.

F_{mag} is the magazine position (20 position) correction factor.

F_{energy} is the energy correction factor for beam other than Cobalt-60, which is used for RPLD calibration.

Similar calculations were carried out for each centre as in table 4.4C above and the results are presented as a summary. Table 4.4D shows calculated RPLD doses after all

correction factors were applied to each RPLD reading for all three centres (data for centre 2 not provided).

Table 4.4D Summary of calculated RPLD doses for centres 3 - 5.

		Average RPLGD dose, Gy		
RPLDs	TPS dose, Gy	Centre 3	Centre 4	Centre 5
1	2.00	2.09	2.11	2.05
2	2.00	2.08	2.08	1.99
3	2.00	2.09	2.08	2.08
4	2.00	2.07	2.11	2.07
5	2.00	2.10	2.15	2.05

Table 4.4E shows the calculated percentage differences between the TPS dose points and the RPLD calculated doses for centres 3 - 5.

Table 4.4E Calculated percentage differences between the TPS calculated and RPLD measured doses for centres 3 - 5.

		Average RPLGD dose, Gy		
RPLDs		Centre 3	Centre 4	Centre 5
1		4.4%	5.3%	2.7%
2		4.0%	4.3%	-0.4%
3		4.3%	4.1%	3.9%
4		3.6%	5.6%	3.3%
5		5.2%	7.5%	2.5%

The results in table 4.4E showed a maximum difference of 7.5% in the high dose gradient region at the edge of the RPLD 1 and 5 detectors. The general trend was that the dose

differences were higher at the field edges. The percentage differences are also plotted and shown in figure 4.15.

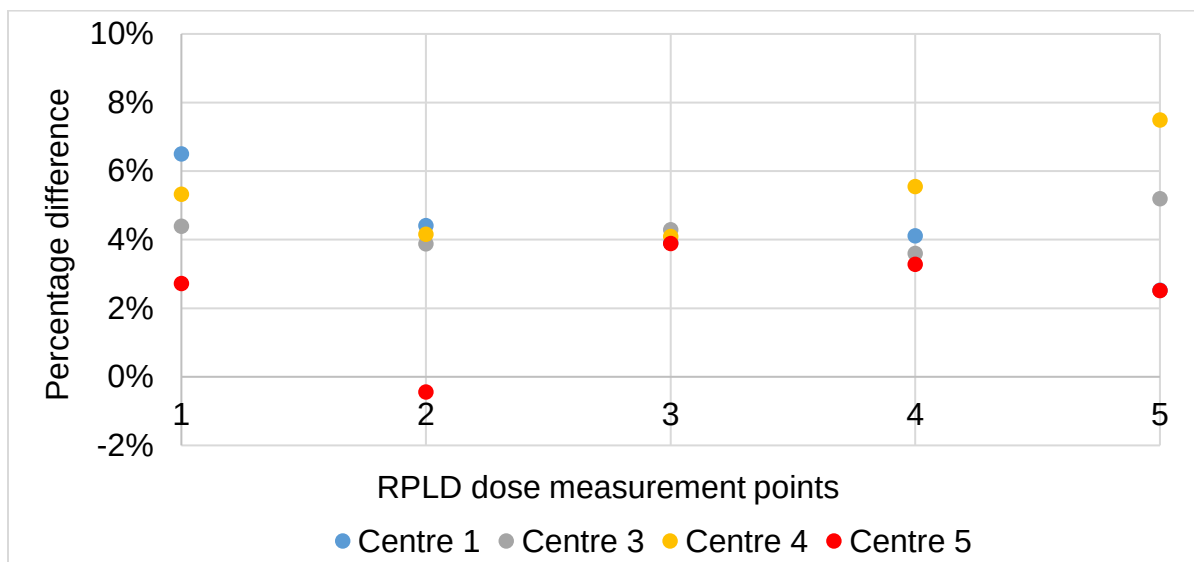


Figure 4.15 Comparison of the calculated percentage difference between the TPS calculated values and the five RPLD doses obtained from participating centres 1, 3 - 5 (the 5 dose measurement points are indicated for each centre). Different colours are used for each of the centres.

Figure 4.15 shows that a variation in the measured dose of more than 6.0% was observed at the superior (RPLD number 1) and inferior (RPLD number 5) edges of the dose distribution. RPLD 3 was placed at the same position as the ionization chamber, and when comparing ionization chamber and RPLD dose, centres 1 and 5 differences were 0.6% and 2.6% respectively while centres 3 and 4 were 8.3% and 6.1% respectively. Centres 5 differences was 2.3% and there was no data for centre 2. However, when comparing ionization chamber with film dose, centres 1 and 2 differences were 2.8% and 6.3% while centres 3 and 4 were 6.5% and 4.5%. There was no data for center 5. The correlation observed was that an increase in differences between film and RPLD audits showed similar trend for centers 1, 3 and 4, which showed consistency in dose differences when calculating dosimetry audit doses from participating centres.

4.5 Uncertainty in handling and measurements with RPLD

The uncertainty associated with the reading, SSDL calibration and RPLD correction factors was calculated and is populated in the uncertainty budget given in table 4.5.

Table 4.5 Uncertainty (U_x) budget for RPLD measurements.

Uncertainty budget RPLD (%) at Reference centre				
Tests	Description	Type A	Type B	Combined U_x
		0.528	0.020	0.528
Reference Participating centre	Sample RPLD, M	0.65		0.65
	Magazine Position	0.52		0.52
	Sensitivity factor	0.09		0.09
	Fading			0.00
	Non-Linearity		0.36	0.36
	Energy correction		0.69	0.69
Center 1		0.837	0.778	1.143
				1.35
Expanded Uncertainty, U		$k=$	2	2.7%

The combined uncertainty when all errors associated with the calibration, correction and RPLD readings were included, was 2.7%. This demonstrated a difference of about 0.7% from the uncertainty obtained during the pilot studies for the establishment of dosimetry audits in reference fields using RPLDs, which was found to be 2.0% (Maselesele, 2018)

4.6 TPS calculated field output factors compared to detector measurements.

Figure 4.16 shows the comparison between the field output factors measured at centre 1 with three different detectors and corrected for detector response, as a function of the set field size, normalised to 1.0 for a 10.0 cm x 10.0 cm reference field size.

