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INTRA-INSTITUTIONAL END TO END TESTING ACCURACY OF MODERN
TECHNOLOGIES AND TECHNIQUES IN RADIOTHERAPY

By

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Submitted in partial fulfillment of the requirements for the degree

MASTER OF SCIENCE



DEPARTMENT OF MEDICAL PHYSICS

SCHOOL OF PHYSICS

2017

Declaration of authenticity

I declare that the research study, *Intra-institutional end to end testing accuracy of modern technologies and techniques in Radiotherapy*, is my own work and that each source of information used has been acknowledged by means of a complete reference. This thesis has not been submitted before for any other research project, degree or examination at any university.

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Dedication

To my mother Norah Muyahabo Thangwana (May her soul rest in peace), my wife Nongebisatsho Elizabeth Ramaloko, my daughter Muyahabo Sharon Ramaloko and finally my son Madikana Thuso Ramaloko jnr.

Abstract

Objective: Intensity Modulated Radiation Therapy (IMRT) treatment techniques have evolved and the current level of interest in IMRT warrants a determination of the accuracy in delivering IMRT, in multiple institutions practicing IMRT. The aim of this study was to (a) perform in-phantom end to end testing accuracy of 3D-Conformal Radiation Therapy (CRT) and different IMRT techniques, (b) check the dosimetric impact of dose delivered with deliberate offsets in the physical positioning of the phantoms using Cone-Beam Computed tomography (CBCT) and (c) use CBCT based IGRT to establish the extrinsic setup errors achieved between set-up and delivery of the planned dose on phantoms. **Materials and Method:** Studies were conducted in 3 institutions. An anthropomorphic phantom and a MatriXX^{Evolution} with MULTICube were CT-scanned and the CT slices were transferred to the treatment planning systems (TPSs). The transferred CT-slices were used to create a patient model and plans were created on hypothetical targets situated adjacent to an organ at risk (OAR). A virtual water phantom was also created in the same TPS and the same plans were created for verification purposes. The plans were transferred to a linear accelerator using a record and verify network system. The phantoms were positioned on the treatment couch and the dose delivered according to the treatment planning protocol. Statistical tools were used to analyse the delivered dose to the planned dose. **Results and discussion:** The end to end testing per institution was found to be less than 5% for dynamic IMRT and 2% for 3D-CRT when comparing planned to the measured dose. Comparison between institutions resulted in less than 7% dose difference for dynamic IMRT and 2% difference for 3D-CRT. Phantom setup errors were found to be less than 6 mm, 4 mm and 3 mm for the pre-treatment, post-correction and post-delivery setups respectively. The dose difference delivered with a deliberate 3mm setup error was found to be less than 1%, 3% and 4% for the Catphan®, Pelvis and Head and Neck plans respectively. **Conclusion:** The overall accuracy of the treatment techniques at each institution was determined successfully. Independent phantom setups are likely to indicate the best possible setup precision as they are much easier to setup reproducibly than a patient with an internal margin for involuntary movement. Pre-treatment imaging was able to detect setup errors of 6 mm in Pelvis cases. Head and neck treatments delivered with advanced techniques are the most sensitive dosimetrically to small setup errors.

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List of Acronyms

2D	2-Dimensional
3D-CRT	3-Dimensional conformal radiotherapy
4D	4-Dimensional
AAA	Anisotropic analytical algorithm
ADH	Addington Hospital
AP	Anterior posterior
ART	Adaptive radiotherapy
CBCT	Cone-beam computed tomography
CI	Conformity index
CN	Conformity number
CT	Computed tomography
CTV	Clinical target volume
DD	Dose difference
dIMRT	Dynamic intensity modulated radiotherapy
DTA	Distance to agreement
DVH	Dose volume histogram
ED	Electron density
EDR2	Extended dose range 2nd generation
EPR	Electron paramagnetic resonance
FF	Full-fan
FFF	Flattening filter free
FOV	Field of view
gated-IMRT	Gated Intensity modulated radiotherapy
GTV	Gross tumour volume
H & N	Head and neck
HF	Half-fan
HI	Homogeneity index
HU	Hounsfield unit
IALCH	Inkosi Albert Luthuli Central Hospital
IGRT	Image guided radiotherapy
IMAT	Intensity modulated arc therapy
IMRT	Intensity modulated radiotherapy
IV	Irradiated volume
kV	kilo-Voltage
kV-CBCT	kilo-Voltage cone-beam computed tomography
kV-CT	kilo-Voltage computed tomography
kVD	kilo-Voltage detector

kVS	kilo-Voltage source
Linac	Linear accelerator
ML	Medio lateral
MLC	Multi-leaf collimator
MRI	Magnetic resonance imaging
MU	Monitor unit
MU/cGy	Monitor units per centiGray
MV	Mega-voltage
MV-CT	Mega-voltage computed tomography
OAR	Organ at risk
OBI	On-board imaging
pCT	Planning computed tomography
PRV	Planning organ at risk
PTV	Planning target volume
QA	Quality assurance
QC	Quality control
RL	Right to left
ROI	Region of interest
RT	Radiotherapy
SI	Superior inferior
ssIMRT	Step and shoot intensity modulated radiotherapy
TLD	Thermo luminescent dosimeter
TPS	Treatment planning system
TV	Treatment volume
UK	United Kingdom
VMAT	Volumetric modulated arc therapy

Chapter 1 - Introduction to the context of the study

1.1 Background

Radiotherapy treatment has evolved with developments in technology. Radiotherapy techniques have transformed from 2 dimensional (2D) to 3 dimensional conformal radiotherapy (3D-CRT) in the past few decades and now intensity modulated radiotherapy (IMRT) and 4-6 dimensional approaches, as well as adaptive radiotherapy and novel stereotactic radiotherapy techniques are available. Most techniques use some form of imaging to confirm patient, field or target position, known as image-guided radiotherapy (IGRT). 3D-CRT uses target and normal structures outlined on multiple transverse images, beam's eye view projections to help with field design, volumetric dose calculations and dose volume histograms (Ezzell, 2003). IMRT is an extension of 3D-CRT that utilizes non-uniform beam intensities that have been created by diverse computer-based optimization techniques (Ezzell, 2003).

The process of determining the treatment volumes of a patient with malignant disease consists of sequentially specifying different tissues, organs, and volumes three dimensionally. These volumes are: clinical target volume (CTV), gross tumour volume (GTV), planning target volume (PTV), irradiated volume (IV), treated volume (TV), organs at risk volumes (OARVs) and planning organ at risk volume (PRVs) (ICRU 62, 1999).

IMRT treatments may be delivered with multi-leaf collimators (MLC) functioning in one of the three basic modes (Podgorsak, 2005):

- (a) The segmented MLC mode, often referred to as the “Static” or “Step and shoot mode” (ssIMRT),
- (b) The dynamic MLC mode, often referred to as the “Sliding or closing window mode” (dIMRT) and
- (c) The intensity or volumetric modulated arc therapy mode, recently referred to as the IMAT, VMAT or RapidArc mode.

RapidArc is an extension of dIMRT but includes rotation of the gantry around a patient (Otto et al 2008). Multi-leaf collimator's leaf motion and the number of monitor units (MU) per gantry

rotation is currently limited during the optimization so that dose rate maxima, gantry rotation speed and leaf translation do not excessively limit the delivery efficiency (Otto, 2008).

In 3D-CRT, leaf location uncertainties of 2 mm may be significant to the output of dose and in general, to the clinical outcome of the patient, since the uncertainty is typically small compared with the aperture size (Ezzell, 2003). However, IMRT leaf location uncertainties of 0.5 mm can cause dose uncertainties of up to 4% (Kung, 2000), and for this reason, the precision of MLC leaf positions accuracy must be maintained to less than 1 mm (Ezzell, 2003). More complex dosimetric aims can be achieved with IMRT, such as creating concavity dose distributions better than 3D-CRT (Ezzell, 2003). RapidArc optimization delivers dose distributions similar to or slightly higher to those from ssIMRT and RapidArc delivery time is range between 1.5 and 3 minutes for a 200 cGy fraction, which is much shorter than other IMRT delivery methods (Otto, 2008).

IMRT challenges are both intrinsic and extrinsic. MLC designs of double-focus or rounded leaf ends cause intrinsic offsets of 0.4 to 1.1 mm depending on location with respect to the central axis, the MLC type and beam energy (Boyer, 1997 and Ezzell, 2003). Transmission through the penumbra and collimators affects the IMRT results at the outside beams and field edges, therefore, accurately modelling penumbra and MLC transmission is critical (Mohan, 2000, Chen, 2000, Azcona, 2002 and Ezzell, 2003). The extrinsic IMRT challenges are structure and target delineation, build up region, mobile and flash targets, dose grid and patient setup, TPS algorithm, margins and radiobiological issues (Ezzell, 2003).

In non-adaptive radiotherapy treatment, the following assumptions are made: Firstly, the patient anatomy and position remain identical to treatment plan for the entire treatment course. Secondly, MLC leaf motions, dose rate and gantry angle operations are expected to operate as per plan. However, in reality it is impossible to achieve all these assumptions. The patient setup, inter- and intra-fractional organ positions and shapes do vary in reality (Barker, 2004, Xing, 2006).

Monitor unit's intrinsic error calculation, MLC motion and gantry angle readouts results in delivered dose deviations from the plan (Ezzell, 2003, Wiersma, 2007). In order to minimize the pitfalls associated with IMRT, various techniques have been coupled within the treatment delivery set-up including breath gating (Gated IMRT), tumour tracking, and more regular image guidance (Fogliata, 2010, Wiersma, 2007, Ling, 2011).

End to end tests help to verify the accuracy of the entire chain (from CT simulation to dose delivery). Ideally, these tests should use a phantom, with a detector (to measure dose), that is CT-scanned and then transferred into the treatment planning system (TPS) (Moran, 2011). Obviously such tests exclude the inaccuracies due to patient motion or volume delineation.

Cone beam computed tomography (CBCT) give a 3D model of the patient pre-treatment and makes it possible to scan patient anatomy pre-treatment and during delivering a fraction of radiotherapy and this process provide knowledge of the position of the target volume for each treatment fraction. This form of IGRT has the ability of ensuring that the reference point for each fraction are the same as in the treatment plan and the setup positions of the target volume (Podgorsak, 2005).

1.2 General statement of the problem

It was announced that almost 60% of cancer patient in the United States of America were being treated with IMRT (Das, 2008). Our statistics shows that currently at Addington (ADH), Greys and Inkosi Albert Luthuli Central (IALCH) Hospitals approximately, 75%, 17% and 23% of all cancer patients are being treated with IMRT, respectively (KZNhealth statistics, 2016 - unpublished). The level of interest in IMRT warrants a determination of the accuracy in delivering IMRT by involving multiple institutions already practising IMRT.

A multiple institution study was performed by defining normal structure and target shapes on CT images of the dosimetric phantoms, planning the treatment using multiple treatments planning systems, and then measured doses with the phantoms were compared to the planned dose from the TPSs. The target and OAR was designed on the phantoms with typical of structure and target

geometries along with the dose constraints and target doses that are currently being encountered at Addington, Greys and IALCH Hospital Oncology Clinics.

The uncertainties in phantom measurements were evaluated. The difference between measurements and predictions may be caused by misinterpretation in the measurement uncertainties, accuracy of dose calculations, treatment plan design and in the dose delivery mechanisms. In addition deliberate offsets in the setup were introduced to investigate the effect on the end to end result.

This study was not necessarily meant to identify the sources of uncertainties but to test the accuracy of the treatment techniques at each institution. The study included target and OAR dose aim for the IMRT planning and typical institutional beam arrangements that were currently used. The dosimetric tools that were available at each site were used to assess the resulting doses.

1.3 Research impact

Intra-institutional end to end testing accuracy of modern technologies and techniques in radiotherapy was intended to test the accuracy of the intra-institutional IMRT systems. In radiotherapy, accuracy in treatment delivery is the key to quality patient treatment.

A patient model was created from CT-scanned phantoms using treatment planning systems. Dose plans were created on the patient model and the dose were delivered to the patient-modelled phantoms using linear accelerators (Linacs). 2D detectors were used to measure the delivered dose. The planned dose was compared with the delivered dose using commercially available software.

Two plans using at least two different treatment techniques per patient model was created. Each plan was treated iteratively by three different (1 Physicist and 3 radiotherapists) personnel independent from each other. Each plan was delivered as per the planning protocol and in addition, a treatment was delivered with a deliberate off-set that was typical of the CTV to PTV margin. Each treatment delivery included a dosimetric measurement in the phantom. Pre-treatment CBCT was also used to determine the off-set from the planned position

Statistical tools were used to analyze the results. The tools included the mean, standard deviations, % difference, distance to agreement and quality indices. Both intended and serendipitous outcome was evaluated.

1.4 Aim

Since the accuracy of dose delivered in radiotherapy is limited by intrinsic and extrinsic uncertainties at the time of the treatment, the aim of this work was:

- (a) To perform end to end accuracy with phantoms at three different institutions using
3D-CRT,
ssIMRT,
dIMRT and / or
RapidArc/VMAT techniques.
- (b) To evaluate the factors influencing IMRT and RapidArc dose calculations
- (c) To check the dosimetric impact on the dose delivered with a typical deliberate offset in the physical positioning of the phantoms.
- (d) To use CBCT based IGRT to establish the extrinsic setup errors achieved between set-up and delivery of the planned dose on phantoms.

Chapter 2 - Literature review

In radiation therapy department, it is highly imperative to verify the entire treatment process when new technologies and methods are introduced. MatriXX^{Evolution} (I'mRT MatriXX user's guide, 2008) is useful in measuring dose in delineated volumes with high accuracy. By substituting a MatriXX^{Evolution} with MULTICube phantom for the patient model, the end to end exercise from CT-scanning to treatment delivery (including TPS patient setup and planning strategies) can be verified. By evaluating the geometric and dosimetric accuracy of the treatment delivery, the measured dose can be compared with the TPS-calculated doses (Dobler, 2010, Han, 2010, Wolfsberger, 2010 and Korevaar, 2011).

2.1 End-to-end testing

Zakjevskii (2016) used Varian TrueBeamTM with a Novel Multiple-Dosimetric Modality phantom to develop an end-to-end test. Zakjevskii designed an end-to-end test to give optimum information in anatomical regions significant to head and neck plans with regard to: a) dosimetric accuracy, b) geometric accuracy, and c) treatment reproducibility. Preliminary end-to-end results were measured using ion chambers and film. The ionisation chamber dose measurements were compared to the TPS calculated dose. Zakjevskii concluded that end-to-end testing process provided baseline values for the geometric and dosimetric accuracy of Varian's TrueBeam system.

Schiefer (2010) was interested on the planning, dose calculation and irradiation process in 23 Swiss oncology centers. A thorax phantom with inhomogeneities was used, in which thermoluminescent dosimeter (TLD) and ion chamber measurements were performed. Absolute dosimetry checks under standard conditions gave less than 1% difference between the ion chamber and the TLD.

Adolfsson (2014) designed and tested end-to-end remote audit system using lithium formate electron paramagnetic resonance (EPR). An EPR dosimetry using alanine was employed for

audits in the UK (Budgell, 2011), Italy (De Angelis, 2005) and Belgium (Shaeken, 2011). Adolfsson (2014) used four clinics, and found that determine absorbed and calculated dose in the target volume agreed to within $\pm 5.5\%$ for the 3D-CRT and $\pm 7.5\%$ ($k=1$) for VMAT/IMRT dose plans.

Ezzell (2009) used a set of test cases to evaluate the overall accuracy of delivery and planning of IMRT process in various centres seeking credentialing for IMRT. The test cases using a variety of IMRT planning and delivery systems for all nine facilities were planned, delivered, measured, and analysed. The agreement between the measured and calculated doses was assessed using an ionisation chamber in low dose and high dose regions, and film dosimetry on coronal planes of field delivered in the phantom, and planar dosimetry for measured field. 3%/3 mm gamma criteria were used to assess dose distributions in planar projection, perpendicular to the central axis. The results were summarized and recommended as the baseline values for all institutions intending to commission IMRT. The report acknowledged that the treatment planning systems and radiation therapy delivery are never perfect.

Rutonjski (2012) reviewed the entire series of activities in 3D-CRT workflow, starting with patient data acquisition up to TPS planning and dose delivery. An anthropomorphic phantom (CIRS Thorax 002 LFC) and ionisation chambers were used to carry out all the measurements. The audit results indicated the failure to meet a certain standard of simple algorithms for the test cases performed and transition to more advanced algorithms was found to be highly desirable.

Kan (2013) compared an Acuros XB (AXB) algorithm calculated dose distribution and an analytical anisotropic algorithm (AAA) calculated dose distribution with measured data next to and within a heterogeneous phantom for IMRT and RapidArc. GAFCHROMIC[®] EBT3 film and TLD was used to measure the dose. The gamma analysis with the 3%/3 mm criteria were found to be 99.5%, 98.7% and 97.7% on the axial plane for the dose-to-medium (AXB_Dm), AAA and dose-to-water (AXB_Dw) algorithms, respectively.

Scott (2008) established the accuracy of five commercially used IMRT TPSs. The Radiological Physics Center (RPC) anthropomorphic thorax phantom (Followill, 2007) with inserts for TLDs,

EBT radiochromic film and an ionisation chamber were used to measure the dose. The predicted dose in the target center was within the test criteria of 5%/3 mm for all TPSs tested. Scott concluded that the convolution superposition algorithm and AAA performed consistently and more accurately than pencil beam algorithms (PBAs) when applied to IMRT planning involving low-density regions.

Aristophanous (2016) demonstrated how ArcCHECK (Sun Nuclear Corp., Melbourne, FL) is currently used to carry out end-to-end testing of VMAT treatments in lung with the hidden target. The three DVH measurement-guided VMAT dose reconstructions achieved 100% of all defined points with the measurements in the unit density target sphere at 3%/3 mm criteria level (composite analysis) for 100% defined profile points for slightly modulated VMAT plans. On the other hand 96% of the points agreed in the highly modulated C-shape plan.

Kinhikar (2007) dosimetrically verified IMRT using an ion chamber, TLD, MOSFET and extended dose range (EDR2) films. The measurement of coronal planar dose was carried out using EDR2 films. TLD's were used to measure point doses in high dose gradient regions whereas an ionisation chambers were found to be more suited to measure point dose in low dose gradient region. Kinhikar concluded that ion chambers gave good agreement between measured and TPS calculated point doses compared to TLD, MOSFET and EDR2 films.

Several authors developed quality assurance protocols suitable for conventional IMRT (Bedford and Warrington 2009, Ling 2008, Ezzel 2009, Qian 2011, Haga 2009 and Schreinbmann 2009) and commercially available dosimetric devices have been tested for QA of un-gated VMAT (Yan, 2010 and Bedford, 2009). Un-gated VMAT dose verification has been verified and validated using delivery log-files (Qian, 2010, Schreibmann, 2009 and Haga, 2009), portal dosimetry (Mans, 2010), and gel dosimetry (Ceberg, 2010). The dose verification protocol to assess the gated VMAT delivery with respiratory scenario has been developed (Qian, 2011).