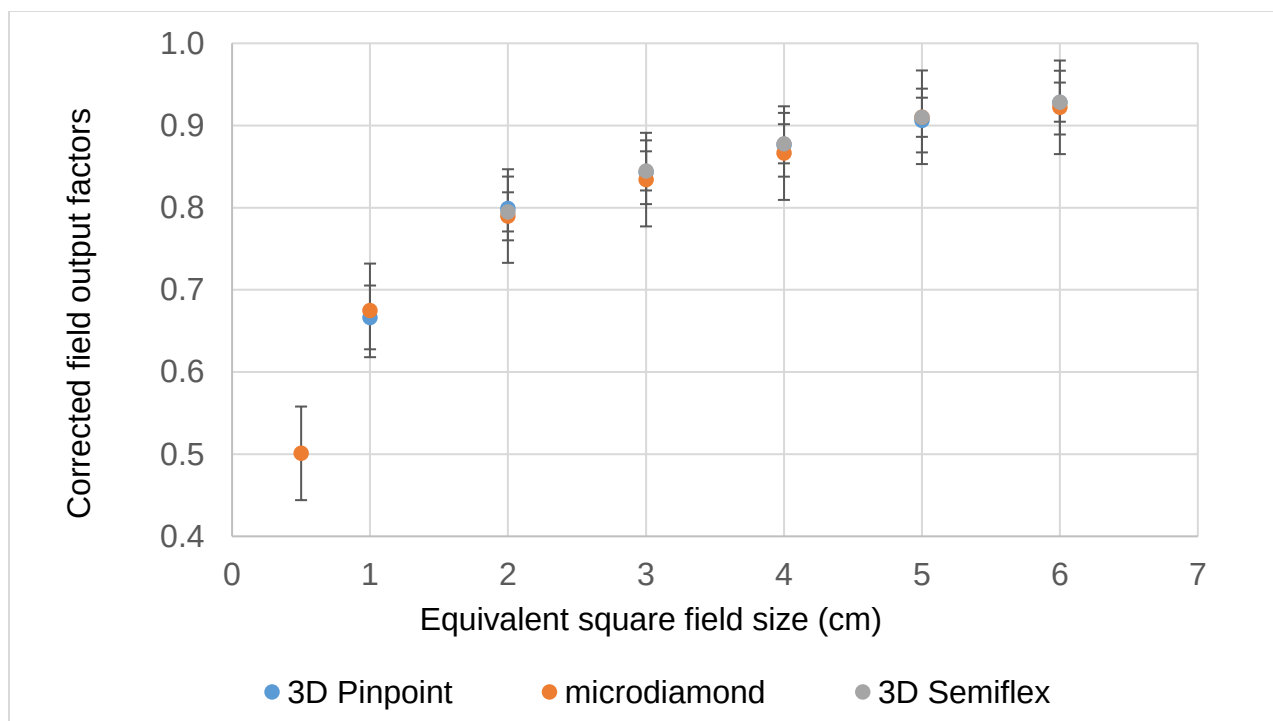


Figure 4.16 Corrected field output factor results from centre 1 measured in a 6 MV flattened beam using three different detectors for 0.5 cm to 6 cm equivalent square field sizes. Error bars show the spread in the data with each detector indicated by a different colour.

Detector data for which field output factors correction factors were not available, are excluded. The results obtained with the different detectors agreed within 1.0%.

Table 4.6 Shows the comparison of the calculated field output factors from the TPS at centre 1 and the field output factors measured at centre 1 with the three different detectors. The table also lists the uncertainty (U_x) of measurements for each field size output factor measurement which was repeated three times.

Table 4.6 Small field output factor calculated by the TPS at centre 1 compared to the measured data using three different detectors. The uncertainties of the measurements (U_x) are provided.

	Centre 1	Measurements					
Equivalent square field size (cm)	TPS field output factors	PTW, 3-D Pinpoint (31022)	U_x (31002)	PTW, micro-diamond (60019)	U_x (60019)	PTW, 3-D Semiflex (31021)	U_x (31021)
0.5	0.401	---	---	0.501	0.4%	---	---
1	0.565	0.666	0.5%	0.675	0.4%	---	---
2	0.787	0.799	0.4%	0.790	0.4%	0.795	0.4%
3	0.841	0.843	0.5%	0.834	0.2%	0.845	0.3%
4	0.885	0.877	0.3%	0.866	0.3%	0.878	0.3%
5	0.900	0.887	0.6%	0.910	0.2%	0.920	0.3%
6	0.920	0.928	0.2%	0.922	0.2%	0.928	0.2%

The uncertainties for the field output factors on the three detectors were within 0.6%. Table 4.7 shows the calculated differences between centre 1 TPS data and corrected field output factors measured at centre 1 using three different detectors.

Table 4.7 The percentage difference between the TPS data and the small field output factors that were measured using three different detectors at centre 1.

Equivalent square field size (cm ²)	PTW, 3-D Pinpoint (31022)	PTW, microdiamond (60019)	PTW, 3-D Semiflex (31021)
0.5	---	17.0%	---
1	16.3%	16.3%	---
2	1.5%	0.3%	1.0%
3	0.3%	-0.8%	0.5%
4	-1.0%	-2.2%	-0.8%
5	0.7%	1.1%	1.1%
6	0.8%	0.2%	0.9%

The results in table 4.6 show a significant difference between the TPS field output factors and measured field output factors when using detectors suitable for small fields. Significant differences were observed at field sizes of 0.5 cm x 0.5 cm and 1.0 cm x 1.0 cm. Table 4.7 shows differences of up to 17.0% higher for small field output factors in the TPS when compared with the measurements. This implies an overdose from very small field segment delivery. This is an indication that the TPS data obtained during commissioning was likely to have been measured with a detector that was not suitable for small field output factor measurements or data for field sizes of less than 4 cm x 4 cm were extrapolated by the TPS.

All the centres indicated that the smallest segment width or length used for complex TPS techniques is 0.5 cm. The TPS field output factors that were requested from the participating centres are given in figure 4.17, normalized to 1.0 in a 10 cm x 10 cm field. These field output factors were calculated from the collapsed cone (CC) algorithm from all participating centres. Figure 4.17 also includes the results of the small field output factors measured with the PTW microdiamond detector at centre 1.