Biplap, et al (2010) verified and compared monitor unit calculation accuracy was for IMRT using a 6 MV radiation beam by employing different methodologies with three different detector phantom combinations. The IMRT plans in a $30 \times 30 \times 30 \text{ cm}^3$ water phantom was created and

measured with 0.6 cm^3 ionization chambers. The 0.6 cm^3 ionization chamber measurements at gantry angle zero degree in a water phantom showed good conformity than other measurements. It was recommended that the reliable technique for IMRT MU verification is the water phantom ionisation chamber point dose measurement.

Low (2003) studied the ionization chamber volume averaging effect in dynamic IMRT beams. Experiments to determine if ionization chambers yield the correct integral doses for sliding window portals in relation to the chamber size, orientation and radiation field size was carried out using a micro ionisation chamber (0.009 cm^3), a Farmer ionisation chamber (0.6 cm^3) and a scanning ionisation chamber (0.125 cm^3). The volume averaging effects errors were found to be significant for smaller homogeneous dose regions for coplanar beams.

2.2 CBCT based IGRT set-up error

Timmermann and Xing (2009) indicated that IMRT alone does not completely solve the problem of beam targeting in radiation therapy. The patient anatomy changes during dose delivery process (intrafractional organ motion) due to patient set-up inaccuracy and voluntary or involuntary physiologic processes related to the patient and changes from day to day (interfractional organ motion). For example, (a) organ motion happens involuntarily for structures that are part of or adjacent to the digestive or urinary systems can also affect the relative position of target volume and (b) changes in the patient's conditions, such as weight loss or gain.

It was reported that the requirement for image guidance and plan adaptation may well be different, due to the difference in the nature and characteristics of organ motion in different disease sites (Langen, 2001 and Xing, 2006). For example, in brain or head and neck studies using static phantoms, daily imaging prior to fractionate treatment seems to be adequate to capture the patient setup error and interfractional anatomy changes. However, for disease sites where intrafractional organ motion changes exist, 3D and 4D imaging should not only be the alternative, instead real-time (gating) imaging feedback with shorter time than that of the

anatomical changes must be added to the treatment. Figure 1 below illustrates the difference between adaptive radiation therapy (ART) and conventional IMRT.

In order to account for the uncertainties caused by patient setup inaccuracy and organ motion and to avoid potential geographic miss of the tumour target, a population-based safety margin encompassing the target is usually introduced. However, the margins are often too small for some patients or too large for others and sufficiently hamper the treatment outcome. Several authors (Yan, 1997; Birkner, 2003; Wong, 2006; Olivera, 2006 and de la Zerda, 2007) argued that this safety margin procedure is fundamentally deficient in that it attempts to tackle a multidimensional internal anatomy change by only a few degrees of freedom because the unreliable correspondence between the anatomies at the times of simulation and the actual treatments represents one of the lacking in safety margin practice quality chain.

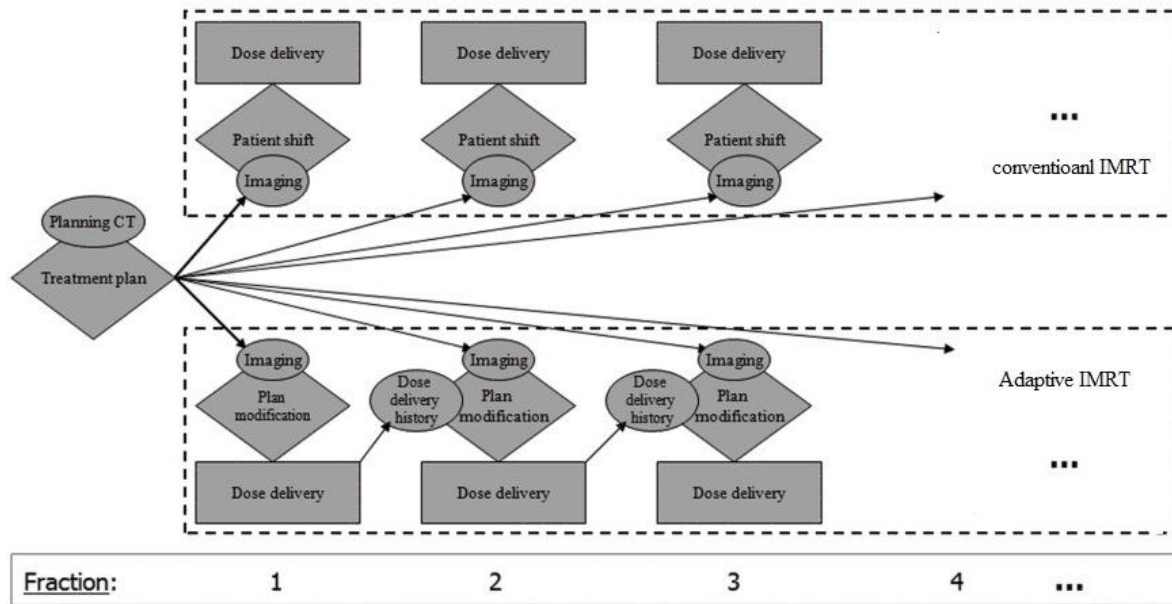


Figure 1: Image-guided conventional IMRT vs. image-guided adaptive IMRT.

Timmermann and Xing (2009) claimed that clinically meaningful ART starts with the introduction of on-board volumetric imaging (viz., OBI-kV-CBCT or Linac-MV-CBCT) in radiation oncology clinics. To establish the patient target motion and set up error using CBCT, pCT and CBCT images must be registered (fused). The registration of pCT and CBCT images may be complicated by number of factors: (a) poor CBCT image quality, (b) rectal contents such

as gas and fecal matters, (c) sheer motion of the lungs and liver, (d) Tumor shrinkage, and (e) patient weight loss and weight gain.

Timmermann (2009) argued that the step toward offline and online adaptive replanning (review) was the segmentation of CBCT images. Since it is impractical to manually segment regions of interest (ROIs) of CBCT image sets, a natural approach is to propagate the contours delineated on the pCT onto the CBCT using software. Robustness, accuracy and efficiency are key characteristics of successful contour mapping and image registration tools.

Lee (2006) emphasized the potential implications of volumetric imaging in ART and analysed the CBCT images acquired during the treatment course for eight rectal cancer patients. The deformation changes to rectal volume of up to 3.77 cm^3 was reported and concluded that a margin-based approach or any other non-volumetric imaging technique will be difficult to cope with tumour motion management during the course of treatment.

Feng Xu (2008) investigated interfractional and an intrafractional setup error that can hamper the precision of radiation therapy, and cone-beam computed tomography (CBCT) was used. 51 patients received CBCT scans for initial setup (pre-correction), re-positioning (post-correction) and after radiation delivery (post-delivery) and the CBCT image was registered to the pCT image. The interfractional setup errors on the X, Y and Z axes were less than 5 mm across the treatment sites. It was concluded that the variation in intrafractional setup error were more prevalent in head and neck tumours and must be taken into consideration during TPS planning.

Cheng K-F (2014) determined the successfulness of the immobilization devices for different imaging sites using megavoltage CT (MVCT). Helical Tomotherapy (Accuray, Sunnyvale, CA) were used on 212 patients treated in 6 sites to determine pre-treatment MVCT based on a verification tool, and thereafter for each patient set-up corrections were noted. Mean systematic and random errors of lateral, longitudinal, vertical directions between immobilization devices of each site was compared. The set-up deviations were noticed in the Orfit system (Orfit Industries NV, Wijnegem, Belgium) of the head and neck region, while the performance of immobilization devices for the abdomen, pelvis and chest sites were also similar. It was concluded that the

results provided evidence for the planning target volume to clinical target volume expansion margins approximations.

Hawkins (2006) evaluated breath-hold kilovoltage (kV) cone-beam computed tomography (CT) of the liver position's residual error after on-line orthogonal megavoltage (MV) image-guided breath-hold liver cancer conformal radiotherapy. Orthogonal MV images were acquired with exhale breath-hold for all thirteen patients before each fraction, the diaphragm for cranio-caudal (CC) alignment and vertebral bodies for medial-lateral (ML) and anterior posterior (AP) alignment and repositioning was done for offsets of greater than 3 mm for all thirteen patients. The cone-beam CT was then performed and registered to the planning CT liver to obtain the residual setup error in the liver position. Random setup errors were found to be less than 3 mm in all axes and systematic errors were less than 2 mm in all axes. Liver offsets of greater than 5 mm were observed in 33% of cases. Offsets greater than 10 mm and liver with deformation greater than 5 mm were identify in a minority of patients. It was concluded that planned position on the great number of patients was within 5 mm for liver position after radiotherapy guided with MV orthogonal imaging.

Létourneau (2005) assessed CBCT online-guided prostate cancer patient setup error where by the stability and magnitude of the residual setup error was determined. Three high-winding coils radiopaque markers were implanted on eight prostate cancer patients and phantom. It was found that for phantom, CBCT image-guided treatment achieves setup accuracy of ± 1 mm whereas for patients, it was generally within ± 1.5 mm. It was concluded that the required after online CBCT correction for the patients were approximately 3 mm margin.

2.3 Dosimetric impact

Dose calculation using CBCT was demonstrated by several authors (Lee, 2008, Yang, 2007, Yoo and Yin, 2006). To compare PTV coverage (dosimetric impact) quantitatively between the TPS measured and calculated dose distributions, the conformity index (CI), conformity number (CN), and heterogeneity index (HI) values must be determined (Koo, 2015).

Qian (2010) reported that the reconstructed dose showed no meaningful difference between the original CBCT-based and original Planning CT (pCT)-based plan, in the absence of setup errors. In the presence of setup errors, it was indicated that the suggested method was capable of showing the dosimetric changes. The results of electron density calibration curves of both CBCT and pCT gave evidence that the commissioned original pCT electron density calibration curve could be used for CBCT dose calculation without introducing meaningful dosimetric consequences. The elliptically shaped target pelvic phantom with single-arc plan was created. The plan was irradiated three times, each with the phantom at a participant target position as per plan. The phantoms were positioned as initially planned, in the first delivery. For the other two deliveries, setup errors were deliberately introduced. The resultant orthogonal dose profiles, dose distributions and DVHs from the CBCT- and pCT-based calculations were compared. The mean target dose difference was 4.6% and 0.8% respectively for the plans with large and moderate setup errors.

Yoo and Yin (2006) determined the cone-beam CT-based treatment planning dosimetric feasibility and compared to CT-based treatment planning. The dosimetric consequence of the HU variation between CBCT treatment plans and conventional CT plans for both patients and phantoms were compared. The isodose distributions between CBCT-based and pCT-based plans agreed well and the dose differences were found to be less than 1% for most phantom cases. It was concluded that the pCT treatment plans were comparable to CBCT treatment plans

Yang (2007) evaluated the accurate achievable dose using a kV-CBCT-based planning. A commercially available treatment planning system was used to calculate and subsequent compared pCT- and CBCT-based dose distributions. Patient and phantom studies were successfully carried out. It was found that the doses computed based on pCT and CBCT agreed to within 1% for the static phantom.

Lee (2008) reconstructed the IMRT dose delivered to a head and neck patient plan using the MLC log-files and CBCT. The electron density calibration and validating the procedures of the dose reconstruction, a cylindrical CT phantom was used. It was found that for the open beam dose calculation, the dose distributions on the same axial slice from the CBCT- and pCT-based

dose calculations were essentially identical; the difference in dose maximum was less than 0.5%. The vertical and horizontal dose profiles for the CBCT- and pCT-based calculations were in agreement to within 1%. It was concluded that there was no significant difference in the calibrations noted over the range of HUs, and the CBCT and pCT HU profiles were in agreement to within 10% except that the CBCT showed a larger fluctuation of HU and reduced HUs at the periphery of the phantom.

Langen (2005) reported on Megavoltage CT (MVCT) images of patients obtained daily on a helical Tomotherapy unit (TomoTherapy, Inc., Madison, WI). The MVCT images were used for patient alignment however they were also used to calculate the treatment plan dose distributions for the patient anatomy of the particular session. The MVCT required a different electron density to CT number calibration curve from original pCT calibration curve. Unlike in Qian (2010), Lee (2008), Yang (2007), Yoo and Yin (2006) kV-CBCT studies where by pCT electron density curve was used. It was concluded that the use of MVCT images for the assessment of each session dose distributions had similar accuracy to that of the initial kVCT dose calculation.

Guan (2009) carried out dose calculation accuracy using CBCT but calibrated the CT number to electron density (ED) using a mini CT QC phantom firmly fixed into an IMRT QA phantom. Three different scan ranges (6 cm, 12 cm and 20.8 cm) were used to determine the HU dependence on the amount of scatter. It was found that the dosimetric difference was largest with the biggest (20.8 cm) scan range.

Olch (2014) recently investigated the dosimetric effects caused by immobilization devices and couch tops. Avoidance of high density structures sets during TPS planning was discussed and included. An important aspect were the recommendations directed at treatment planning system vendors, clinical physicists, and device vendors on how best to take measurements of attenuation and surface dose, and how to report all these values. An appeal was made to all vendors to work together to provide accurate couch top models in all commercially available planning systems. It was found that immobilization devices, couch tops, and combinations of such equipment can have a significant impact on patient setup and dosimetry. Attenuation through couch tops especially carbon fibre ranges from 2% for normally incident beams through the central uniform

portion to 6% for highly oblique beams and may attain as much as 17% for more dense sections of the couch tops. The manual adjustment of TPS calculated MU was discouraged, as this practice introduces errors in the patient treatment plan and correction methods for couch attenuation may lead to an under- or over dose of part of the treatment volume. It was recommended that the couch top and all immobilization devices being incorporated in the TPS optimization process (couch modelling) because couch inclusion into the treatment planning process results in acceptable dose optimization and calculation accuracy. The same couch top in planning CT scanning, treatment simulator and treatment delivery must be used.

Srinivasan (2014) summarized studies on dosimetric evaluation of CBCT-based planning for Varian OBI (Varian medical systems, Palo Alto, CA) system, Siemens MVision (Siemens AG Healthcare Sector, Erlangen, Germany) system and Elekta XVI (Elekta oncology systems, Stockholm, Sweden, AB) systems.

Rong (2009) investigated the HU to electron density stability conversion and evaluated the dose calculation accuracy using anatomic site-specific calibration. The CT number (HU) for various structures, and in addition mean, near minimum and near maximum doses to target volumes was analysed. 2% difference between the pCT and CBCT based planning methods was reported. It was concluded that the HU to electron density conversion is stable and could be used directly.

Dunlop (2015) used HU mapping on inhomogeneous and homogeneous phantoms. The dosimetric drawback because of HU variation for CBCT by comparing isodose, DVH and dose distribution was analysed. The results indicated a variance of less than 1% and good agreement in isodose volumes. It was recommended to use a single HU-electron density calibration curve for both pCT- and CBCT- based planning.

Ding (2007) compared the mean, near minimum and near maximum doses between plans calculated with kV-CBCT and conventional CT. The dose difference for a complex inhomogeneous phantom was found in the calculated dose to targets to be less than 1%. It was concluded that the kV-CBCT images can be used to compute dose distribution and generate dosimetric parameters accurately in radiation therapy.

According to Van Zijtveld (2007) the conventional CT HU mapping to that of CBCT was used prior to dose calculation and compared the CBCT planning to that of conventional pCT planning for IMRT head and neck patients. The overall difference between the mapped conventional pCT and CBCT scan was found to be within 1%. It was suggested that (with Elekta XVI system) there was a need to generate separate electron density-HU linearity graph specifically for CBCT based plan.

Chapter 3 Study design, materials and methodology

3.1 Research design and material used

Eclipse™ version 8.6/8.9 (Varian® Medical Systems, Palo Alto, CA) and Monaco (Elekta® Medical Systems, Stockholm, AB) was used for treatment planning and target delineation. The PTV delineation was performed by a multi-disciplinary team based on all image data. All phantoms were treated with 6 MV photons (Table 4) on a Trilogy® linear accelerator with IGRT™ couch top (Varian Medical Systems, Palo Alto, CA) and Elekta VersaHD® linear accelerator with Connexion™ couch top (Elekta Medical Systems, Stockholm, AB).

The I'mRT MatriXX^{Evolution} with MULTICube (IBA-dosimetry group, GmbH, Schwarzenbruck, Germany), Catphan® 504 (Phantom Laboratory, Inc., Salem, NY) and anthropomorphic (Phantom Laboratory, Inc., Salem, NY) phantoms were CT-scanned and the CT slices were exported to TPSs. The transferred CT-slices were used to create a patient model and the plans were created on hypothetical targets and OAR. The RT-plans were transferred to the linac using an Aria™ (Varian® Medical Systems, Palo Alto, CA) and Mosaik™ (Elekta® Medical Systems, Stockholm, AB) record and verify (R&V) systems. The phantoms were positioned on the treatment couch and the dose delivered as per each treatment planning protocol.

3.2 Research Methodology

3.2.1 End to end testing accuracy of 3D-CRT, IMRT and RapidArc

End-to-end accuracy testing of 3D-CRT, IMRT and RapidArc plans were carried out using the water, OCTAVIUS® 4D 1500 (PTW-Freiburg, GmbH, Freiburg, Germany) and MatriXX^{Evolution} with MULTICube phantoms. The entire process is summarized in Figure 4, where by the MatriXX^{Evolution} based plan measurement was analysed using COMPASS® software (IBA-dosimetry group, GmbH, Schwarzenbruck, Germany) and VeriSoft® software (PTW-Freiburg, GmbH, Freiburg, Germany).



a



b1



b2



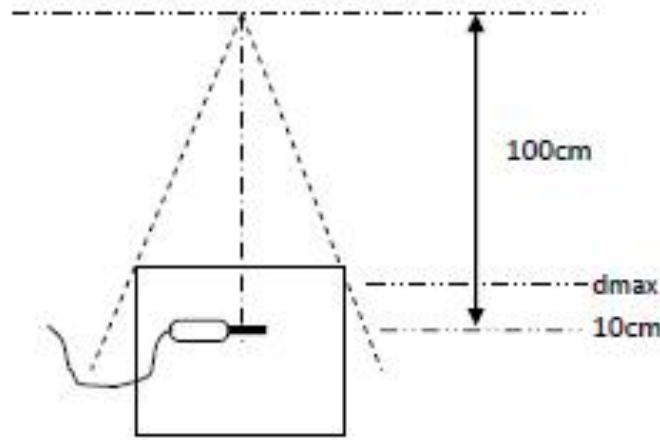
b3

Figure 2a: (a) shows the end-to-end test flow chart with MatriXX^{Evolution} and MULTICube phantom, (b₁) shows the sagittal plane set up of MatriXX^{Evolution} with the MULTICube phantom, (b₂) shows the coronal plane set up of MatriXX^{Evolution} with the MULTICube phantom and (b₃) shows the gantry mount of MatriXX^{Evolution} with Perspex.



c

Figure 2b. (c) Shows the end-to-end test flow chart with water phantom



d

Figure 2c. (d) shows the setup for the ionisation chamber water phantom IMRT dose calibration. A FC65-G ionisation chamber (IBA-dosimetry group, GmbH, Schwarzenbruck, Germany) and TM30013 ionisation chamber (PTW-Freiburg, GmbH, Freiburg, Germany) were used to measure point doses in water phantoms.