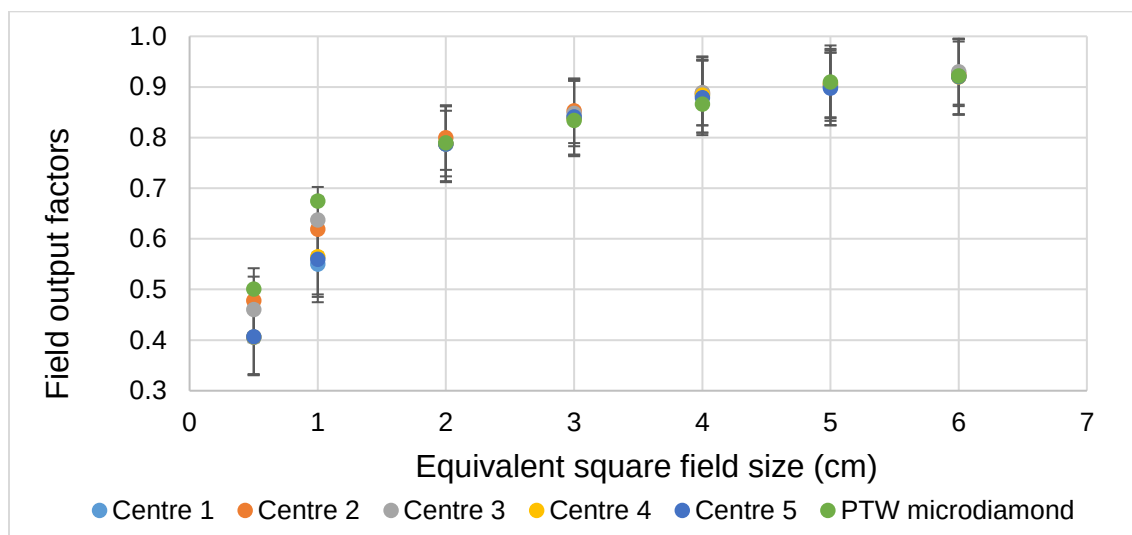


Figure 4.17 Comparison of TPS field output factor data received from the five participating centres with the field output factors measured with the PTW microdiamond detector (green dots). Error bars show the spread in the TPS data points for each field size, and each centre is indicated in a different colour.

The error bars in figure 4.17 were used to indicate the spread between the field output factors being used by the different centres. The standard deviation for the TPS field output factors for all the centres agreed within 1.0% for field sizes above of 2.0 cm x 2.0 cm and above. The maximum difference when comparing TPS field output factors from each centre to those measured with microdiamond detectors was 1.3% for 2.0 cm x 2.0 cm field size and 2.6% for other field sizes (3.0 cm x 3.0 cm to 6.0 cm x 6.0 cm). The results were comparable to the datasets published by the RPC, where measured output factors for field sizes of 2.0 cm x 2.0 cm and above were reproducible within standard deviations ranging from 0.1% to 2.4%; the absolute difference was found to range from 1.8% to 3.5% (Followill et al, 2012). However, for field sizes smaller than 2.0 cm x 2.0 cm the data from this study shows a standard deviation of up to $\pm 8.0\%$ at field sizes of 0.5 cm x 0.5 cm. This illustrates the importance of verifying the commissioning of small fields of less than 2.0 cm x 2.0 cm using measured data field sizes less than 2.0 cm x 2.0 cm. The results presented above show that these TPS beam models underestimated the field output factors for small fields. The audited centres should therefore have paid attention to limiting the size of the smallest segments that were used in IMRT or VMAT planning to those that were within a known and acceptable uncertainty.

5. Discussions

This study focused on several steps that were investigated and researched as part of developing a national end-to-end dosimetry audit methodology for complex techniques. A radiotherapy equipment survey was conducted at 54 centres around the country. This was followed by an accelerated film dosimetry audit. The end-to-end audit included treatment planning of a well-described case with specified dose point calculations, based on a given histology and prescription. Plan evaluation and approval was followed by measurements during treatment delivery of the plan at the linac using an ionization chamber and RPLDs in a CIRS head and neck phantom. The clinical implementation of small field dosimetry was investigated.

Radiotherapy is used in most of the cancer treatment regimens and remains an important curative treatment modality for localized tumors (Muhammad et al., 2016; Khan, 2014). Radiotherapy involves complex processes and technologies which bring considerable risk of doing harm if not handled appropriately (Chen and Kuo, 2017). There is a variation in the availability and application of complex technologies and some centres only deliver 2-D and 3-D treatment techniques as standard treatments as a result of resource constraints. On the other hand, implementation of IMRT, VMAT and other rotational treatment techniques has seen a rapid increase in many centres around the globe (IAEA, 2016) and in South Africa, based on the survey conducted in this study. These techniques have been advancing over the years and are increasingly complex. New challenges arise when different types of TPSs and algorithms are being used and these require changes in commissioning and quality management programs. The need for accurate dose measurements and audits can be conducted for quality improvement using different types of phantoms and detectors (Meyer, 2007; Starkschall et al., 2000). Dosimetry audits are an important tool to ensure dose accuracy and to establish whether adequate quality management systems are in place for safe treatment. This study focused on the development of an end-to-end methodology for advanced techniques and identified challenges that can arise when auditing the entire radiotherapy chain.

Dosimetry audits have been implemented in the past fifty years for reference beam dosimetry, operated by the two largest audit networks, which are the IAEA/WHO and the IROC-H. These institutions have been conducting dosimetry audits for reference beams in linacs and Cobalt-60 teletherapy treatment machines (Schreiner et al., 2009). The IAEA/WHO focuses not only on the reference beam dosimetry services but also on the development of different audit methodologies as well as promotion of dosimetry auditing and quality improvement (IAEA, 2022; Izewska et al., 2020). End-to-end methodologies are often not piloted or resourced well enough to support routine participation (Ibbott and Thwaites, 2015). The IROC-H mostly provides comprehensive support to centres that participate in clinical trials and require credentialling (Followill, 2016). Other dosimetry audit methodologies have been developed to meet the demands of QA in the radiotherapy processes (Wesolowska et al., 2019; Mehrens et al., 2016).

Postal dosimetry audits in the past fifty years have served as a tool to improve radiotherapy practices and the accuracy of radiation dosimetry over time (Izewska et al., 2019; Izewska et al., 2001). Consistencies in radiotherapy audit results and better outcomes on patient treatments have also been observed worldwide (Kry et al., 2018; Palmer et al., 2011; Izewska et al., 2001). Postal dose audit programmes with a limited scope provide verification of a few dose points and beam parameters (IAEA, 2016). Dosimetry audits for reference beam alone are not adequate to evaluate the entire end-to-end radiotherapy process. A well-developed end-to-end dosimetry audit methodology can be an efficient and important tool (Izewska et al., 2020). These audits can also play a crucial role for centres that plan to implement new complex techniques.

The IAEA/WHO has employed the use of anthropomorphic phantoms for commissioning of TPSs. Custom made phantoms have been used for performing end-to-end audit studies (Izewska et al., 2016; IAEA, 2008). This resulted in the development of relevant procedures, which were tested in multicentre studies and implemented at the national level through pilot audit runs (Izewska et al., 2020).