Typical plans were developed for different sites and the beam arrangements used in this study are summarized in Table 1.

Table 1: Summary of beam arrangements

	Site	3D-CRT	dIMRT	ssIMRT	RapidArc
H&N Plans	Energy	6MV	6MV	6MV	6MV
	Field/Arc	4 Fields	5 Fields	5 Fields	1 Arc
	Gantry angle	Sequential	*BAO	*BAO	179-181°
Pelvis Plans	Energy	6MV	6MV	6MV	6MV
	Field/Arc	4 Fields	5 Fields	5 Fields	1 Arc
	Gantry angle	Sequential	*BAO	*BAO	179-181°
Catphan® Plans	Energy	6MV	6MV	6MV	6MV
	Field/Arc	4 Fields	5 Fields	5 Fields	1 Arc
	Gantry angle	Sequential	*BAO	*BAO	179-181°

*BAO is the Beam Angle Optimization routine that optimizes the best possible gantry angle on the Eclipse™ TPS.

3.2.1.1 End to end testing with MatriXX^{Evolution} and OCTAVIUS phantom

3.2.1.1.1. RT plans and Dose constraints.

The pCT of the MatriXX^{Evolution} with MULTICube phantom was acquired and hypothetical targets (pseudo PTV and pseudo OAR) were created. Pelvis big target, Pelvis small target, Head and Neck big target, Head and Neck small target and CatPhan plans were created. Table 1 summarizes beam arrangements and table 2 summarizes the dose constraints used to produce treatment plans for 3D-CRT, IMRT and RapidArc delivery.

Table 2: Summary of target volume and critical structures' dose constraints

Critical structure	DVH constraints	Target Volume	DVH constraints
Spinal Chord	$D_{2\%} < 50\text{Gy}$	H&N	$D_{98\%} > 66\text{Gy}$
Right Parotid	$D_{50\%} < 25\text{Gy}$	PTV	$D_{2\%} < 70\text{Gy}$
Left Parotid	$D_{50\%} < 25\text{Gy}$		
Brain Stem	$D_{2\%} < 54\text{Gy}$	H&N	$D_{98\%} > 72\text{Gy}$
Right Lens	$D_{2\%} < 50\text{Gy}$	GTV	$D_{2\%} < 75\text{Gy}$
Left Lens	$D_{2\%} < 50\text{Gy}$		
Right optic Nerve	$D_{2\%} < 55\text{Gy}$	Pelvis	$D_{98\%} > 50.4\text{Gy}$
Left optic Nerve	$D_{2\%} < 55\text{Gy}$	PTV	$D_{2\%} < 55\text{Gy}$
Pituitary glands	$D_{2\%} < 45\text{Gy}$		
Optic Chiasm	$D_{2\%} < 55\text{Gy}$	Pelvis	$D_{98\%} > 52\text{Gy}$
Right Femur Head	$D_{50\%} < 50\text{Gy}$	CTV	$D_{2\%} < 56\text{Gy}$
Left Femur Head	$D_{50\%} < 50\text{Gy}$		
Rectum	$D_{50\%} < 55\text{Gy}$	Cuboid	$D_{98\%} > 30\text{Gy}$
Bladder	$D_{50\%} < 65\text{Gy}$	PTV	$D_{2\%} < 33\text{Gy}$
Rectangular	$D_{50\%} < 25\text{Gy}$		
Circular	$D_{50\%} < 25\text{Gy}$		

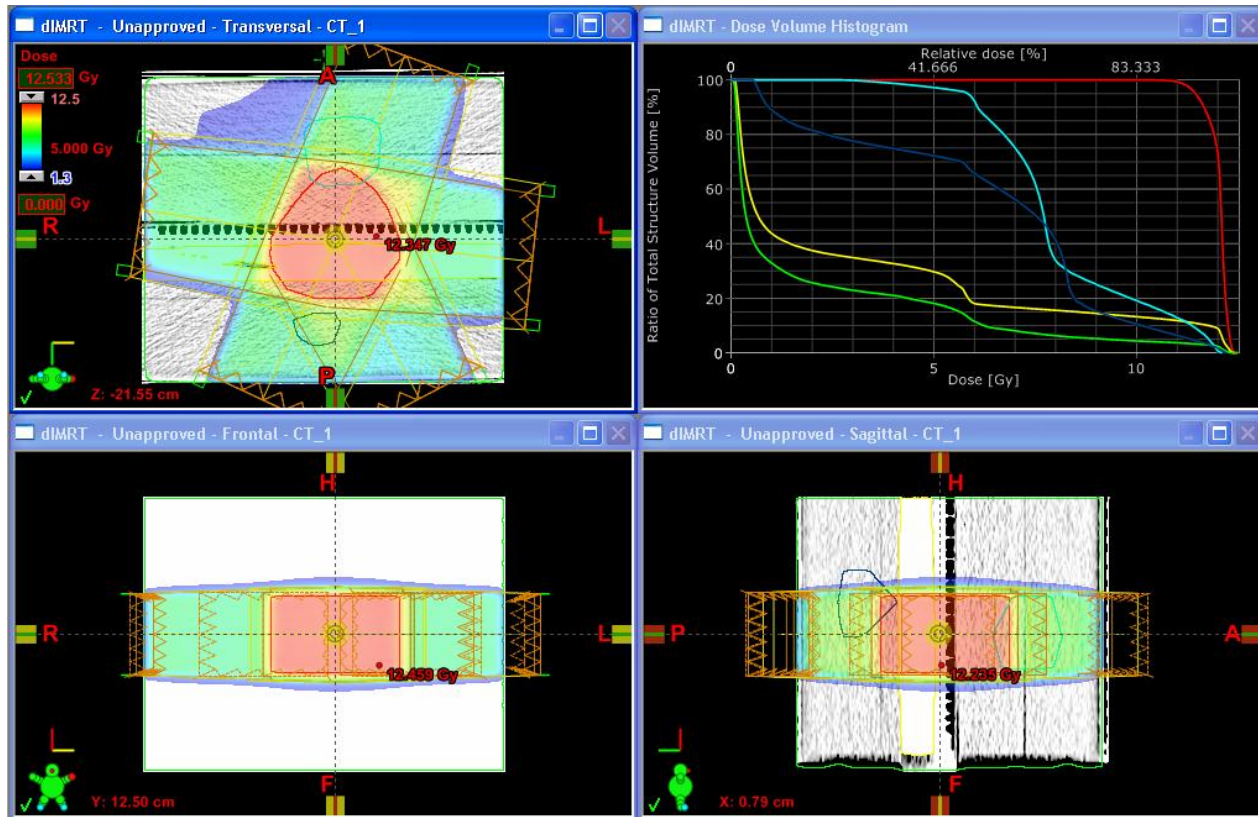


Figure 3: A screenshot of DIMRT plan for MatriXX^{Evolution} with the MULTICube phantom. The plan consists of 4 ports and is typical of a pelvic treatment. The axial (top left), sagittal (bottom right) and coronal (bottom left) view through the isocentric plane are shown in addition the dose-volume histogram (top right). On the dose-volume histogram, red represents the PTV, light blue the bladder, dark blue the rectum, yellow is the matriXX body (detectors) and green is the matriXX body (phantom)

3.2.1.1.2. 3D detector array measurements (Verification).

The RT plan was copied in to the Delta4 (3D detector array) and the dose was computed on the Delta4 patient model. Delta 4 was used for Addington hospital, an OmniPro I^mRT at Greys hospital and an OCTAVIUS 4D at IALCH. The plans were verified, the dose difference (DD) and distance to agreement (DTA) were also carried out on various criteria ranging from 2%/2mm up to 6%/4mm. Figure 4 summarizes the Delta4 verification results with 3%/3mm pass criteria for DIMRT plan.

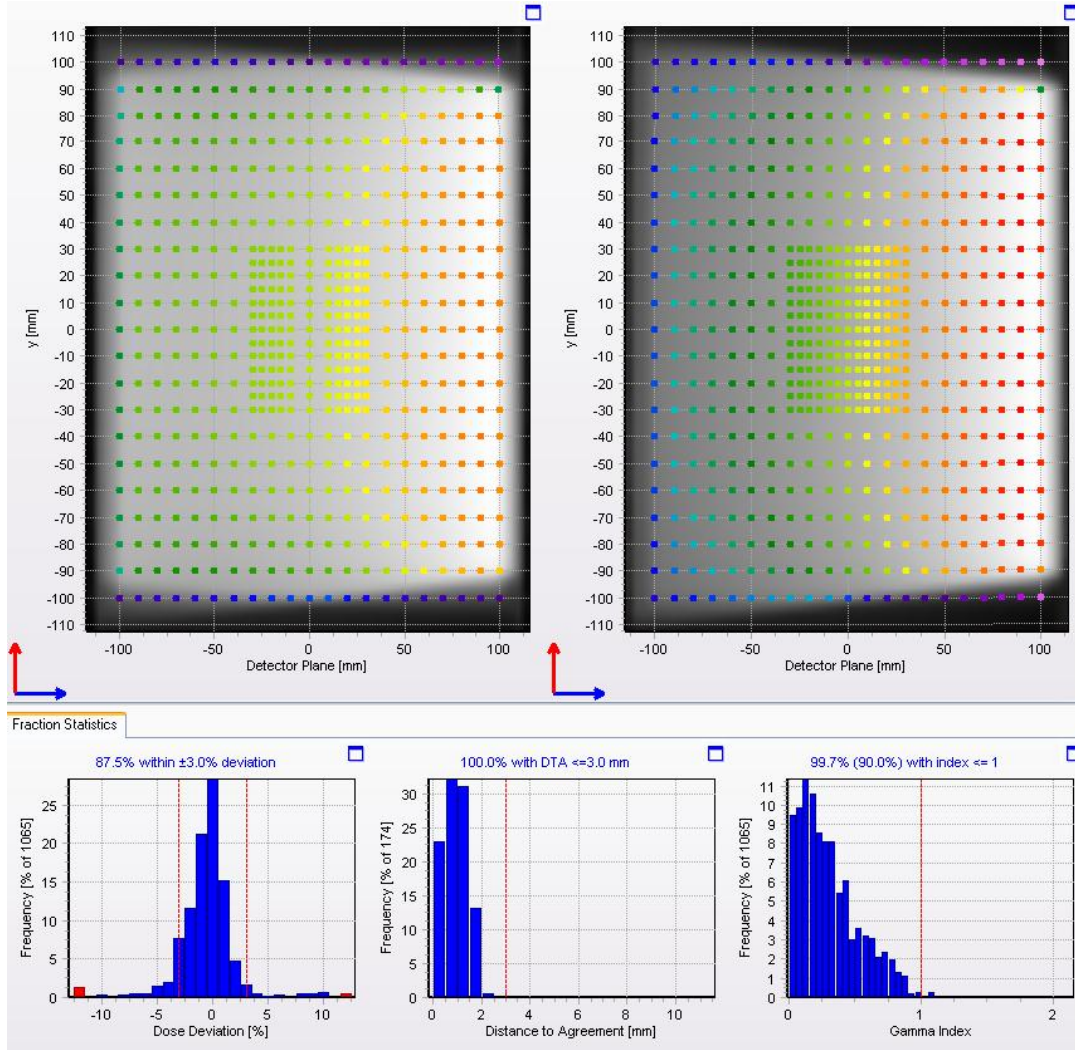


Figure 4: A screenshot of delta4 verification results with 3%/3mm pass criteria for dIMRT plan. The detector planes (top right and left) display of dose measured with 2 detector planes arranged perpendicular to each other in a cube phantom. The dose difference (bottom right), distance to agreement (bottom middle) and Gamma index (bottom right) are also shown.

3.2.1.1.3. Dose measurements and analysis.

The MatriXX^{Evolution} based plan was measured and analysed using COMPASS® software (IBA-dosimetry group, GmbH, Schwarzenbruck, Germany) and VeriSoft® software (PTW-Freiburg, GmbH, Freiburg, Germany) in absolute mode to provide comparison with the TPS-computed dose in the low- and high dose gradient regions. Figure 5 below summarizes the dIMRT measured dose compared with the TPS dose using COMPASS software.

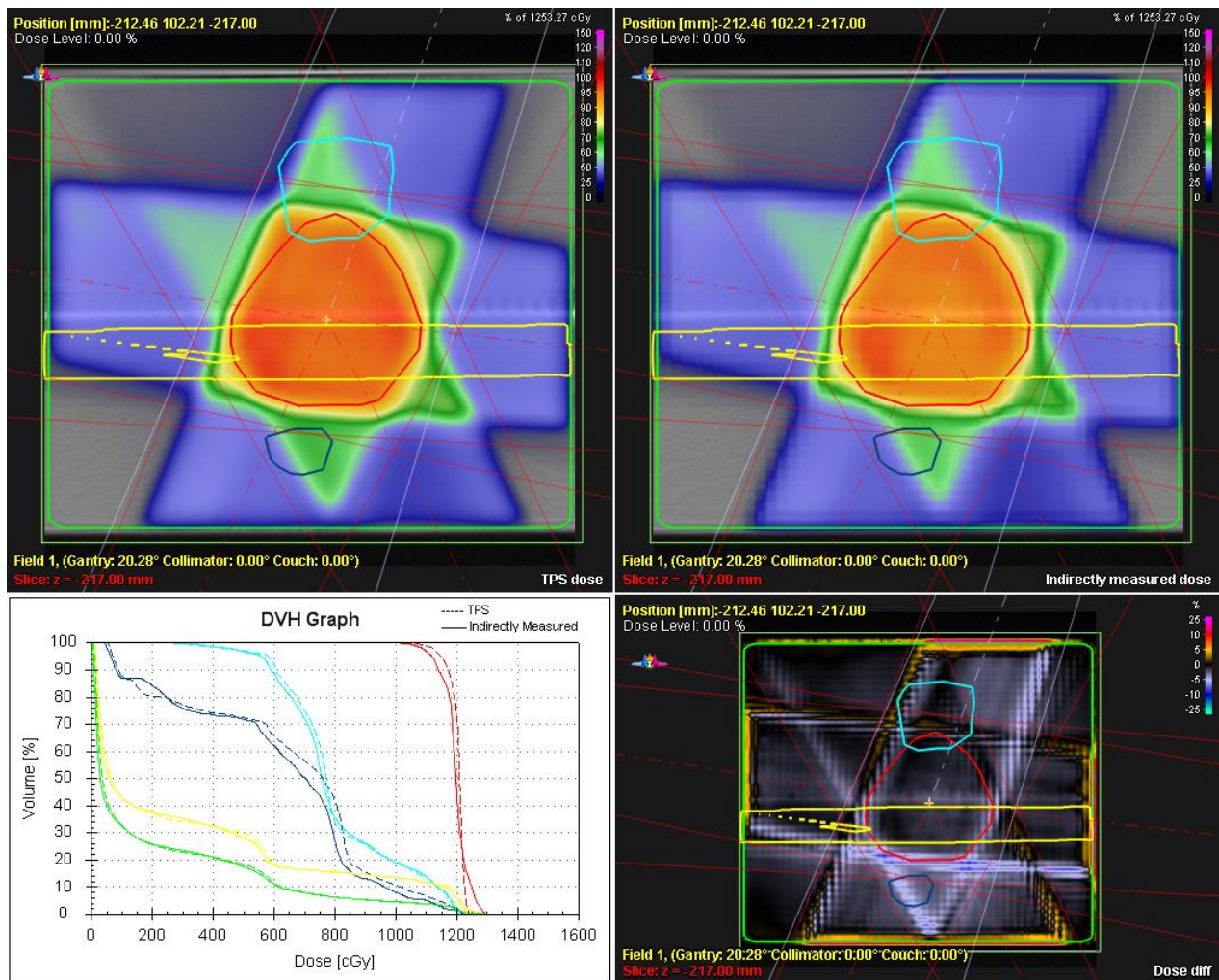


Figure 5: A screenshot of the DIMRT delivery showing the measured and planned doses using COMPASS® software. The Eclipse™ TPS calculated dose distributions (top left), Compass® software measured dose distributions (top right), DVH comparison (bottom left) and dose distribution differences (bottom right) are shown. On the dose-volume histogram, red represents the PTV, light blue the bladder, dark blue the rectum, yellow is the matriXX body (detectors) and green is the matriXX body (phantom)

3.2.2.1 End to end testing with water phantom

3.2.2.1.1. Virtual water phantom and Dose constraints.

A virtual water phantom ($20 \times 20 \times 20 \text{ cm}^3$) was created in the Eclipse™ TPS. Typical plans were created on the virtual water tank with the depth of measurements determined by the BAO

for each field per treatment technique. Table 3 and 4 summarizes beam arrangements and dose constraints used to produce treatment plans for 3D-CRT, IMRT and RapidArc delivery respectively. Figure 11 depicts the dIMRT plan in a water phantom.

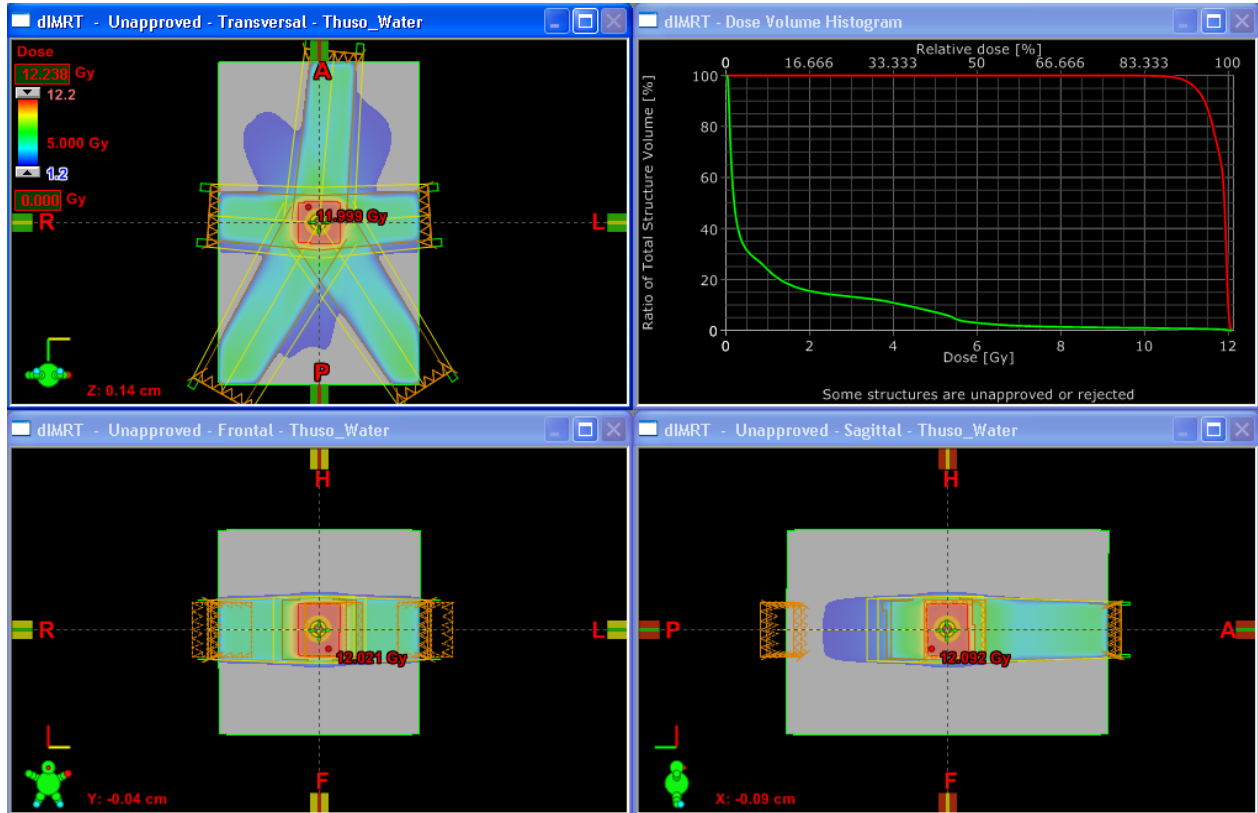


Figure 6: The dIMRT plan for a water phantom geometry. The axial (top left), sagittal (bottom right) and coronal (bottom left) views through the isocentric plane are shown in addition the dose-volume histogram (top right). On the dose-volume histogram, red represents the PTV and green is the body (water phantom)

3.2.2.2. 3D detector array measurements (Verification).

The RT plan was copied in to the Delta4 (3D detector array) and the dose was computed on the Delta4 patient model. A 3% DD and 3mm DTA acceptability criteria between the measured dose profiles and the calculated TPS dose profiles was used on the low dose and high dose gradient regions respectively.

3.2. 2.3. *Dose measurements and analysis.*

The FC65-G and TM30013 Farmer ionisation chambers were used to measure a point dose in the water phantom at isocenter. The TPS calculated isocenter point dose was compared with the delivered isocenter point dose for the 3D-CRT, IMRT and RapidArc treatment plans. The measured IMRT dose was corrected using correction scheme (see figure 2d) developed by Low (2003) and Biplap (2010).

3.3. *Factors influencing IMRT and RapidArc*

The Catphan® phantom was CT scanned and CT slices transferred into the Eclipse™ TPS. Patient model was created and the factors influencing IMRT and RapidArc calculation speed and accuracy were fully investigated.

3.3.1. *Time and grid size.*

Planning parameters influencing calculation time of dIMRT, ssIMRT and RapidArc was investigated. The calculation grid size was varied from 1 to 5mm at an intervals of 1mm. The average factor with which the calculation time increased was calculated and the correlation coefficient was calculated and compared.

3.3.2. *Dose distributions.*

The dose distribution was calculated for dIMRT, ssIMRT and RapidArc plans. The near minimum dose (D_{98}), mean dose (D_{50}) and near maximum dose (D_2) were calculated and compared.

3.3.3. *Monitor Unit (MU).*

The number of MU was calculated for the dIMRT, ssIMRT and RapidArc according to beam arrangement in table 1. The average MU and the standard deviation was calculated and compared.

3.4 CBCT based IGRT assessment of set-up error.

Two plans (big target and small target) per treatment site per phantom (patient model) were created (see figures 7, 8 & 9) and each RT plan was assigned CBCT setup fields. Thereafter, each plan was transferred to the Linac, CBCTs were setup, acquired and the RT plans were treated iteratively by four different personnel (1 Physicist and 3 Radiotherapists) independent from each other. Table 3 below summarizes the CBCT plan acquisition parameters.

Table 3: Summary of the CBCT plan set up and acquisition parameters

	H&N		Pelvis		CaTPhan
	Small target	Big target	Small target	Big target	
Vert (cm)	15.4	15.5	11.3	11.3	15.3
Lng (cm)	25.1	25.4	97.5	97.5	57.4
Lat (cm)	0.6	0.5	1	1	2.1
Scan width (cm)	17.5	17.5	16.2	16.2	15.2
Scan center (cm)	0	0	0	0	0
Scan z-zero (R)	0	0	0	0	0
Scan Type	Single cone-beam	Single cone-beam	Single cone-beam	Single cone-beam	Single cone-beam
Bow-tie	FF-Filter	FF-Filter	HF-Filter	HF-Filter	FF-Filter
PA/ axis (cm)	25	25	45	45	25
RL/axis (cm)	25	25	45	45	25
Slices	59	59	52	52	56
Slice thickness (mm)	2.97	2.97	3.00	3.00	3.00
Y-Pixels (cm)	0.0488	0.0488	0.0879	0.0879	0.0488
X-Pixels (cm)	0.0488	0.0488	0.0879	0.0879	0.0488

In this work, the CBCT was firstly acquired using half-fan mode (80 mA, 125 kVp, 8216 ms, 3mm slice thickness and 512 X 512 X 51 matrix size) with a half-bowtie filter (Pelvic study). Secondly, a CBCT was acquired with ‘full-fan’ CBCT mode (100 kVp, 20 mA, 7060 ms, 3mm slice thickness and 512 X 512 X 51 matrix size) with full-bowtie filter (H & N and CaTPhan studies). Both the resolution and image size of the CBCT was manually selected before image acquisition.

Acquired CBCT images were registered to the relevant RT plan. In the first acquisition (pre-treatment setup), the phantom was positioned as initially planned. In the second acquisition (post-correction setup), the phantom was positioned after applying shifts obtained from the

CBCT. In the third acquisition (post-delivery setup), the phantom was deliberately positioned incorrectly after delivering treatment.

The pre-treatment and post-correction setup errors were performed as initially planned but setup errors were deliberately instituted for the post-delivery setup. The couch was moved 3mm in the anterior-posterior (AP) direction, right-left (RL) and superior-inferior (SI) direction by the three independent (2 in the same direction and 1 in an opposite direction) participants. The whole exercise was repeated five times with all three different participants. The resultant dose distributions, orthogonal dose profiles and DVHs from the RapidArc calculations were compared.

3.4.1. Anthropomorphic phantom (small target).

A pelvis plan was created for an elliptically shaped target of 5.0 cm in the major axis, 4.1 cm in the minor axis and 6.1 cm in length. Three CBCTs were acquired per RT plan treatment delivery, each with the phantom positioned by a participant according to the plan.

3.4.2. Anthropomorphic phantom (Big target).

A pelvis plan was created for an elliptically shaped target of 12.4 cm in the major axis, 11.3 cm in the minor axis and 8.6 cm in length. Three CBCTs were acquired per RT plan treatment delivery, each with the phantom positioned by a participant according to the plan.

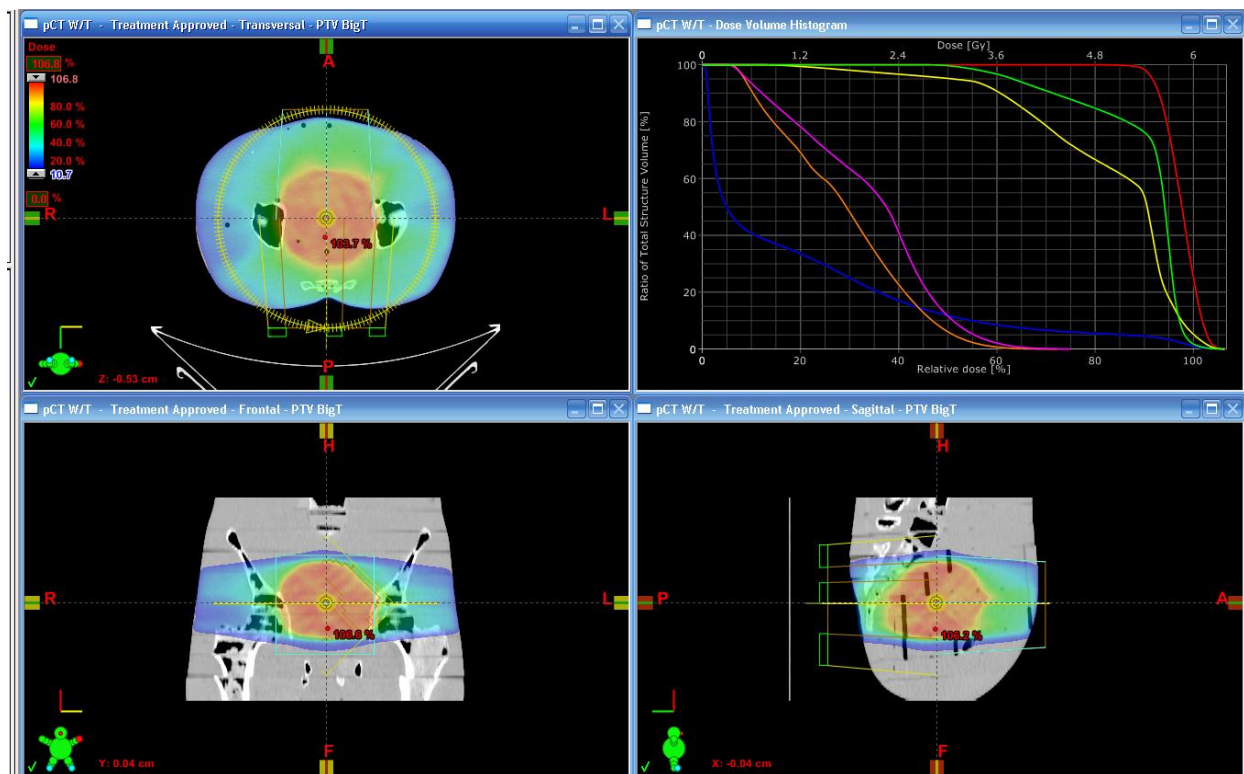


Figure 7: A screenshot of an anthropomorphic phantom (Pelvis Big target) RapidArc plan. The axial (top right), sagittal (bottom left) and coronal (bottom right) view through the isocentric plane are shown in addition the dose-volume histogram (top left). On the dose-volume histogram, red represents the PTV, green is the bladder, yellow is the rectum, orange is the right femoral head, purple is the orange is the left femoral head and blue is the phantom body.

3.4.3. Anthropomorphic phantom (small target).

A H & N plan was created for an elliptically shaped target of 3.0 cm in the major axis, 2.1 cm in the minor axis and 2.1 cm in length. Three CBCTs were acquired per RT plan treatment delivery, each with the phantom positioned by a participant according to the plan.

3.4.4. Anthropomorphic phantom (Big target).

A H & N plan was created for elliptically shaped target of 8.2 cm in the major axis, 6.6 cm in the minor axis and 5.4 cm in length. Three CBCTs were acquired per RT plan treatment delivery, each with the phantom positioned by a participant according to the plan. Figure 8 below summarizes the head and neck target anthropomorphic phantom plan

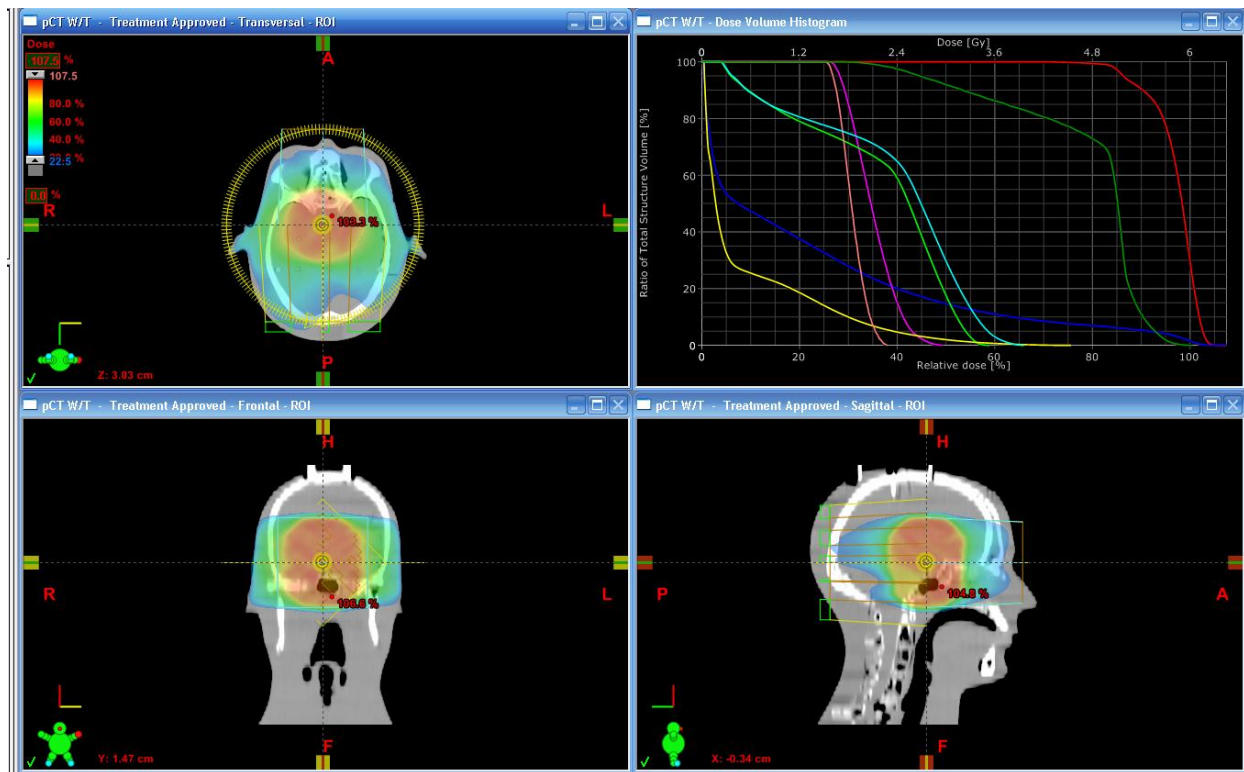


Figure 8: A screenshot of an anthropomorphic phantom (H & N big target) RapidArc plan. The axial (top right), sagittal (bottom left) and coronal (bottom right) views through the isocentric plane are shown in addition the dose-volume histogram (top left). On the dose-volume histogram, red represents the PTV, green is the brainstem, yellow is the spine, orange is the right eye, purple is the left eye, light green is the left parotid, light blue is the right parotid and blue is the body.

3.4.5. Catphan® phantom.

A circular shaped target was created of 3.6 cm in diameter and 5.1 cm in length. Three CBCTs were acquired per RT plan treatment delivery, each with the phantom positioned by a participant according to the plan. Figure 9 below summarizes the H & N target Catphan® phantom plan

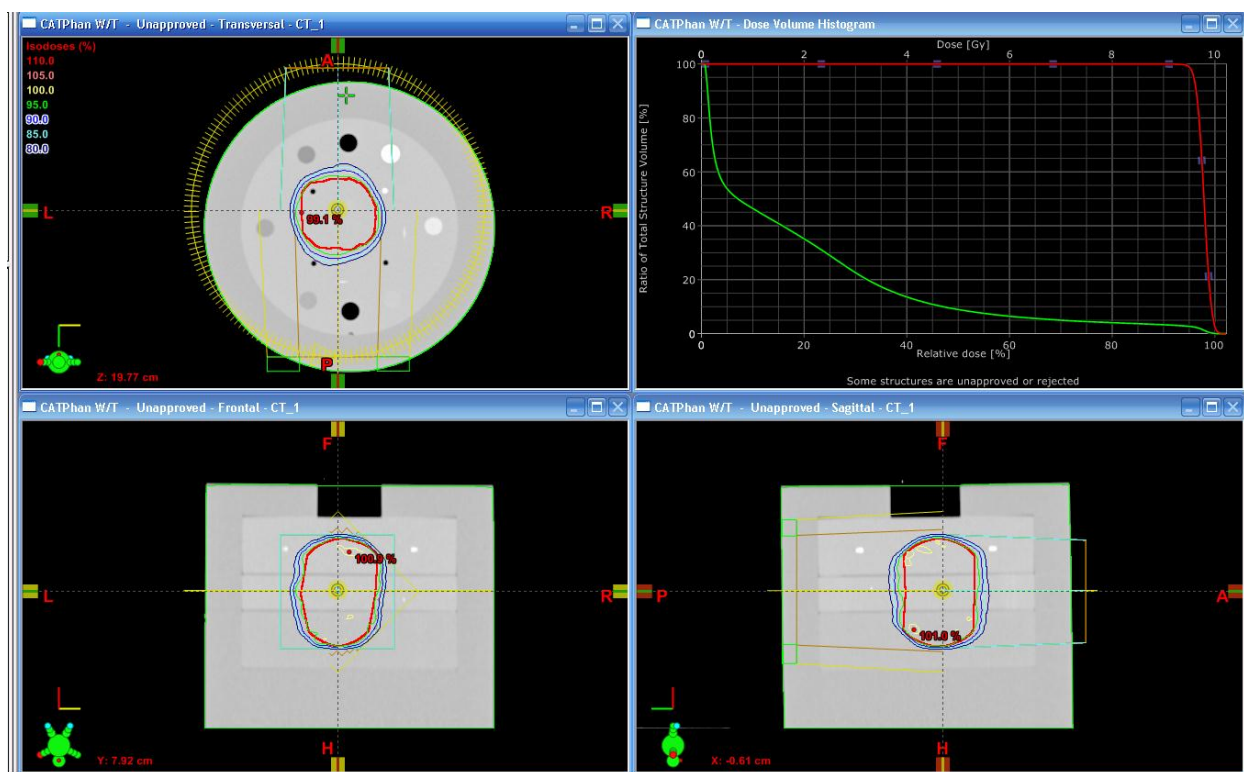


Figure 9: A screenshot of the Catphan® phantom plan. The axial (top right), sagittal (bottom left) and coronal (bottom right) view through the isocentric plane are shown in addition the dose-volume histogram (top left). On the dose-volume histogram, red represents the PTV and green is the body.

3.4.6. *Offline/Online Review.* The CBCT images were acquired and the “save match” button was used to create the spatial registration object (SRO). The “save match” button saves the SRO to the information system (database) which also saves all of the acquired images to the information system (so that pCT/CBCT image pairs appear as paired images for Offline/Online Review).