The IROC-H also uses customized anthropomorphic QA phantoms to credential sites that are using advanced technologies to deliver complex treatment plans using IMRT and VMAT (Mehrens et al., 2016). The audits have also shown potential benefits for 3-D CRT treatment techniques. The failure rate for IROC-H, IMRT head and neck phantom was reported to be around 10.0% to 15.0% which demonstrated the need for developments in audit methodologies that interrogate each part of the end-to-end treatment process (Followill, 2016).

Most radiotherapy centres in South Africa participate in the IAEA/WHO reference dosimetry audits for high energy photon beams. Very limited willingness to participate in end-to-end dosimetry audits was observed (Maselesele et al., 2019). Even though part of the licensing conditions from the regulator is to have a comprehensive quality management system in place, centres still do not voluntarily participate in end-to-end independent audits. Hence the need for developing and piloting an end-to-end dosimetry audit methodology for complex treatment techniques in South Africa, justifies this study.

The initial phase of the study involved fielding a questionnaire to 54 centres around the country. A very poor response was received, noting that only 9 centres responded. This limited response had a negative impact on the research since the results collected could not reasonably provide a representative snapshot of the situation in the country. Of the nine responses, eight were delivering treatment with IMRT techniques and seven were treating with a combination of both IMRT and VMAT techniques, which implies that complex treatment techniques were likely to be highly utilized and implemented. With regard to participation in the IAEA/WHO reference beam audit programme, only seven centres out of nine reported previous participation in the IAEA/WHO reference dosimetry postal audits. Results were reported to be within the $\pm 5.0\%$ tolerance limit. Two centres reported no participation in any reference beam dosimetry audit. In this case, only the mandatory pre-licensing independent verification was therefore carried out by an independent medical physicist following acceptance testing and initial commissioning of the treatment unit.

From the results of the survey, each centre indicated the existence of equipment that is used for patient specific QA, which is apparently performed as part of the standard workflow for pretreatment plan verification of both IMRT and VMAT treatment techniques. It is general knowledge that patient specific QA aims to confirm that the TPS plan can be delivered by the linac within the stated tolerances. This however implies a level of redundancy since the patient specific QA does not necessarily pick up local treatment planning errors associated with beam modeling, detector calibration and small field data acquisition (Bulski et al., 2015). Treatment planning algorithms that are not modeled correctly result in patient specific QA verification that is not sensitive to systematic errors (Rutonjski et al., 2012). This implies that plan verifications can pass even when TPS data is wrong.

Small field film dosimetry audits from four centres, showed significant inconsistencies when comparing stated and measured dose. In this part of the study, a 4.0 cm x 4.0 cm field size was selected since it is considered the smallest field size for TPS data measurements using standard detectors below which suitable detectors for small field sizes are mandatory. The disagreement in the results from the film dosimetry audit when comparing stated dose to measured dose, ranged from 2.8% to 6.5%, is of concern because the accuracy of film dosimetry is expected to be within 5.0% (Marroquin et al, 2016). The result indicated that small field dosimetry may be inconsistently implemented.

Five centres participated in the initial phase of the end-to-end audit and performed on-site CT scanning of the CIRS head and neck phantom. Treatment planning was carried out with the involvement of the entire radiotherapy team. The oncologists delineated the target and OAR volumes based on a typical patient histology and dose prescription that was provided. The results received from the participating centres demonstrated that there was poor agreement amongst clinicians on the delineation of volumes.

It was also stated by the centres that the CIRS head and neck phantom did not provide sufficient contrast to clearly visualize the target(s) or parotids, and this also complicated comparison of the treatment planning results. The data received from participating

centres demonstrated varying understanding and interpretation of the histology and prescription. The variation on the delineated target volume of about $\pm 15.7\%$ showed that each centre would potentially treat patients with similar histology, differently.

The MUs calculated by the TPS for both IMRT and VMAT showed a significant variation in treatment delivery of the same dose prescription, which impacts on treatment time, workload and compliance with internal margins. The mean dose to the target was evaluated and the variation was within 1.5%. There were clearly major differences in the metrics used for plan evaluation and approval, as well as a lack of adherence to stated tolerance doses for the OARs. It is evident that most of the audited centres do not strictly comply to ICRU recommendations for prescribing and reporting or to QUANTEC guidance, respectively (Emami, 2013; ICRU, 2010).

Four centres participated in the onsite audit, which included dose measurements with an ionization chamber and RPLDs. Reference dose output measurements with an ionization chamber were within $\pm 2.0\%$, which was in line with requirement for linac dose stability (AAPM, 2009). When comparing the dose measurement for RPLD 3 placed at the same position where the ionization chamber dose measurements were carried out, it was observed that the dose measurements with RPLDs were within 5.0% while for measurement with ionization chamber, a maximum of up to 6.5% difference was observed. The maximum difference between the TPS calculated doses and the RPLD measured doses were up to 7.5% at the distal and proximal edges of the dose distribution (RPLD 1 and 5). These differences were attributed to partial irradiation of the RPLDs close to the edge of target.

In this study the combined uncertainty for the dose measurements with the RPLDs was 2.7% compared to the IAEA/WHO uncertainty of 2.0% when using TLDs (Izewska et al., 2008). The uncertainty obtained using RPLDs was in close agreement with that reported in other literature (Maselesele, 2018). The determination of the overall uncertainty for the entire end-to-end audit methodology presented here was not possible due to the variable data received from the participating centres and the low coverage in the number of

participants. The dose measurement results that were obtained in this study showed a difference of up to 7.5% from the expected dose values, and this demonstrates that quality improvement and dosimetry audits should be advocated in centres that are treating with complex techniques.

The significant difference of up to 17.0% when comparing the small field output factors calculated by the TPSs with those measured with three different detectors, also indicated that it is important to measure small field output factors for TPSs with a suitable detector and to properly model the TPS during commissioning, especially for small field size field output factors that would otherwise be extrapolated by the TPS.

Table 5.1 below summarizes the results obtained in this study and provides the percentage uncertainties in the data analyzed from the participating centres. For TPS target doses the results are reported for both the mean and the maximum doses. For serial OARs (Spinal cord, Brain, Brainstem, and mandible), the values reported are for the organs giving the lowest and highest percentage differences. Only one parallel structure (Parotid) was delineated, and the results are reported as the highest percentage differences. The lowest and the highest percentage differences are reported from the dose measurements with both the ionization chamber and the RPLDs that were obtained during the treatment plan deliveries. More voluntary participation should be encouraged from different centres to identify appropriate tolerance and action levels.

Table 5.1 Summarized audit findings.

Audited parameters.	Lowest Percentage Difference (%), Hounsfield Unit (HU) or uncertainty in percentage.	Highest Percentage Difference (%)/HU or uncertainty in percentage.
Film dosimetry.	2.8%	6.3%
CT to Electron density calibration.	---	3.0%
CT dose contribution (measured with RPLD).	---	2.0%
CT number accuracy.	---	15 HU
TPS organs delineation (Comparison based on all 5 participating centres).		
Target volume size	---	15.7%
Serial organ at risk volumes.	4.3%	35.7%
Parallel organ at risk volumes.	---	15.9%
TPS Doses (Comparison based on all 5 participating centres).		
Target, mean dose.	---	1.2%
Target, maximum dose.	---	5.5%
Target, minimum dose	---	18.4%
Serial organs at risk dose.	5.7%	18.2%
Parotid dose.	---	13.1%
Treatment delivery (Comparison based on 4 participating centres).		
End-to-end in phantom (Ionization chamber).	-2.0%	6.5%
End-to-end in phantom (RPLD 3, non-dose gradient point)	3.9%	4.3%
Small field dosimetry (Comparison based on 4 participating centres).		
TPS commissioning field output factor data for 0.5 cm equivalent square fields.	---	17.0%

Dosimetry audits can be a useful tool when commissioning a TPS or implementing new treatment techniques, as a means to verify and establish baseline quality management data, tolerances and action levels. To ensure that steps are not skipped in the audit process, a workflow diagram is proposed for the establishment of an end-to-end audit

methodology as in figure 5.1. The workflow that is proposed assumes that data on the treatment unit(s), QA equipment, TPS type and beam characteristics will be obtained from the audited centre through an initial audit form questionnaire prior to shipping of the phantom and detectors or organizing an onsite visit. The phantom and the detectors are then shipped to the audit centres with well-defined step by step procedure with a data collection form aligned to a specific end-to-end audit with an ionization chamber and RPLDs. TPS beam data such as the small field output factors should be requested separately prior to the audit, including measured data if it is available. The form should also indicate the smallest segment allowable in the TPS for treatment planning as well as plan evaluation and approval criteria.

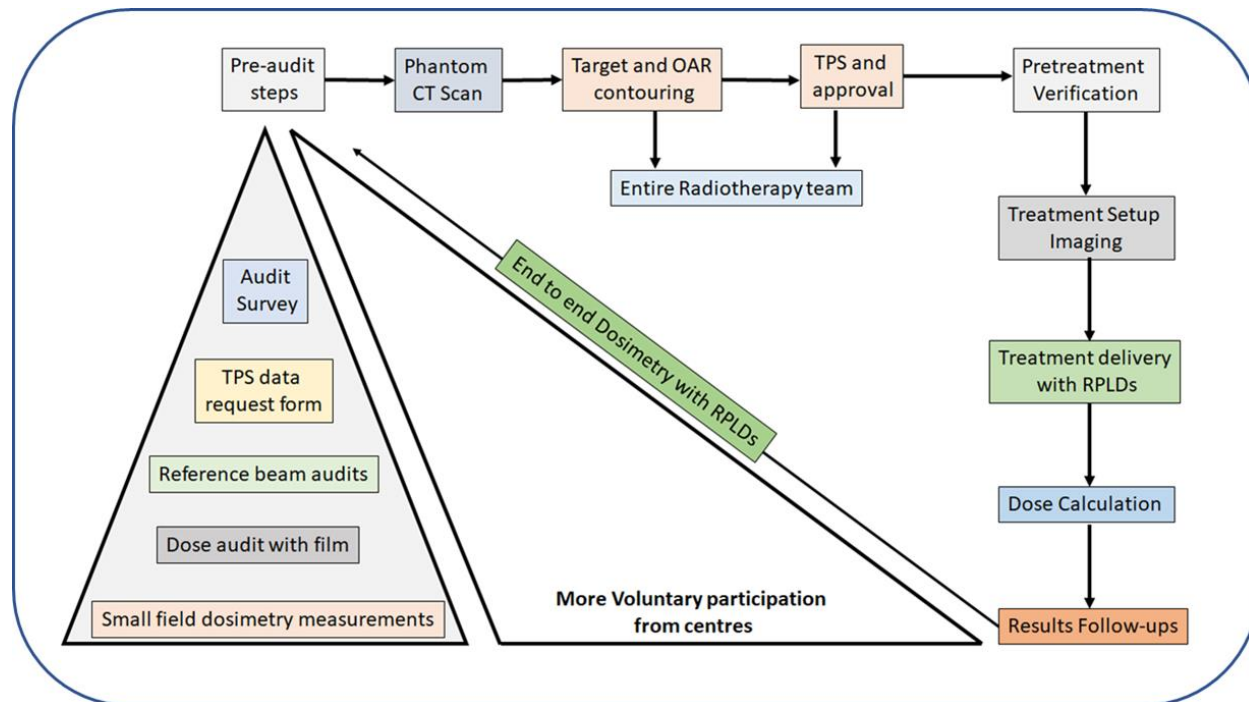


Figure 5.1 A workflow diagram proposed for an end-to-end audit.

The dosimetry audit results obtained from this study have been evaluated and compared with suggested limits published in the IAEA Human Health Series no. 31 (IAEA, 2016), which suggested the accuracy that is achievable in several different steps of the radiotherapy process and included strategies for improving the results. It also

recommends that all forms of radiotherapy should be applied as accurately as reasonably achievable (AAARA) with technical and biological factors considered. Accuracy and precision in radiotherapy is also related to factors such as training, adequate staffing levels, QA and QC tools specific to the techniques being used. For consistency in prescribing, recording and reporting of external beam radiotherapy (EBRT), the recommendations of the ICRU reports (ICRU, 2010; ICRU, 1999; ICRU, 1993) or other recognized consensus groups, should be implemented (IAEA, 2016).

Table 5.2 is a summary of the published levels of accuracy that are thought to be practically achievable (IAEA, 2016) compared with the results obtained in this study. Also provided are action levels, which define the range of acceptability, beyond which corrective action is required.

Table 5.2 Comparison of estimates of external beam radiotherapy uncertainties (IAEA, 2016) with the findings obtained in the study.