Once two associated images (pCT/CBCT) were available, the automatic 3D/3D match was performed. The system shifts the two superimposed images relative to each other during the match and calculates the couch correction values and the couch shift was then applied. Using “Offline/Online review” the paired images were analysed and compared in terms of: (a) pre-correction setup error (b) post-correction setup error and (c) post-delivery setup error for all independent participants.

3.5 Dosimetric impact of dose delivered with deliberate offset.

The acquired original CBCTs attached in to the plan were transferred into the TPS. The original pCT contours were mapped (copied) into RT plan acquired and registered original CBCTs. The Eclipse optimization process was carried out on the acquired RT plan registered CBCTs and the Analytical Anisotropic Algorithm (AAA) calculation algorithm was used to calculate the dose on mapped CBCT.

3.2.4.1. Anthropomorphic phantom (Pelvis: big and small target).

The original acquired and RT plan registered CBCT with and without deliberate error calculated dose distributions per technique per patient model were analysed and compared with the original pCT computed dose distributions. The results are summarized in chapter 5.

3.2.4.2. Anthropomorphic phantom (H & N: big and small target).

The original acquired and RT plan registered CBCT with and without deliberate error calculated dose distributions per technique per patient model were analysed and compared with the original pCT computed dose distributions. The results are summarized in chapter 5.

3.2.4.3. Catphan® phantom.

The original acquired and RT plan registered CBCT with and without deliberate error calculated dose distributions per technique per patient model were analysed and compared with the original pCT computed dose distributions. The results are summarized in chapter 5.

Chapter 4 Formulae

When comparing dose measurements with TPS calculated plans, tools are available (Mutic and Purdy, 1998) that include (i) Distance to agreement, (ii) dose difference, (iii) correlation coefficient, and (iv) paired t -test.

4.1 Correlation coefficient

The correlation coefficient r describes how well two data-distributions are correlated to each other and it is denoted by:

$$r = \frac{\sum (X_i - \bar{X})(Y_i - \bar{Y})}{\sqrt{\sum (X_i - \bar{X})^2 \sum (Y_i - \bar{Y})^2}} \quad (1)$$

Where by, X_i is the value in position i , $\bar{X}$ is an average, Y_i is the calculated value in position i and $\bar{Y}$ is the calculated average.

The following scenario best describe r :

- $r = 1$; Two distributions are highly correlated
- $r = 0$; No statistical correlation between the two distributions
- $r = -1$; Two distributions are highly inversely correlated.

4.2 Gamma function (Γ)

The Γ function includes the dose difference function and the distance to agreement (DTA) function. Dose difference (δ_{Dose}) is the difference in dose between two dose matrices at the same point. The DTA is the distance between the nearest point in the measured distribution containing the same dose value and the dose point in the calculated distribution (Mutic and Purdy et al 1998). Figure 1 shows the difference between the Γ , DTA and dose difference in 1 dimension (1D).

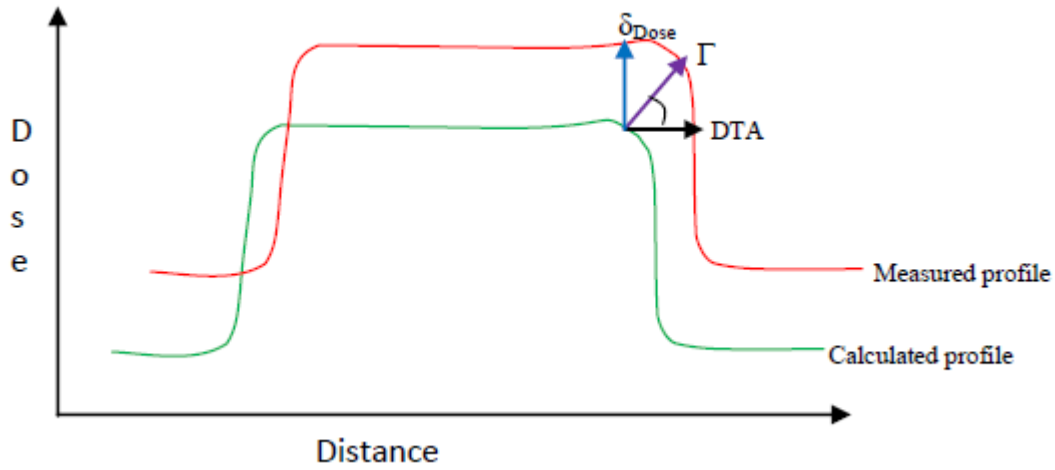


Figure 10: Difference between Γ , DTA and DD

4.2.1 Gamma Method

When comparing two dose distributions, misjudgement in the agreement of two dose distributions may occur in the following (Compass user guide, 2011):

- The difference between two dose distributions can be large in high-gradient regions, even if the isodoses are relatively close to each other.
- The isodose distance between two dose distributions can be large in low-gradient regions, although the difference in dose may be quite small.

The gamma method combines both low dose- and high dose gradient regions in to single factor called the Gamma index (γ). The γ for measurement point r_m is denoted by:

$$\gamma(r_m) = \min \{ \Gamma(r_m, r_c) \} \forall \{ r_c \} \quad (2)$$

where by:

$$\Gamma(r_m, r_c) = \sqrt{\frac{r^2(r_m, r_c)}{\Delta d_M^2} + \frac{\delta^2(r_m, r_c)}{\Delta D_M^2}} \quad (3)$$

$$r(r_m, r_c) = |r_c - r_m| \quad (4)$$

and

$$\delta(r_m, r_c) = D_c(r_c) - D_m(r_m) \quad (5)$$

where, r_m is the position of a single measurement point, r_c is the spatial location of the calculated distribution relative to the measurement point, Δd_M is the passing criterion for isodose distance, ΔD_M is the passing criterion for dose difference, $D_c(r_c)$ is the calculated dose in r_c and $D_m(r_m)$ is the measured dose in r_m .

The following scenario exists in γ :

- $\gamma(r_m) \leq 1$; The calculation pass the set criterion
- $\gamma(r_m) > 1$; The calculation fail the set criterion

4.3 Paired t-test

Rosie Shier et al (2004) indicated that the paired t-test can be used to compare two different methods of measurement or treatment where the measurements/treatment is applied to the same phantom.

4.3.1 Procedure

To test the null hypothesis that the true mean difference is zero, the procedure is as follows:

- Calculate the difference between the two measurements on each pair: $d_i = y_i - x_i$ (6)
- Calculate the mean difference: $\bar{d}$
- Calculate the standard deviation of the difference and use it to calculate the standard error of the mean difference: $SE(\bar{d}) = \frac{s_d}{\sqrt{n}}$ (7)
- Calculate the t-statistics: $T = \frac{\bar{d}}{SE(\bar{d})}$ (8)
- Use tables of the t-distributions to compare your value for T to the t_{n-1} distribution

Rosie Shier et al (2004) suggested that the calculation of a confidence interval for the mean difference reveals limits within which the true difference is likely to lie. A 95% confidence interval for the true mean difference is given by:

$$\bar{d} \pm (t^* \times SE(\bar{d})) \quad (9)$$

Where, t^* is the 2.5% point of the t-distribution on $n-1$ degrees of freedom.

Furthermore, Koo et al (2015) and ICRU report no 83 (2010) gave the indexes as another tool that can be used for comparing the measured and the TPS calculated dose distributions. The tools include homogeneity index, conformation number and conformity index.

4.4 Homogeneity index

Homogeneity index (HI) of the target volume (as defined by the ICRU 83) is denoted by:

$$HI = \frac{(D_{2\%} - D_{98\%})}{D_{50\%}} \quad (10)$$

Where by, $D_{2\%}$ represents the near maximum dose received by 2% of the PTV, $D_{98\%}$ represents the near minimum dose received by 98% of the PTV, and $D_{50\%}$ represents the dose received by 50% of the PTV.

- $HI = 0$, indicates a more homogeneous plan, and
- $HI = 1$, indicates a less homogeneous plan

4.5 Conformity index

The conformity index (CI) as defined by the Radiation Therapy Oncology Group is denoted by:

$$CI = \frac{V_{RI}}{TV} = \frac{D_{50}}{D_{98}} \quad (11)$$

Where by, V_{RI} is the volume of reference isodose and TV is the PTV volume. TV includes the entire PTV and it is recommended by ICRU 83 report that D_{98} be used for delineating the TV. The D_{50} was used instead of V_{RI} for the purpose of this study.

- $CI = 1$, is an ideal conformation, and
- $CI > 1$, indicates the irradiation of healthy tissues.

4.6 Conformation number

The conformation number (CN) is evaluated to consider the irradiation of healthy tissue (Koo et al, 2015). The CN is denoted by:

$$CN = \frac{TV_{RI}}{TV} \times \frac{TV_{RI}}{V_{RI}} = \frac{D_2}{D_{98}} \times \frac{D_2}{D_{50}} \quad (12)$$

TV and TV_{RI} represent the PTV volume and the volume covered by the reference isodose line, respectively.

- The first fraction indicates the quality of target coverage, and
- The second fraction represents the volume of healthy tissue irradiated with the reference isodose or higher

4.7 IMRT Phantom-chamber calibration factor

Linear accelerators are calibrated to deliver 1 cGy/MU for 100 cm Source Surface Distance (SSD) in water at depth of d_{max} (1.63 cm for Addington Hospital 6MV beam) for 10 cm × 10 cm set field size. Biplap (2010) and Low (2003) indicated that for measurements in IMRT fields using ion chamber in water, the dose to water must first be measured to check the calibration constancy factor (CCF), which is the ratio of calibration dose (1 cGy/MU) to the measured dose at d_{max} .

The calibration constancy factor (CCF) is correlated with a known dose in the TPS, usually 200 cGy to be delivered at 10 cm depth in water, to get the calibration factor for water phantom – ionisation chamber combination. This is given by the following equation:

$$CF(W) \approx \frac{D_{TPS}}{D_M \times N_{D,W} \times K_{Q,Q0} \times K_{T,P} \times CCF_{d_{max}/d_{10}}} \quad (13)$$

where D_{TPS} is the TPS calculated dose, D_M is the measured dose, $K_{Q,Q0}$ is the specific beam quality correction factor and CCF is the calibration constancy factor, K_{TP} is the ion chamber temperature and pressure correction and N_{DW} is the absorbed dose to water ionisation chamber calibration factor.

Chapter 5 Results and Discussion

5.1 End to End testing

5.1.1 End to End testing with 2D array phantom results

The end to end testing (illustrated in figure 2) was carried out in ADH and IALCH. The results are summarized in Tables 4, 5, 6, 7, 8 and 9.

Table 4: Summary of the EclipseTM (ADH) and MonacoTM (IALCH) TPS beam arrangements and plans showing the calculated doses for each of the techniques.

	Eclipse ver 8.6 (ADH)				Monaco ver 5.11 (IALCH)			
Plan	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
Prescribed dose (cGy)	200	200	200	200	200	200	200	200
Beam energy (MV)	6	6	6	6	6	6	6	6
# of Fields/ Arcs	4	5	5	1	4	5	5	1
Beam Angle (°)	0	25.4	20.3	179-181	0	0	0	180-
	90	96.3	96.3		90	45	45	180
	180	152.1	152.1		180	135	135	
	270	204.9	204.9		270	225	225	
		273.8	278.9			315	315	
TPS Dose (cGy)	202.5	202	201.5	204.7	195.4	190.5	194.7	208.3
D ₉₈ (min dose)	193.0	195.7	187.0	199.7	175.0	155.0	167.4	171.7
D ₅₀ (Mean dose)	202.5	202.0	201.5	204.7	195.4	190.5	194.7	208.3
D ₂ (max dose)	206.0	207.3	205.7	207.0	215.8	205.0	209.4	244.0

5.1.2 3D/2D array phantom verification results

The Delta4 and OCTAVIUS were used to verify all the plans. The different criteria were used to pass the plans. Table 6 illustrates the different criteria that were used to pass the plans and it was evident that 6%/4mm is necessary for all plans to pass by 100%. Table 5 below attest to the Mutic and Purdy (1998) sentiment that the gamma index is the correct tool to verify modern treatment techniques, because most plans would have failed to reach acceptable passing criteria

by using only % DD. The same argument can be extended to the DTA, wherein most plans would reach acceptable passing criteria with ease and provide false passes upon comparison.

Table 5: Summary of the ADH and IALCH verification results for all techniques using different passing criteria

Plan	100% of all calculated points with $\Gamma \leq 1$							
	Delta4 (ADH)				OCTAVIUS 4D 1500 (IALCH)			
	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
Pass 2%/2mm criteria	75.7%	53.0%	76.0%	68.7%	82.7%	66.7%	86.0%	73.9%
Pass 3%/3mm criteria	96.0%	71.1%	93.5%	91.8%	98.6%	83.6%	96.9%	94.9%
Pass 4%/4mm criteria	100.0%	90.0%	99.1%	96.8%	100.0%	93.3%	99.9%	96.5%
Pass 5%/5mm criteria	100.0%	98.7%	100.0%	98.7%	100.0%	99.9%	100.0%	99.3%
Pass 6%/4mm criteria	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Point dose (cGy)	203.83	202.23	203.70	205.72	203.83	202.23	203.70	205.72
100% of all calculated points within % dose difference (DD)								
Pass 2% DD criteria	46.9%	21.0%	45.7%	37.7%	66.8%	66.7%	65.4%	61.8%
Pass 3% DD criteria	70.0%	37.1%	70.8%	63.6%	80.7%	67.9%	81.2%	75.5%
Pass 4% DD criteria	81.3%	60.7%	79.5%	77.7%	91.3%	80.2%	89.6%	77.6%
Pass 5% DD criteria	85.0%	74.9%	83.9%	85.9%	94.8%	84.6%	94.5%	95.1%
Pass 6% DD criteria	85.0%	72.9%	86.8%	91.0%	95.9%	92.4%	96.5%	98.6%
100% of all calculated points within mm of distance to agreement (DTA)								
Pass 2mm DTA criteria	91.1%	84.9%	82.8%	83.9%	95.6%	94.3%	92.9%	94.8%
Pass 3mm DTA criteria	98.5%	93.7%	95.6%	95.0%	99.5%	96.1%	98.8%	96.9%
Pass 4mm DTA criteria	100.0%	97.5%	100.0%	98.7%	100.0%	99.9%	100.0%	100.0%
Pass 5mm DTA criteria	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

5.1.3 2D array phantom measured dose results analysis

The MatriXX^{Evolution} with Compass and OCTAVIUS with VeriSoft were used to measure the delivered dose. Table 6 illustrates the results obtained.

Table 6: Summary of measured doses from ADH and IALCH obtained using MatriXX^{EVOLUTION} with COMPASS® and OCTAVIUS with VeriSoft® respectively.

	MatrixX with COMPASS ® ver 2.1				OCTAVIUS with VeriSoft ® ver 1.8			
Plan	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
Measured Dose (cGy)	203.97	203.90	199.70	204.77	196.13	193.37	198.27	215.17
D ₉₈ (min dose)	189.83	195.63	180.40	185.90	176.57	156.17	169.13	175.30
D ₅₀ (Mean dose)	203.97	203.90	199.70	204.77	196.20	193.37	198.23	215.17
D ₂ (max dose)	210.67	210.10	213.27	216.67	216.57	206.97	213.33	249.80

The measured dose was compared with the planned dose. Figures 11, 12, 13, and 14 illustrate the DVH's from both the measured and planned doses for all the hypothetical OARVs and PTVs for 3D CRT, dIMRT, ssIMRT and RapidArc respectively. The results are from ADH

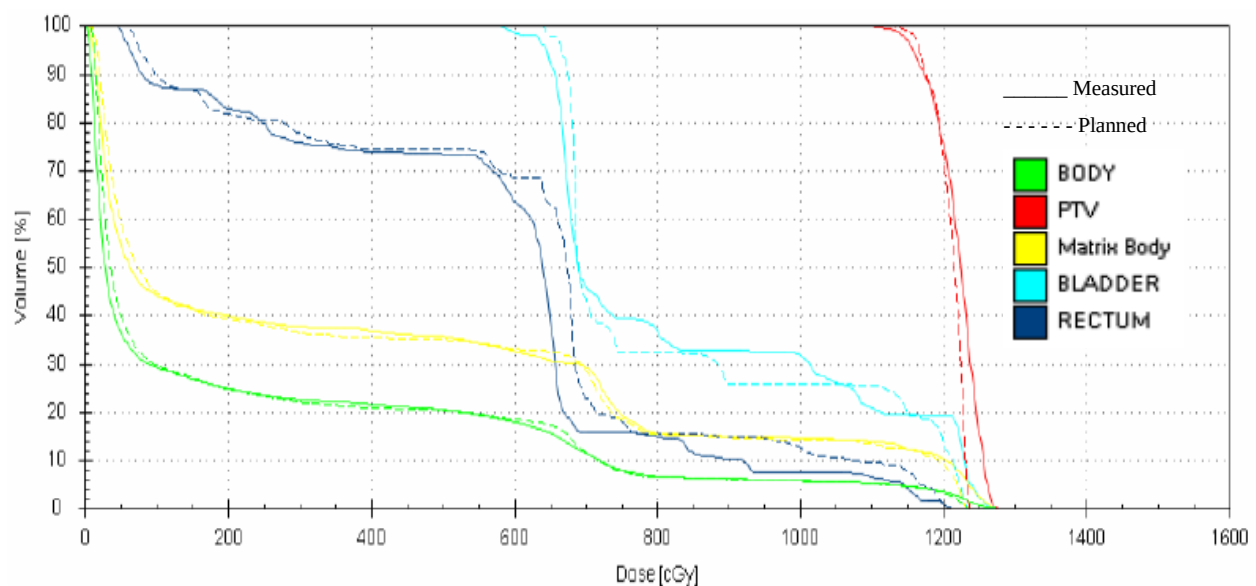


Figure 11: Summary of DVH comparison for 3D-CRT case from ADH. The dotted line is the Eclipse® TPS planned dose and the solid line is the MatriXX measured dose.

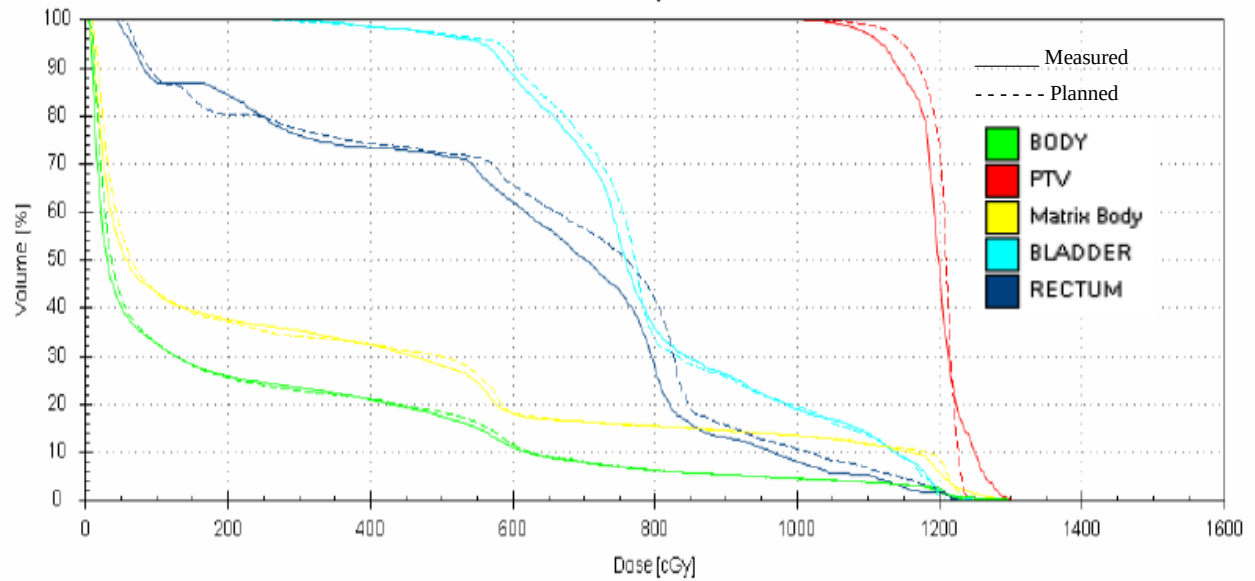


Figure 12: Summary of DVH comparison for dIMRT case from ADH. The dotted line is the Eclipse® TPS planned dose and the solid line is the MatriXX measured dose.

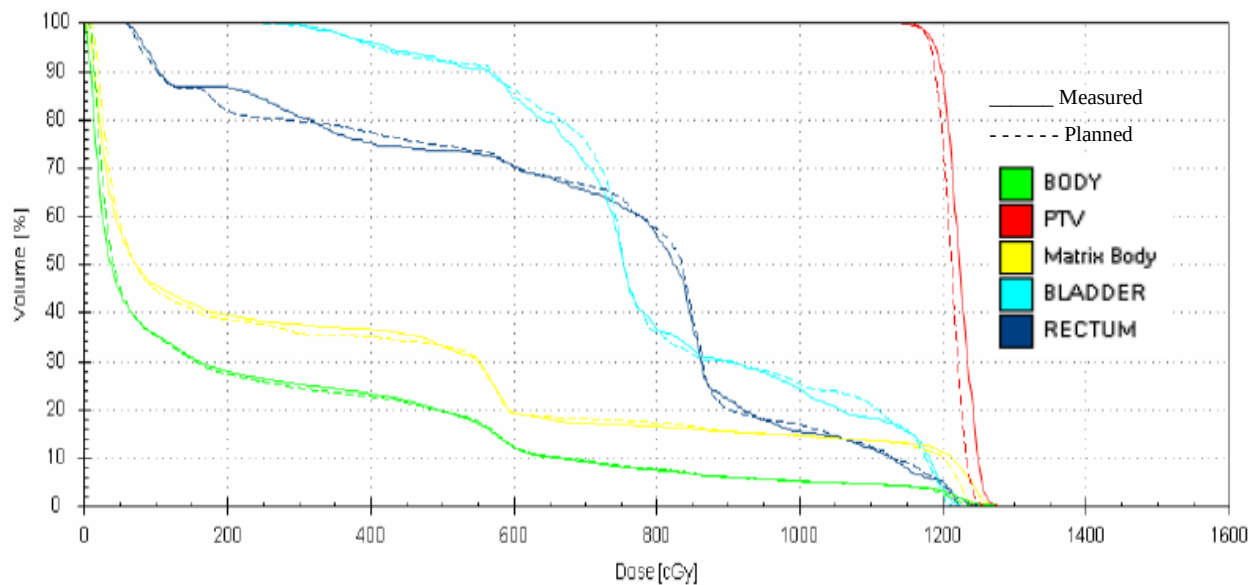


Figure 13: Summary of DVH comparison for ssIMRT case from ADH. The dotted line is the Eclipse® TPS planned dose and the solid line is the MatriXX measured dose.

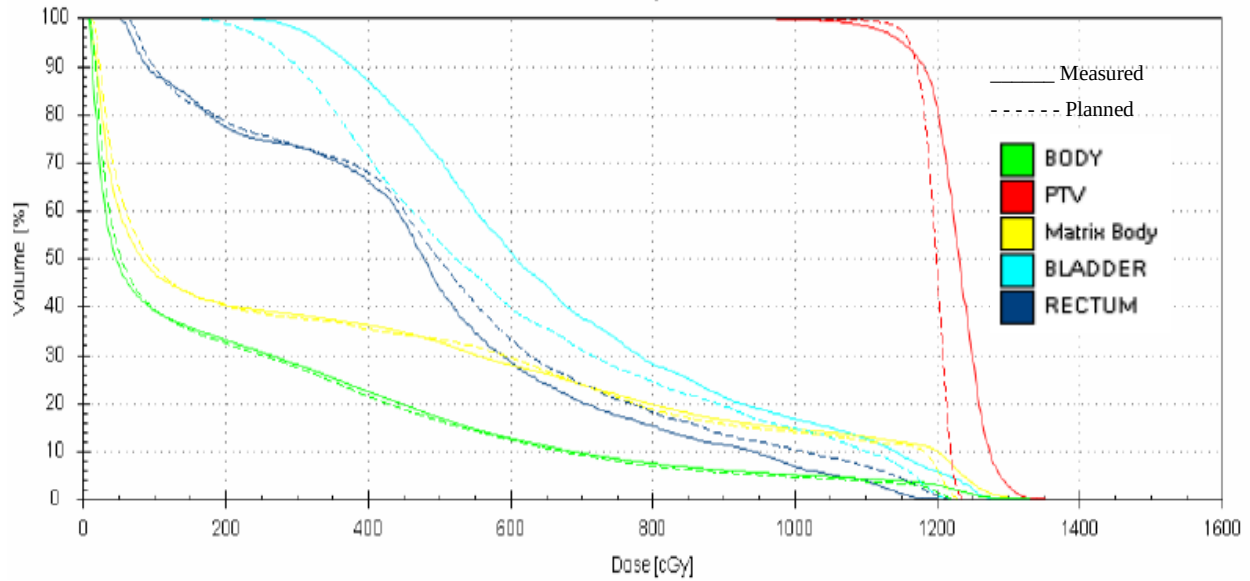


Figure 14: Summary of DVH comparison for RapidArc case from ADH. The dotted line is the Eclipse® TPS planned dose and the solid line is the MatriXX measured dose.

The delivered doses and TPS planned doses were also compared. Table 7 illustrates the comparison between the measured and planned dose distributions.

Table 7: Comparison of the planned and measured doses obtained using MatriXX^{EVOLUTION} with COMPASS® at ADH and OCTAVIUS with VeriSoft® at IALCH.

Plan	% difference							
	ADH				IALCH			
	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
Measured/Plan Dose	-0.72	-0.94	0.89	-0.03	-0.38	-1.50	-1.83	-3.30
D ₉₈ (min dose)	1.64	0.03	3.53	6.91	-0.90	-0.75	-1.04	-2.10
D ₅₀ (Mean dose)	-0.72	-0.94	0.89	-0.03	-0.41	-1.50	-1.81	-3.30
D ₂ (max dose)	-2.27	-1.35	-3.68	-4.67	-0.36	-0.96	-1.88	-2.38

The 3D-CRT and ssIMRT measured doses compared very well with the planned dose, whereas the minimum and maximum doses for the dIMRT and RapidArc techniques gave bigger differences respectively. The dose differences in dynamic treatment mode can be attributed to factors ranging from detector resolution, MLC leakage, detector sampling time and the accuracy of the TPS dose calculation algorithms.

5.1.4 End to End testing with water phantom results

The end to end testing was carried out as illustrated in figure 4 and results are summarized in table 9 and 10. The Grey's hospital results were included and tabulated in table 11.

Table 8: Summary of EclipseTM and MonacoTM TPS beam arrangements and calculated doses

	Eclipse ver 8.6 (ADH)				Monaco ver 5.11 (IALCH)			
Plan	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
Prescribed dose (cGy)	200	200	200	200	200	200	200	200
Beam energy (MV)	6	6	6	6	6	6	6	6
# of Fields/ Arcs	4	5	5	1	4	5	5	1
Beam Angle (°)	0	25.4	20.3	179-181	0	0	0	180-180
	90	86.2	86.2		90	45	45	
	180	147	147		180	135	135	
	270	210	210		270	225	225	
		273.8	273.8			315	315	
TPS Dose (cGy)	196.7	197.3	198.4	195.3	196.7	190.5	194.7	208.3
D ₉₈ (min dose)	180.1	182.8	182.7	190.6	180.1	155.0	167.4	171.7
D ₅₀ (Mean dose)	196.7	197.3	198.4	195.3	196.7	190.5	194.7	208.3
D ₂ (max dose)	199.9	203.1	204.8	198.6	199.9	205.0	209.4	244.0

The Delta4 and OCTAVIUS were used to verify all the plans. The 3%/3 mm criteria was used to pass the plans and 100% of the defined points were found to be $\Gamma \leq 1$. The measured dose compared well with the TPS planned dose

Table 9: Summary of verification (Delta4 from ADH and OCTAVIUS from IALCH), dose delivered and comparison of doses from ADH and IALCH.

	Delta4 ver 2.1 (ADH)				OCTAVIUS 4D 1500 (IALCH)			
Plan	3D-CRT	ssIMRT	dIMRT	RapidArc	3D-CRT	ssIMRT	dIMRT	VMAT
	100% of all calculated points with $\Gamma \leq 1$							
Pass 3%/3mm criteria	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
	FC-65G ion chamber (ADH)				TM30013 ion chamber (IALCH)			
Measured Dose (cGy)	197.07	197.27	198.23	195.83	197.43	192.13	196.10	210.50
	% difference							
	ADH				IALCH			
Plan/measured Dose	-0.19	0.02	0.08	-0.27	-0.37	-0.86	-0.72	-1.06

5.1.5 End to End testing phantom results discussion

The measured doses compared well with the planned doses from institution to institution, even though Grey's hospital did not have DVH-based measurement software. The hospital MatriXX^{Evolution} phantom point dose measurement was used instead and the measured point dose with MatriXX^{Evolution} was found to be less than 9 % for both D_{50} and D_2 of the planned doses. The complete summary is tabulated in Table 11 and 12.

Table 10: Summary of the dose differences between measured and planned doses for the 3 different institutions

	Mean dose (D_{50}) vs Measured dose (cGy)					
	MatriXX ^{Evolution} /Octavius			FC65-G/TM30013 ion chamber		
	ADH	Greys	IALCH	ADH	Greys	IALCH
3D-CRT	-0.67%	1.27%	-0.41%	-0.19%	-0.75%	-0.37%
ssIMRT	-0.87%	3.69%	-1.50%	0.02%	-0.58%	-0.86%
dIMRT	0.93%	6.41%	-1.81%	0.08%	0.27%	-0.72%
VMAT	-0.03%	-	-3.30%	-0.27%	-	-1.06%

Table Table 11: Summary of the % difference between measured and planned doses for the 3 different institutions

	Maximum dose (D_2) vs Measured dose (cGy)					
	MatriXX ^{Evolution} /Octavius			FC65-G/TM30013 ion chamber		
	<i>ADH</i>	<i>Greys</i>	<i>IALCH</i>	<i>ADH</i>	<i>Greys</i>	<i>IALCH</i>
3D-CRT	-2.27%	4.61%	-0.36%	1.42%	-0.24%	1.25%
ssIMRT	-1.35%	7.85%	-0.96%	2.87%	1.42%	6.48%
dIMRT	-3.68%	8.91%	-1.88%	3.25%	2.25%	6.55%
VMAT	-4.67%	-	-2.38%	1.39%	-	14.73%

The 2D array phantom planned doses (D_{50}) and measured doses (D_{50}) from ADH and IALCH were found to be less than 1% and 3.5% respectively for all the treatment plans. IALCH hospital gave much larger mean dose differences for more complex treatment techniques for mean doses, which was not observed at ADH. However, the dose differences increased with complexity of the plans and the maximum doses (D_2) at ADH and IALCH was found to be less than 5% and 2.5% respectively.

The water phantom planned doses (D_{50}) and measured doses from ADH and IALCH hospital was found to be less than 0.3% and 1.1% respectively for all the treatment plans. The mean doses did not vary with complexity in treatment techniques. However, the much difference with complexity of the plan was visible on the water planned phantom maximum doses (D_2) of both ADH and IALCH was found to be less than 3.5% and 14.7% respectively. The high dose difference from IALCH can be attributed to Monte Carlo dose calculation algorithm.

The water phantom planned doses (D_{50} and D_2) and measured point doses from Grey's hospital agreed to be less than 0.8% and 2.5% respectively. The identical ionisation chamber (FC-65G), IBA dosimetry electrometer and IBA MatriXX^{Evolution} 2D array were used at Grey's and ADH.

5.2 Factors influencing IMRT and RapidArc planning

The calculated time, dose distributions quality indicators and MU for all available special procedures as a function of grid sizes are summarized in Table 12.

Table 12: Summary of factors influencing the planning of a ssIMRT delivery

Grid size (mm)	Time (min)	Dose distributions (cGy)			MU
		D ₉₈	D ₅₀	D ₂	
1.0	1.16	11.78	12.13	12.44	355
2.0	0.21	11.76	12.11	12.42	355
3.0	0.11	11.72	12.1	12.41	355
4.0	0.091	11.68	12.08	12.4	355
5.0	0.086	11.03	12.05	12.35	355

5.2.1 Time and grid size.

Planning parameters influencing the calculation time of dIMRT, ssIMRT and RapidArc plans were investigated. The average calculation time as a function of grid size was calculated, compared and is summarized in figure 15.

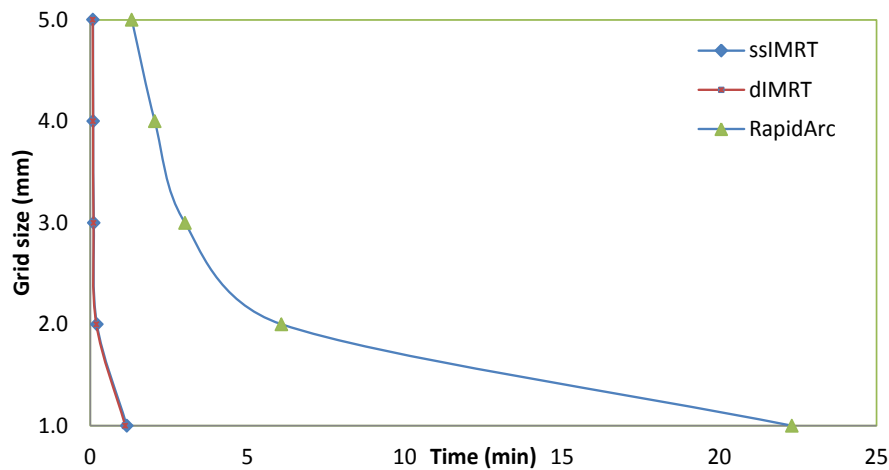


Figure 15: The plot of grid size versus time to calculate special procedures.

5.2.2. Dose distributions.

The dose distribution was calculated for dIMRT, ssIMRT and RapidArc plans. The minimum, mean and maximum doses as a function of grid size were calculated, compared and are summarized in figure 16 (D₉₈), 17 (D₅₀) and 18 (D₂) respectively.

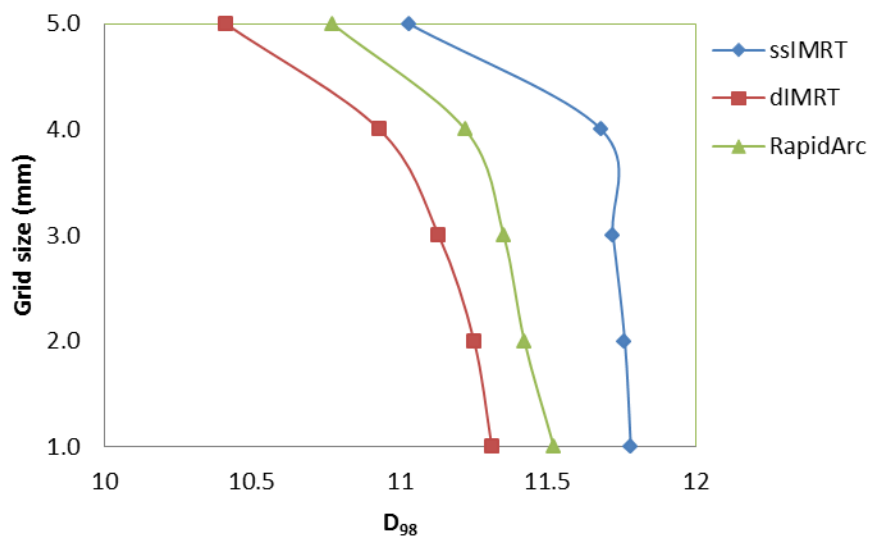


Figure 16: The plot of grid size versus minimum doses of special procedures.

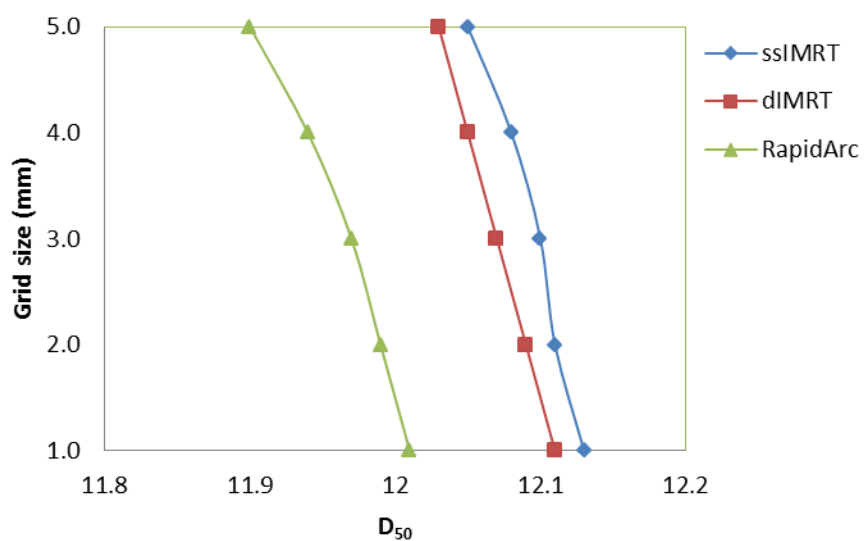


Figure 17: The plot of grid size versus mean doses of special procedures.