	Uncertainties and action levels, IAEA human health series No. 31 (IAEA, 2016)			Results from this study	
Audited parameters	Dose ($k = 1$)	Spatial or CT number ($k = 1$)	Action level ($\sim k = 2$)	Uncertainties	Suggested action level
CT number accuracy	---	20 HU	30 HU	15 HU	15HU
Treatment delivery uncertainties					
EBRT end-to-end in phantom	3–10%	2 mm	5–15%/3 mm	6.5%	10%

6. Conclusions.

The response received from the survey to invite participation in a national dosimetry audit for advanced radiotherapy techniques, was poor and more advocacy is needed to increase voluntary participation. From the data received, most centres appeared to access technology that includes FFF beams, IMRT and VMAT capabilities.

Out of nine centres, only 4 participated in the film dosimetry audit. The comparison between the 4.0 Gy stated dose and the measured dose on the film for 4.0 cm x 4.0 cm field sizes showed differences of up to 6.5%. This indicated that there was poor standardization in small field dosimetry. Audits of well-defined steps in the radiotherapy process are therefore needed prior to embarking on an end-to-end process in order to avoid systematic errors.

A difference and lack of consistency amongst the centres when it comes to interpretation of histology and compliance to ICRU recommendations for the prescription and dose reporting was observed (ICRU, 2010; ICRU, 1993). A major difference was observed in the application of clinical protocols, which implies that similar disease sites are managed differently at different centres. Engagement with the clinical oncology profession is needed to resolve this.

The significant variation in MUs required for treatment delivery of the same dose prescription was observed when comparing the treatment plans from the different centres. This pointed to a lack of small field size limitation in the planning process, indicating the underestimation of small field output factors, and results in differences in the workload and use factors of the treatment delivery equipment.

There was better correlation between centres on some OAR delineation, but poor results were observed on achieving dose constraints. Only the dose constraints for the spinal cord and the brain volumes were within the QUANTEC stated doses for all the centres. This study revealed that QUANTEC guidelines are not used diligently. This study recommends more intensive clinical auditing of key TPS processes prior to further development of more comprehensive end-to-end audits.

Follow ups were also made where planning results did not display conclusive information like adequate dose coverage and high doses to OARs. It was however observed that participating centres were very reluctant to provide further information. The option of sharing DICOM RT files would have expedited a more comprehensive and direct analysis, but this option was not available to this study.

The dose from the selected TPS points were calculated and compared with the doses measured with an ionization chamber and five RPLDs in the CIRS phantom. The uncertainty budget of the measurements when using RPLDs were in close agreement with the uncertainties of the IAEA/WHO on TLDs (Izewska et al., 2008). The study demonstrated and concluded that ionization chambers and RPLDs can be used for dosimetry audits on complex treatment techniques since they can be removed and reinserted easily inside a phantom. Better reproducibility should in principle be achieved when the end-to-end setup remains constant for all steps in the process.

Some dosimetry audits focus on phantoms with a well-defined normal anatomy and digitally imported target volumes, which are then clearly visible on the phantom images. This limits the need for the oncologists to apply their minds on volume delineation of OARs and plan approval only, and this limits the involvement of the entire team. In order to invite more clinical participation, this study introduced the concept of establishing an end-to-end phantom dosimetry audit methodology wherein a head and neck target was independently delineated by the oncologist based on a typical treatment histology and prescription. This revealed differences in interpretation of the given histology and prescription amongst the different radiotherapy teams. Clinical leadership is therefore important to the development of an end-to-end audit methodology. Better consensus may be achieved if additional hypothetical diagnostic workup information is provided in the patient histology. Digital target volumes should be provided only when anthropomorphic phantoms do not have adequate anatomical detail for target definition.

For the audit methodology to achieve similar goals like the IAEA/WHO audit approach (which includes confidential follow-ups by external experts) and the IROC-H approach (which allows participation in clinical trials), more audits (involving different treatment sites

and different phantoms) are required, and this should be encouraged. Quality improvement measures should be encouraged to ensure good practice and improve compliance to licensing conditions.

Since the study only used a head and neck CIRS anthropomorphic phantom, additional efforts are needed to audit techniques that interrogate the treatment of other disease sites.

The study showed that it is important to measure the small field output factors using detectors suitable for small fields. The smallest segment selected on the TPSs should be guided by the smallest field size used for measuring field output factor that can be accurately measured with a suitable detector and verified. Reliance on extrapolated data introduces significant differences in the field output factors. There was clear evidence that centres did not carefully implement IAEA TRS 483 (IAEA, 2017) when commissioning their systems for advanced technologies.

Field size (or segment) limitations for complex treatment must also be considered since they play a vital role in dose calculation accuracy. This study also concluded that additional information should be audited, including details of the TPS modelling of small field sizes (especially below 2.0 cm x 2.0 cm). A more detailed data request form providing such information, is therefore recommended going forward.

Radiotherapy centres should be encouraged to participate in independent dosimetry audits using remote services or on-site visits. A comprehensive QA programme should be in place in every radiotherapy department. Routine QC procedures should be implemented according to published recommendations and local regulatory requirements.

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Appendix A

Ethics approval

Human Research Ethics Committee (Medical) 50 years 1966 – 2016

Research Office Secretariat: Faculty of Health Sciences, Philip Tobias Building, 3rd Floor, Office 301,
29 Princess of Wales Terrace, Parktown, 2193 Tel +27 (0)11-717-1252 /1234/2656/2700
Private Bag 3, Wits 2050, email: zanele.ndlovu@wits.ac.za
Office email: hrec-medical.researchoffice@wits.ac.za
Website: www.wits.ac.za/research/about-our-research/ethics-and-research-integrity/



Ref: W-CJ-171016-2

16/10/2017

TO WHOM IT MAY CONCERN:

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical).

Investigator: Mr H V Maselesele (student no. 1773639).

Project title: Development of a dosimetry audit methodology for advanced radiotherapy.

Reason: This study uses only treatment equipment, commissioning data and application of advanced radiotherapy techniques. There are no human participants.

A handwritten signature in black ink, appearing to read "Peter Cleaton-Jones".

Professor Peter Cleaton-Jones

Chair: Human Research Ethics Committee (Medical)



Copy – HREC (Medical) Secretariat: Zanele Ndlovu, Rhulani Mkansi, Lebo Moeng.