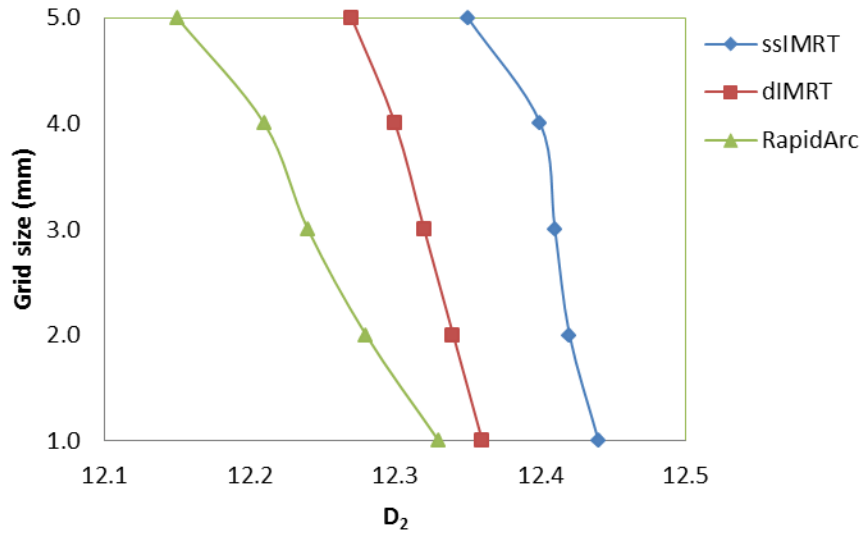


Figure 18: The plot of grid size versus maximum doses of special procedures.

5.2.3. Monitor Unit (MU).

The number of MU was calculated between dIMRT, ssIMRT and RapidArc plans. The average MU as a function of grid size were calculated, compared and is summarized in figure 19.

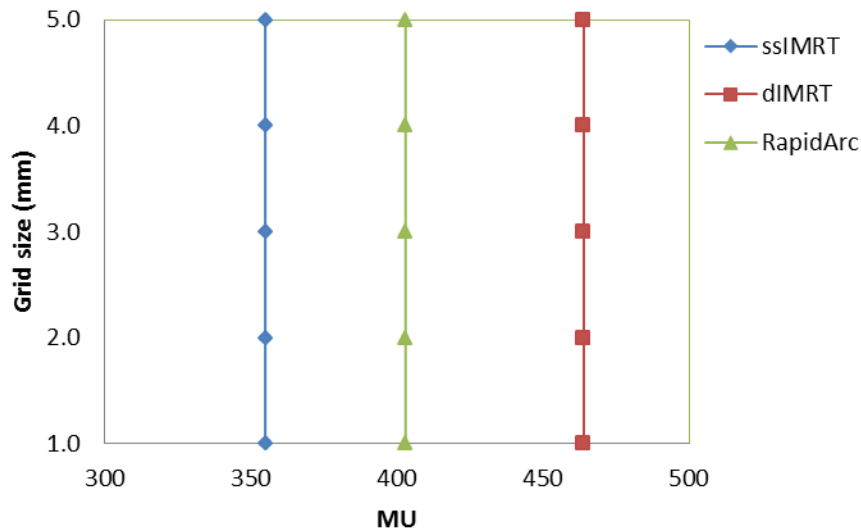


Figure 19: The plot of grid size versus MU calculated from special procedures.

All treatment techniques indicated some degree of agreement with varying grid size, however the calculation time was completely different for RapidArc plans and it is affected by the number of control points to be calculated over the entire arc.

5.3 CBCT based IGRT assessment of set-up error.

The primary role of the CBCT based planning without error was used as an intermediate between pCT based planning and CBCT with error based planning (Timmermann, 2009) in order to identify:

- (1) the inaccuracies in the conversion of CT values to electron densities due to increased scatter contribution by CBCT based dose calculation.
- (2) the degree of variance when calculating between the two modalities that may distort the results of this study if significant variance exists.
- (3) the resulting dose calculation congruent between kV-CBCT plans and pCT-based plans since an inherent level of variance exists between the two modalities.

Figures 20, 23 and 26 depict the pre-treatment pCT and CBCT matching. Figures 21, 24 and 27 depict the post-correction pCT and CBCT matching. Figures 22, 25 and 28 depict the post-treatment pCT and CBCT matching.

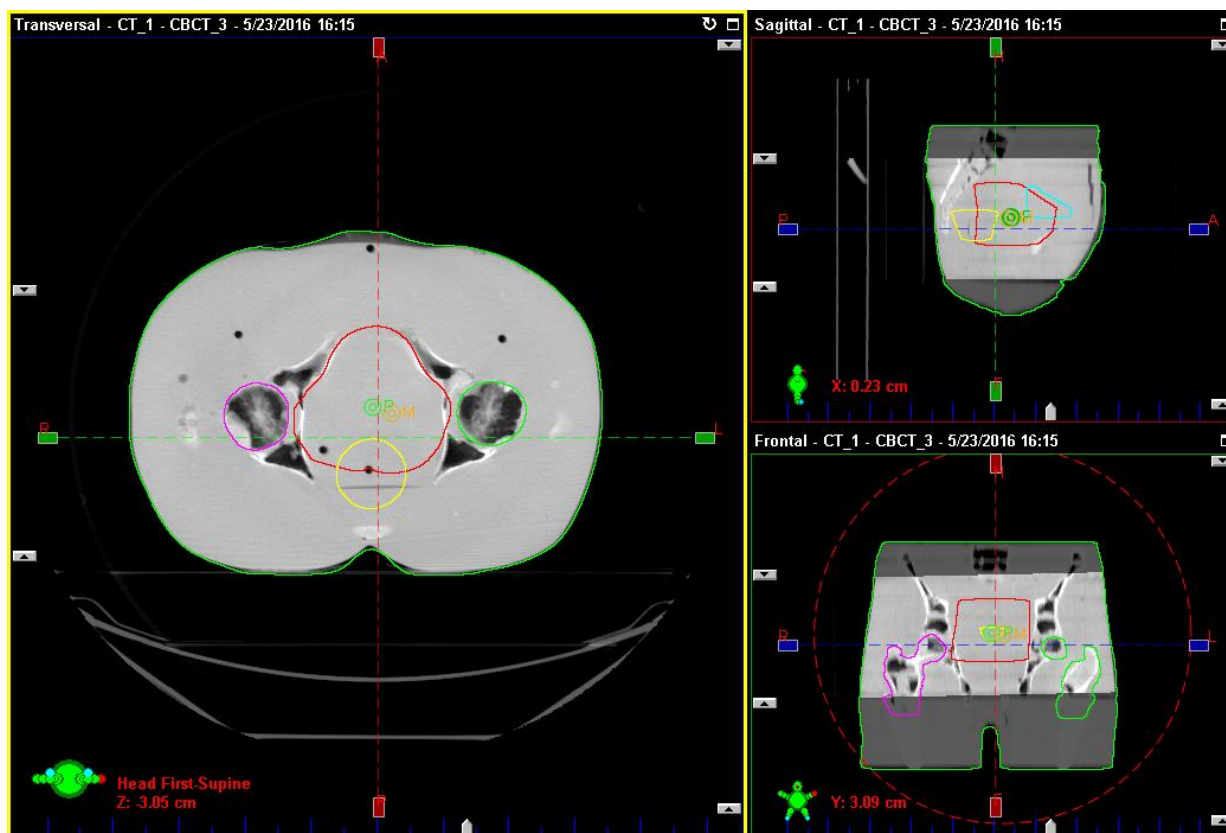


Figure 20: A screenshot of the pre-treatment pCT and CBCT on-line matching (Pelvis). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT)

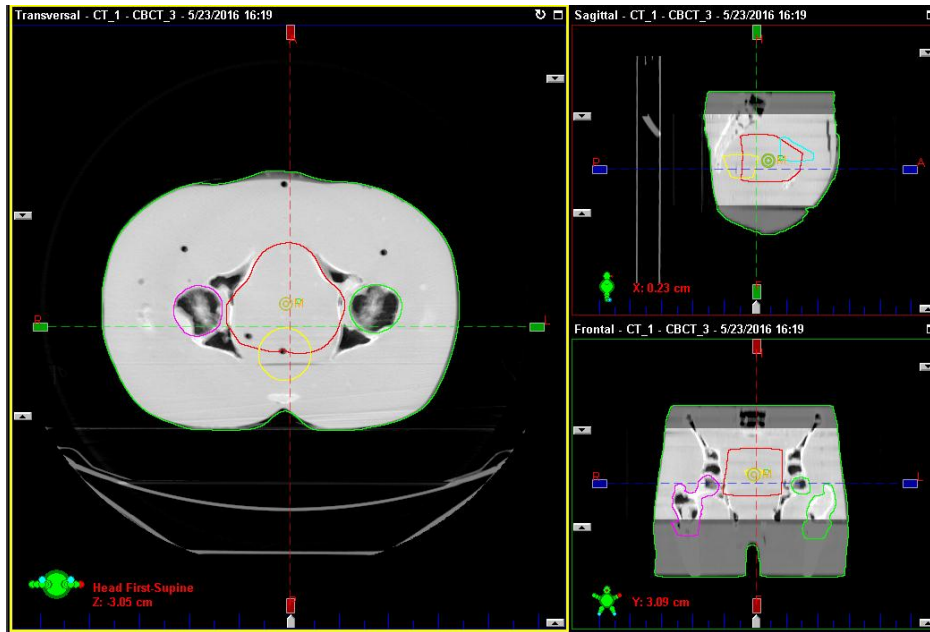


Figure 21: A screenshot of the post-correction pCT and CBCT on-line matching (Pelvis). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

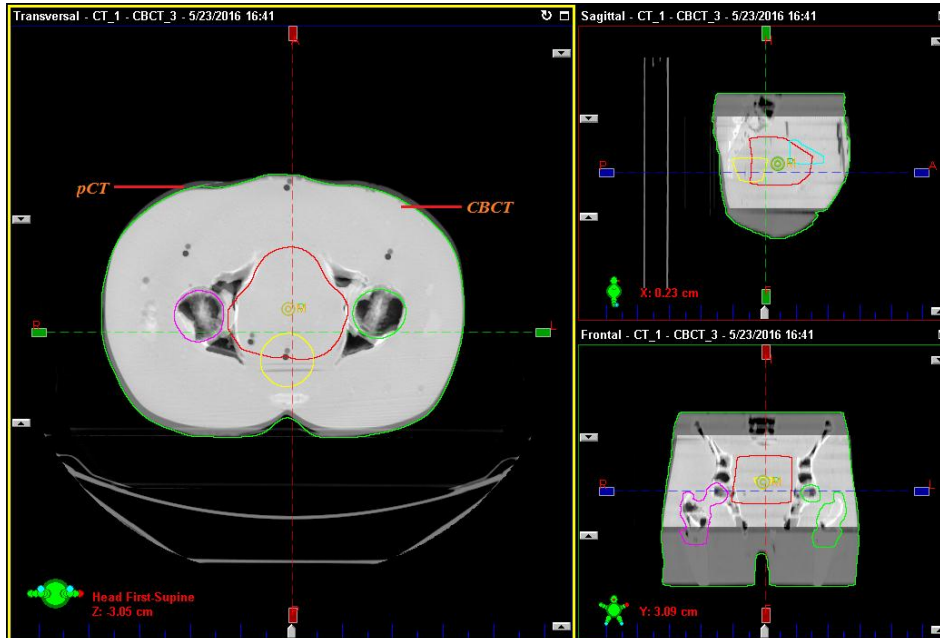


Figure 22: A screenshot of the post-treatment pCT and CBCT on-line matching with deliberate 3mm offset (Pelvis). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

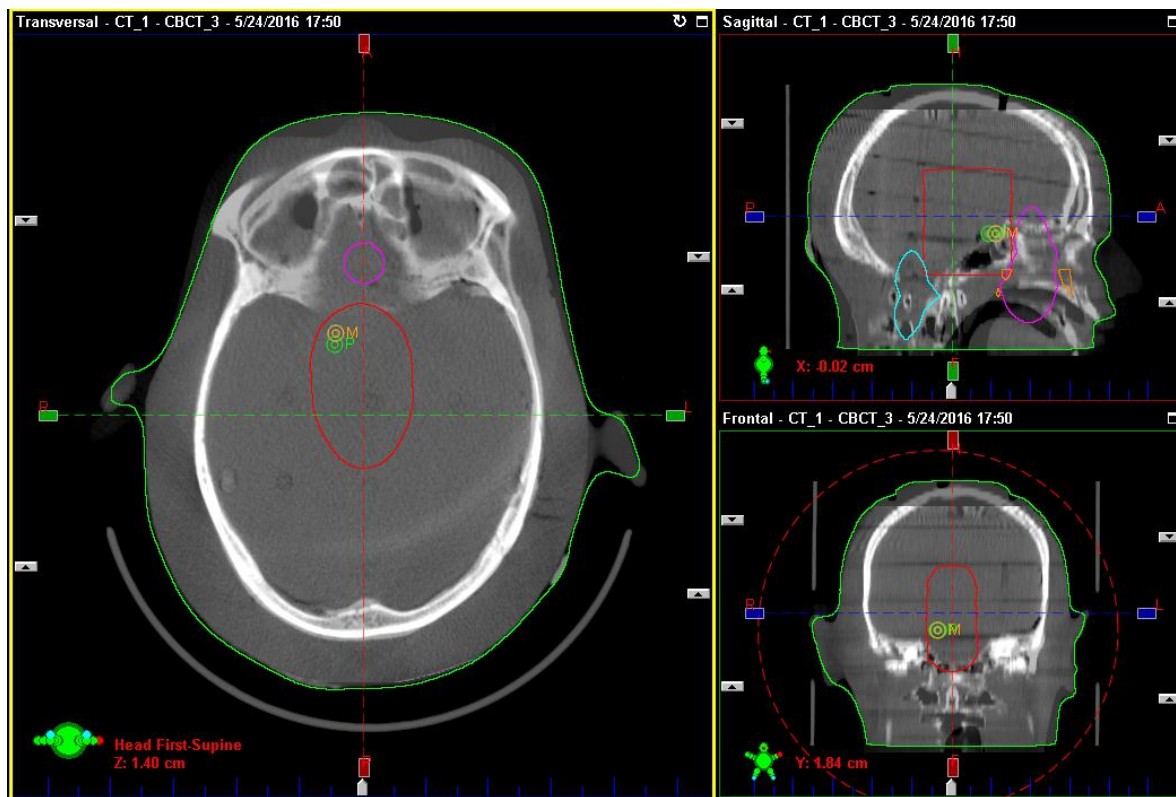


Figure 23: A screenshot of the pre-treatment pCT and CBCT on-line matching (H&N). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

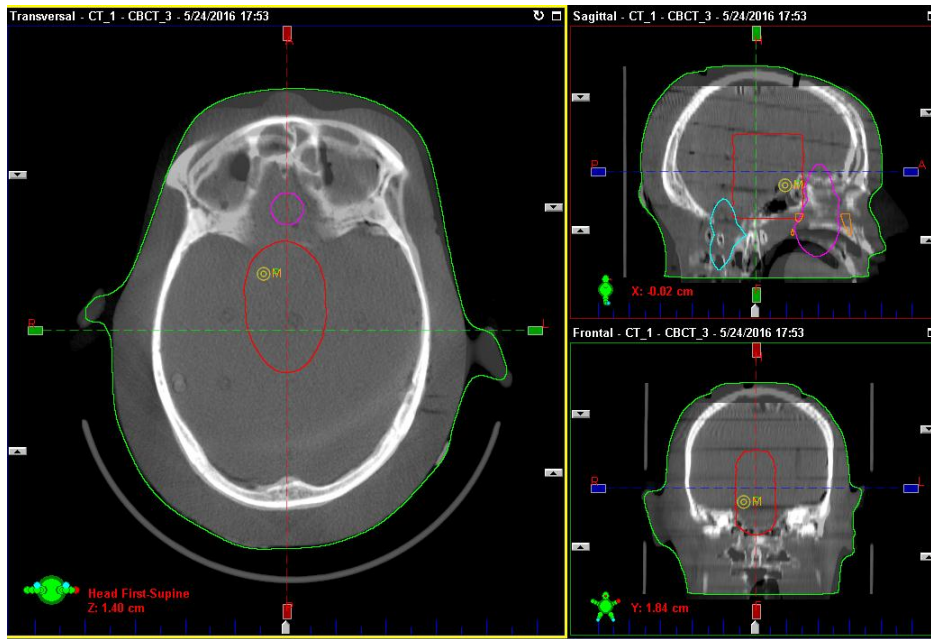


Figure 24: A screenshot of the post-correction pCT and CBCT on-line matching (H&N). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

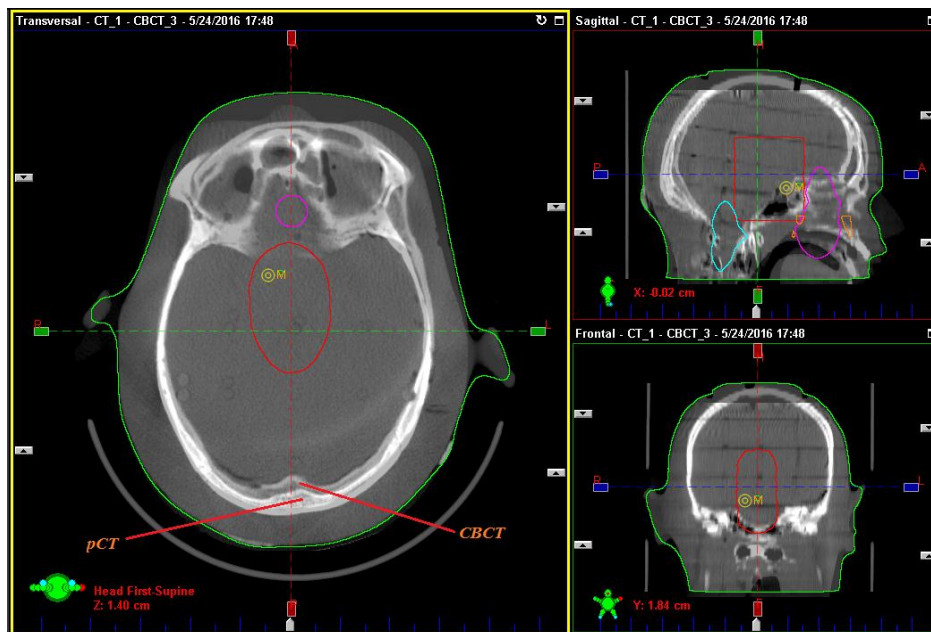


Figure 25: A screenshot of the post-treatment pCT and CBCT on-line matching with deliberate 3mm offset (H&N). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