Appendix B

Annexure A: Linear accelerator licensing conditions

ANNEXURE A

Conditions

- 50 The licence holder shall ensure that:
- a. All the applicable quality control tests are performed at the prescribed frequencies as specified in the SASQART guidelines that are available at <https://sites.google.com/site/radiationcontroldoh/> -> Electronic Devices -> Ionising Radiation -> Radiotherapy
 - i. These tests are documented as prescribed in the SASQART guideline, and
 - ii. All tests comply with all the requirements as prescribed in the applicable SASQART guideline.
 - b. At all times the services of a sufficient number of medical physicists are retained to ensure that optimal technical support and supervision are available to provide for effective patient, operator and public protection. "Sufficient number of medical physicists" means the number of medical physicists as specified in the latest document of SAMPS that is available at:
<https://sites.google.com/site/radiationcontroldoh/> -> Electronic Devices -> Ionising Radiation -> Radiotherapy -> Minimum Staffing Levels for Radiation Oncology Physicists.
 - c. No radiation therapist operates a radiation oncology treatment unit for patient treatment without a second radiation therapist or a medical physicist or a radiation oncologist being present to verify treatment parameters.
 - d. Dose verification, applicable to the relevant technology and deemed by the resident medical physicist to be an acceptable form of verification, is performed on all patients receiving megavoltage photon therapy within 7 days after the first fraction or before 20% of the total prescribed dose has been delivered (whichever is sooner). Deviations of more than 10% from the calculated dose must be reported to the medical physicist immediately.
 - e. A comprehensive quality management system for radiation safety has been compiled and protocols, procedures, policies, instructions, tests, evaluations and rules are performed and documented in accordance with the system. This local system must include, but not limited to, the chart check protocol, the roles and responsibilities of the respective members of the radiation oncology team and the peer review mechanisms in place.
 - f. Independent verification of the results of quality control tests is an essential component of any quality control program. To ensure redundancy and adequate monitoring, a second qualified medical physicist must independently verify the implementation, analysis and interpretation of the quality control tests at least annually. This independent check must be documented.
 - g. All suspected radiation occurrences are immediately reported to the Director: Radiation Control. A "radiation occurrence" means a single event or series of events occurring in the course of the use of a listed electronic product which has resulted in injurious or potentially injurious exposure of any person to ionising radiation as a direct result of the use of that product. The responsible person and medical physicist must investigate the circumstances of the exposure, the possible effects on a person(s) concerned and decide on the action to be taken.

Signed at Pretoria on 28 September 2022



for Chief Executive Officer

Appendix C

Data collection form



Development of national dosimetry audit methodology for advance radiotherapy.

This project is part of International Atomic Energy Agency (IAEA) in collaboration with NMISA as the SSDL in South Africa for member states to develop audit methodology for advance radiotherapy following the adopted reference standard audits performed on all centers in South Africa.

All information will be treated with confidentiality and only the audit steering committee (SASCRO, SAMPS, RadCon(SAHPRA), NMISA and IAEA) has access to the outcome of the project. Centers will be given formal feedback of the outcome.

Proposed audit instructions (Inputs can be added at the end of page 3).

Download CT scans from the drop box to the CD or any other storage device
Load CT scans on the treatment planning system.

Location:

\\ Advance RT..\\Head and Neck CT\\S108310\\S30

Use all processing tools available on your TPS to create the body contour and other structures.

Radiation Oncologist should use the provided histology to delineate the target volume(s) and all organs at risks (OAR) associated with the audit case below.

Please note the scans are from CIRS RMI phantom, not actual patient.
Note that this is the only information provided for audit purpose and you can add notes during delineation (to assist with formulating the methodology).

Audit Case for Head and Neck:

- **Cancer of the Oral cavity**
- **Stage 2 with positive nodes.**
- **Target volume to be given 70 Gy in 35 fractions.**

- (i) The Radiation Oncologist must be the one to decide on the advanced radiotherapy technique to use.
- (ii) The Radiation Therapists must begin with treatment planning process and plan must be approved by Radiation Oncologists before reporting.

Report the following from approved Treatment plan.

Team of Radiation Oncologists, Radiation Therapist/Dosimetrist and Medical Physicist:

(a) Technique chosen:

Elaborate:

.....

(b) For target volume(s):

Give information about the following:

Time spent on delineation of target volume (s):.....

Superior border:

.....

Inferior border:

.....

Anterior Border:

.....

Posterior Border:

.....

(c) Total volume(s) of the target (cm³):

(d) Define local prescription and Dose normalization option(s):

.....

(e) Description of organ at risk delineated:

Description	Delineation time	Dose constraints	Volume (cm ³)

(f) Treatment Planning system report:

TPS name:.....

Algorithm:.....

MLC description & geometry:

.....

.....

MLC width description:.....

TPS Data collection information:

Output Factor minimum field size:.....and maximum field size.....

PDD: Minimum field size..... and Depth.....

Maximum field size..... and Depth.....

Imaging Protocol and frequency (kV, MV, CBCT etc):.....

.....

Pre-planning verification system:

Verification Criteria:.....

Please complete target volume(s) information:

Description	Volume Cm ³	Mean dose Gy (%)	Minimum dose Gy(%)	Maximum dose Gy(%)	Approved coverage by RO	

Please complete organ at risk information.

Description	Volume Cm ³	Mean dose Gy (%)	Minimum dose Gy(%)	Maximum dose Gy(%)

Attach dose coverage print out or screen shot at the following transverse slices:

- | | | |
|--------------------|-------------------|----------------|
| 1. Sagittal = -0.1 | Transverse = +0.3 | Coronal= -10.0 |
| 2. Sagittal = -0.1 | Transverse = -0.2 | Coronal= -10.0 |
| 3. Sagittal = -0.1 | Transverse = -1.7 | Coronal= -10.0 |
| 4. Sagittal = -0.1 | Transverse = -2.7 | Coronal= -10.0 |
| 5. Sagittal = -0.1 | Transverse = -3.7 | Coronal= -10.0 |

Add print out or screen shot for the following slices as well:

1. Coronal view across the centre of the tumor.
2. Sagittal view across the centre of the tumor.

- NB:** (i) Please attach DVH and Treatment plan summary with this report
- (iii) Please Attach TPS electron density curve or data with this report and send back to the sender email: humbulani.maselesele@up.ac.za Tel: 0123542317

Appendix D

Normal tissue tolerances for standard fractionation (Emami, 2013).

Organ	Endpoint	Rate (%)	Dose-volume parameter	D_{max} (Gy)	D_{mean} (Gy)
Brain	Symptomatic necrosis	<3 <5		<60 <65	
Brainstem	Necrosis or cranial neuropathy	<5 <5	D100 <54 Gy D1–10 cc ≤59 Gy	<64 Point	
Spinal cord	Grade ≥2 myelopathy	<1		50	
Optic nerve & chiasm	Optic neuropathy	<3 3–7		<55 55–60	<50
Retina	Blindness	<1		<50	
Cochlea	Hearing loss	<15			≤45
Parotid 1	Grade 4 xerostomia	<20			<20
Parotid 2		<20			<25
Mandible	ORN	<5		<70 Point	
Pharyngeal constrictors	PEG tube dependent Aspiration	<5 <5			<50 <60
Larynx	Grade ≥2 edema	<20	V50 <27%		<44
Brachial plexus	Clinically apparent nerve damage	<5		<60	
Lung	Symptomatic pneumonitis	5	V5 <42%, V20 <22%		7
		10	V20 <31%		13
		20	V20 <40%		20
		30			24
		40			27
Esophagus	Grade ≥2 esophagitis	<30	V35 <50% V50 <40% V70 <20%	<74 Point	
	Grade ≥3 esophagitis	≤10	V60 <30%		<34
Heart	Pericarditis	<15	V30 <46%		<26
	Long-term cardiac mortality	<1	V25 <10%		
Liver	RILD, normal liver	<5			≤30
	RILD, liver disease	<5			≤28
Kidney 1	Renal dysfunction	<5	Equivalent of 1 kidney <18 Gy		
Kidney 2	Renal dysfunction	<5			<18
Stomach	Ulceration		D100 <50 Gy		
Small Bowel	Acute grade ≥3 toxicity	<10	V15 <120 cc		
	Late obstruction/perforation	<5	V50 <5%		
Rectum	Grade ≥2/≥3 late toxicity	<10/<15	V50 <50%		
	Grade ≥2/≥3 late toxicity	<10/<15	V60 <35%		
	Grade ≥2/≥3 late toxicity	<10/<15	V65 <25%		
	Grade ≥2/≥3 late toxicity	<10/<15	V70 <20%		
	Grade ≥2/≥3 late toxicity	<10/<15	V75 <15%		
Bladder	Grade ≥3 late toxicity	<6 ?	D100 <65 Gy V65 ≤50% V70 ≤35%		

Appendix E

RPLD dose determination factors

After reading the RPLDs irradiated by Cobalt-60 beam, dose is determined using equation (1).

$$\mathbf{Dose} = \mathbf{M} \times \mathbf{N_{RPLD}} \times \mathbf{f_{unif}} \times \mathbf{f_{mag}} \times \mathbf{f_{scf}} \times \mathbf{f_{fad}} \times \mathbf{f_{lin}} \quad (1)$$

Where;

M is the RPLD reading

N_{RPLD} is the calibration factor.

F_{unif} is the beam off axis correction factor.

F_{mag} is the magazine position correction factor.

F_{scf} is the sensitivity correction factor.

F_{fad} is fading correction factor.

F_{lin} is dose nonlinearity correction factor

Dose calibration factor (N_{RPLD}) was calculated from the reference signal using equation (2) below.

$$\mathbf{N_{RPLD}} = \frac{\mathbf{D_{ref,corr}}}{\mathbf{GS_{corr}}} \quad (2)$$

Where D_{ref,corr} is the Co-60 given dose corrected for dose non-uniformity if the phantom.

GS_{corr} is the corrected RPLD signal given by:

$$\mathbf{GS_{corr}} = \mathbf{M} \times \mathbf{f_{unif}} \times \mathbf{f_{mag}} \times \mathbf{f_{scf}} \times \mathbf{f_{fad}} \times \mathbf{f_{lin}}$$

The dose from the glass signal for each user set was calculated using equation (3) below.

$$\mathbf{Dose_{user}} = \mathbf{GS_{user,corr}} \times \mathbf{N_{RPLD}} \quad (3)$$

If irradiation is performed using linear accelerator, correction for the RPLD dependence on energy (f_{energy}) must be done by obtaining a correction function using radiation beam energies of know beam quality (Pdd, 10cm) given by equation (4)

$$\mathbf{f_{energy}} = \mathbf{m(Pdd,10cm)} + \mathbf{c} \quad (4)$$

Where m is the gradient and c is the y intercept of the curve obtained from the beam energy function.

For irradiated RPLDs, the absorbed dose is calculated using equation (4) corrected for all parameters that affect the RPLD irradiation and reading.

$$\text{Dose} = M \times N_{\text{RPLD}} \times f_{\text{holder}} \times f_{\text{mag}} \times f_{\text{scr}} \times f_{\text{rad}} \times f_{\text{lin}} \times f_{\text{energy}} \quad (4)$$

Analysis of Uncertainty of RPLD system for Co-60 and Linac beams

Uncertainty is estimated in two ways, one called Type A, where estimates are done using statistical data (repeated measurements) and the other is Type B where any other method or information including calibration certificates, manufacturer specifications etc, can be used.

Uncertainty of RPLD measurements will be analysed for all the parameters required to calculate dose from the RPLD which is irradiated by a beam of known characteristics. The dose calculated from a RPLD is given by equation (4) above. In this section, the uncertainty of each parameter on the equation will be discussed. Three sessions (n) of measurement readout are taken, with each having five readings, repeated by Dose ace RPLD reader. The average in each section is computed using equation (5) below.

$$\text{Average}(\bar{x}) = \sum_1^n \left(\frac{x_1 + x_2 \dots x_n}{n} \right) \quad (5)$$

The estimated standard derivation of the measurement is also calculated using equation (6) below.

$$s = \sqrt{\frac{\sum_1^n (x_n - \bar{x})^2}{n - 1}} \quad (6)$$

Once the data for estimating uncertainty is available the standard uncertainty for type A can be calculated using equation (7) below.

$$\sigma = \frac{s}{\sqrt{n}} \quad (7)$$

For type B equation (8) for rectangular distribution can be used. However, for type B uncertainty other equation can be used depending on the distribution.

$$\sigma = \frac{a}{\sqrt{3}} \quad (8)$$

Where a is the semi range between the upper limit and lower limit on the distribution.

Uncertainties must be expressed in the same units and once that is done the combined uncertainty can be calculated using equation (9).

$$U_c = \sqrt{a^2 + b^2 + a^2 \dots} \quad (9)$$

Where $a, b, c \dots$ are the standard uncertainty converted to the same unit.

The combined uncertainty is scaled by using the coverage factor (k) as in table 3.9, for a stated level of confidence, which can be obtained from student t-test the tables. This will result in calculation of expanded uncertainty as in equation (10) below.

$$U = U_c \times k \quad (10)$$

Table 2. Some of the commonly used coverage factors and the level of confidence associated with them.

Coverage factor, k	Level of confidence
1.0	68.0 %
2.0	95.456 %
2.58	99.0 %
3.0	97.0 %