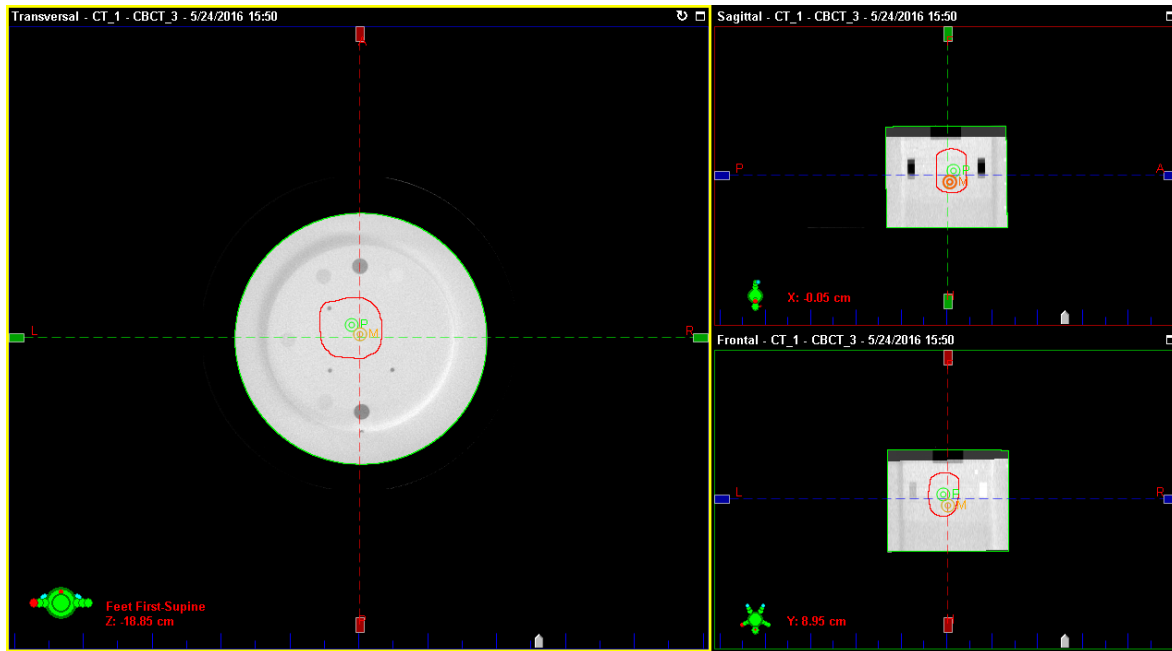


Figure 26: A screenshot of the pre-treatment pCT and CBCT on-line matching (Catphan®). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

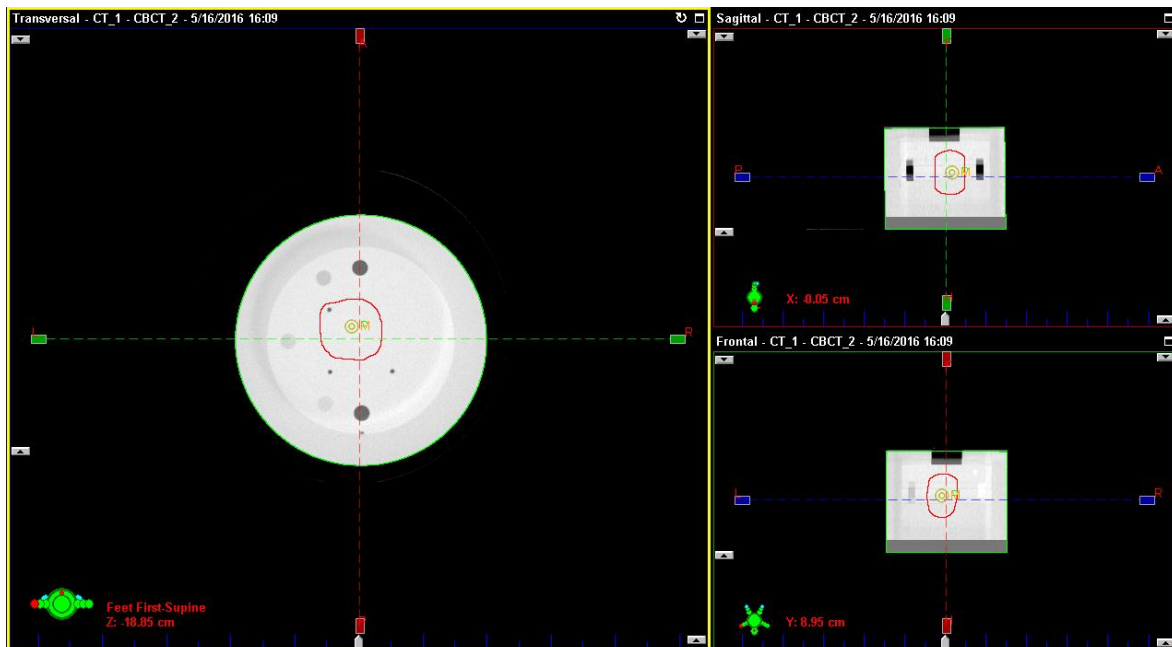


Figure 27: A screenshot of the post-correction pCT and CBCT on-line matching (Catphan®). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

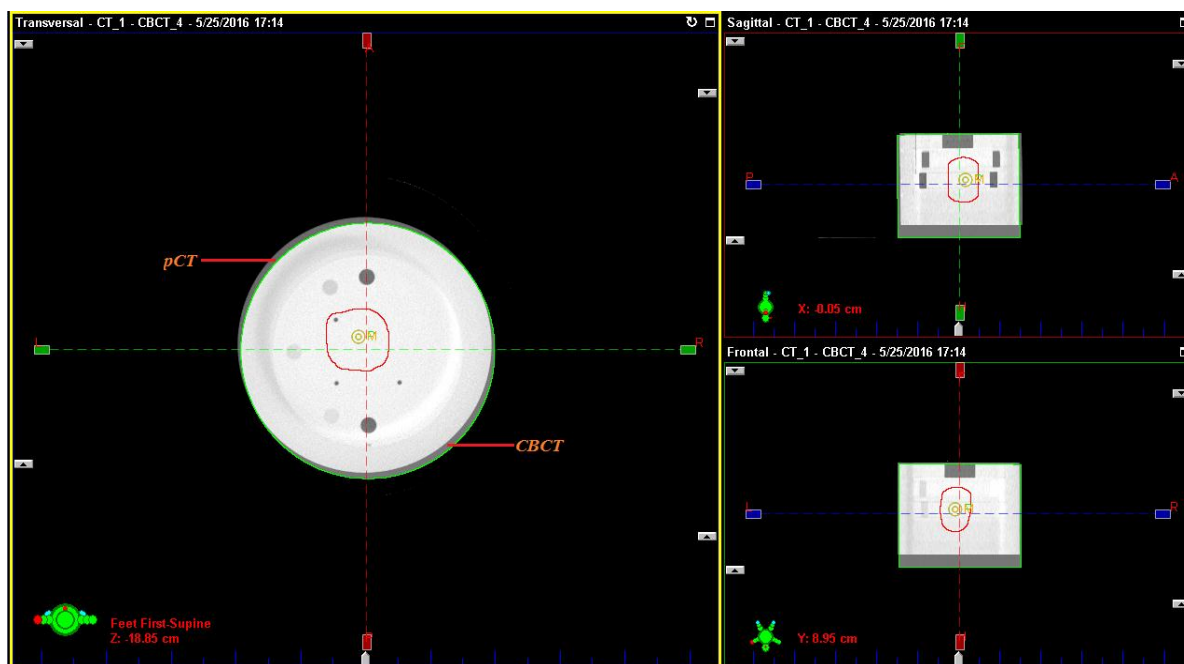


Figure 28: A screenshot of the post-treatment pCT and CBCT on-line matching with 3mm offset (Catphan®). The axial (right), coronal (bottom left) and sagittal (top left) views are shown. On the image, the P represents the planning isocenter (pCT) and M represents the matching isocenter (CBCT).

5.3.1.1. Anthropomorphic phantom (Pelvis small target).

For the pelvis plan with an elliptically shaped target, setup errors were deliberately introduced for the post treatment deliveries. The physicist in this study reproduced the correct setup and the other three participants (Radiotherapists) represented a typical inter-fraction setup error. The resultant setup errors from RapidArc treatment technique are summarized in Tables 14, 15, 16, 17 and 18. In this study, the mean indicates the set-up error and 1δ (represents the 68% probabilities) the systematic error (Timmermann, 2009).

Table 13: Summary of RapidArc pelvis small target setup errors

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	90.2	90.2	90.5	89.8	90.3
<i>Pre-correction set up errors</i>					
X-axis(mm)	10.9	3.0±1.0	5.0±4.0	-2.0±3.0	-2.0±4.0
Y-axis(mm)	96.4	-1.0±11.0	1.0±11.0	-4.0±13.0	-3.0±12.0
Z-axis(mm)	1.2	-1.0±2.0	2.0±2.0	1.0±2.0	0.0±2.0
<i>Shift: Post correction set up errors</i>					
X-axis(mm)	10.9	3.0±1.0	-1.0±4.0	0.0±3.0	-2.0±3.0
Y-axis(mm)	96.4	-3.0±12.0	-5.0±7.0	1.0±11.0	-3.0±12.0
Z-axis(mm)	1.0	-2.0±1.0	-2.0±2.0	-2.0±4.0	-2.0±3.0
<i>Post. delivery set up errors</i>					
X-axis(mm)	10.9	-1.0±2.0	3.0±5.0	-1.0±3.0	4.0±3.0
Y-axis(mm)	96.4	-1.0±13.0	-2.0±7.0	3.0±8.0	3.0±12.0
Z-axis(mm)	1.1	2.0±1.0	-1.0±2.0	-2.0±2.0	-2.0±5.0

The pre-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm Z-axis. From the Table 13 it was evident that the system suffers from a systematic error of up to 13 mm in the longitudinal direction (Y-axis). A systematic error was less than 4 mm in the X- and Z-axis

The post-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm. A systematic error of less than 12 mm was observed in the longitudinal direction. A systematic error was less than 4 mm in the X- and Z-axis

The post-delivery set up error was found to be less than 2 mm after substituting the intentionally introduced 3 mm in X-axis while the inter-participant worst case scenario was found to be 3 mm. A systematic error of less than 13 mm was observed in the longitudinal direction. A systematic error was less than 5 mm in X- and Z-axis

5.3.1.2. Anthropomorphic phantom (Pelvis Big target).

The pre-correction set up error was found to be less than 5 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm in the Z-axis. From the Table 14 it was evident that the system suffers from a systematic error of up to 13 mm in the longitudinal direction. The systematic error was less than 5 mm in the X- and Z-axis

Table 14: Summary of RapidArc pelvis big target setup errors

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	90.2	90.2	90.5	89.8	90.3
<i>Pre-correction set up errors</i>					
X-axis(mm)	10.9	1.0±3.0	1.0±5.0	-2.0±3.0	-2.0±4.0
Y-axis(mm)	96.4	-5.0±12.0	-5.0±14.0	-4.0±13.0	-3.0±12.0
Z-axis(mm)	1.2	-1.0±2.0	2.0±2.0	1.0±2.0	0.0±2.0
<i>Shift: Post correction set up errors</i>					
X-axis(mm)	10.9	0.0±4.0	-1.0±4.0	0.0±3.0	-2.0±3.0
Y-axis(mm)	96.4	-4.0±13.0	-4.0±13.0	-4.0±13.0	-3.0±12.0
Z-axis(mm)	1.0	0.0±3.0	-1.0±0.2	-2.0±4.0	-2.0±3.0
<i>Post. delivery set up errors</i>					
X-axis(mm)	10.9	-2.0±4.0	1.0±5.0	-3.0±3.0	2.0±3.0
Y-axis(mm)	96.4	-1.0±13.0	-3.0±12.0	-3.0±10.0	0.0±12.0
Z-axis(mm)	1.1	1.0±3.0	-2.0±6.0	-2.0±2.0	-2.0±5.0

The post-correction set up error was found to be less than 4 mm in the X-axis while the inter-participant worst case scenario was found to be 5 in the X-axis. A systematic error of less than 13 mm was observed in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

The post-delivery set up error was found to be less than 2 mm after substituting the intentionally introduced 3 mm in X-axis while the inter-participant worst case scenario was found to be 3 mm in the X-axis. The systematic error of less than 13 mm was observed in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

5.3.1.3. Anthropomorphic phantom (H&N small target).

The pre-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 3 mm in the Z-axis. From the Table 15 it was evident that the system suffers from a systematic error of up to 10 mm in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

Table 15: Summary of RapidArc H&N small target setup errors

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	87.8	91.9	92.2	91.6	92.3
<i>Pre-correction set up errors</i>					
X-axis(mm)	14.7	-1.0±4.0	-1.0±4.0	-2.0±4	-1.0±3
Y-axis(mm)	26.0	0.0±10.0	-1.0±10.0	1.0±10.0	2.0±9.0
Z-axis(mm)	1.2	-3.0±3.0	-3.0±3.0	-1.0±3.0	-1.0±3.0
<i>Shift: Post correction set up errors</i>					
X-axis(mm)	14.7	1.0±2.0	-5.0±3.0	-5.0±3.0	-4.0±3.0
Y-axis(mm)	26.0	0.0±10.0	1.0±10.0	1.0±10.0	2.0±9.0
Z-axis(mm)	1.0	0.0±1.0	-4.0±2.0	-3.0±3.0	-4.0±3.0
<i>Post. delivery set up errors</i>					
X-axis(mm)	14.7	0.0±1.0	-4.0±3.0	-4.0±4.0	-3.0±4.0
Y-axis(mm)	26.0	0.0±10.0	-2.0±10.0	-1.0±7.0	-2.0±10.0
Z-axis(mm)	1.1	0.0±1.0	-2.0±2.0	-2.0±6.0	-2.0±2.0

The post-correction set up error was found to be less than 1 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm in the X-axis. A systematic error of less than 10 mm was observed in the longitudinal direction. The systematic error was less than 3 mm in the X- and Z-axis

The post-delivery set up error was found to be less than 1 mm after substituting the intentionally introduced 3 mm in X-axis while the inter-participant worst case scenario was found to be 4 mm in the X-axis. The systematic error of less than 10 mm was observed in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

5.3.1.4. Anthropomorphic phantom (H & N Big target).

The pre-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm in the Z-axis. From the Table 16 it was evident that the system suffers from systematic error of up to 13 mm in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

Table 16: Summary of RapidArc H&N big target setup errors

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	87.8	91.9	92.2	91.6	92.3
<i>Pre-correction set up errors</i>					
X-axis(mm)	14.7	-1.0±3.0	-1.0±3.0	-2.0±3.0	-1.0±2.0
Y-axis(mm)	26.0	0.0±10.0	1.0±10.0	1.0±10.0	2.0±9.0
Z-axis(mm)	1.2	-3.0±3.0	-3.0±3.0	-1.0±3.0	-1.0±3.0
<i>Shift: Post correction set up errors</i>					
X-axis(mm)	14.4	4.0±4.0	-5.0±3.0	-5.0±3.0	-4.0±3.0
Y-axis(mm)	26.0	0.0±10.0	1.0±10.0	1.0±10.0	2.0±9.0
Z-axis(mm)	1.0	0.0±1.0	-4.0±2.0	-3.0±3.0	-4.0±3.0
<i>Post. delivery set up errors</i>					
X-axis(mm)	14.4	0.0±1.0	-3.0±3.0	-1.0±3.0	-3.0±3.0
Y-axis(mm)	26.0	0.0±10.0	-2.0±10.0	2.0±11.0	2.0±10.0
Z-axis(mm)	1.1	0.0±1.0	-2.0±2.0	2.0±3.0	2.0±2.0

The post-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 3 mm in the X-axis. A systematic error of less than 10 mm in the longitudinal direction was observed. The systematic error was less than 4 mm in the X- and Z-axis

The post-delivery set up error was found to be less than 0 mm after substituting the intentionally introduced 3 mm in X-axis while the inter-participant worst case scenario was found to be 3 mm in the X-axis. The systematic error of less than 10 mm was observed in the longitudinal direction. The systematic error was less than 3 mm in the X- and Z-axis

5.3.1.5. Catphan® phantom.

The pre-correction set up error was found to be less than 3 mm in the X-axis while the inter-participant worst case scenario was found to be 5 mm in the Z-axis. From the Table 17 it was evident that our system suffers from systematic error of up to 13 mm in the longitudinal direction. The systematic error was less than 4 mm in the X- and Z-axis

Table 17: Summary of Catphan® phantom setup errors

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	88.8	91.1	91.4	90.8	91.2
<i>Pre-correction set up errors</i>					
X-axis(mm)	15.1	1.0±5.0	1.0±4.0	-1.0±1.0	0.0±2.0
Y-axis(mm)	57.1	-2.0±10.0	-13.0±12	-3.0±7.0	-3.0±6.0
Z-axis(mm)	2.1	2.0±0.6	0.0±1.0	0.0±1.0	-1.0±2.0
<i>Shift: Post correction set up errors</i>					
X-axis(mm)	15.1	-1.0±1.0	-1.0±1.0	-2.0±2.0	-1.0±0.0
Y-axis(mm)	57.1	1.0±12.0	-3.0±7.0	-3.0±7.0	-3.0±7.0
Z-axis(mm)	2.1	0.0±1.0	0.0±1.0	-1.0±1.0	-2.0±1.0
<i>Post. delivery set up errors</i>					
X-axis(mm)	15.1	-1.0±1.0	-1.0±2.0	-3.0±3.0	0.0±4.0
Y-axis(mm)	57.1	-3.0±7.0	-5.0±8.0	-4.0±7.0	-5.0±10.0
Z-axis(mm)	2.1	1.0±2.0	0.0±3.0	0.0±3.0	-1.0±2.0

The post-correction set up error was found to be less than 2 mm in X-axis while the inter-participant worst case scenario was found to be 3 mm but other participant managed to achieve the 0 mm set up error in the Z-axis. The systematic error of less than 12 mm was observed in the longitudinal direction. The systematic error was less than 5 mm in X- and Z-axis

The post-delivery set up error was found to be less than 2 mm after substituting the intentionally introduced 3 mm in X-axis while the inter-participant worst case scenario was found to be 3 mm but other participant managed to achieve the 0 mm set up error in the X-axis. The systematic error of less than 10 mm was observed in the longitudinal direction. The systematic error was less than 4 mm in X- and Z-axis

5.4 Dosimetric impact of dose delivered with deliberate offset.

Figures 29 and 30 show the dose distributions obtained from registered CBCT acquired without deliberate (W/T) error and with deliberate (W) error for Pelvis big and small target plans respectively. Figure 31 and 32 show the dose distributions obtained from RT registered CBCT acquired W/T error and W error for H & N big and small target plans respectively. Figure 33 shows the dose distributions from RT registered CBCT acquired W/T error and W error for Catphan® phantom plan.

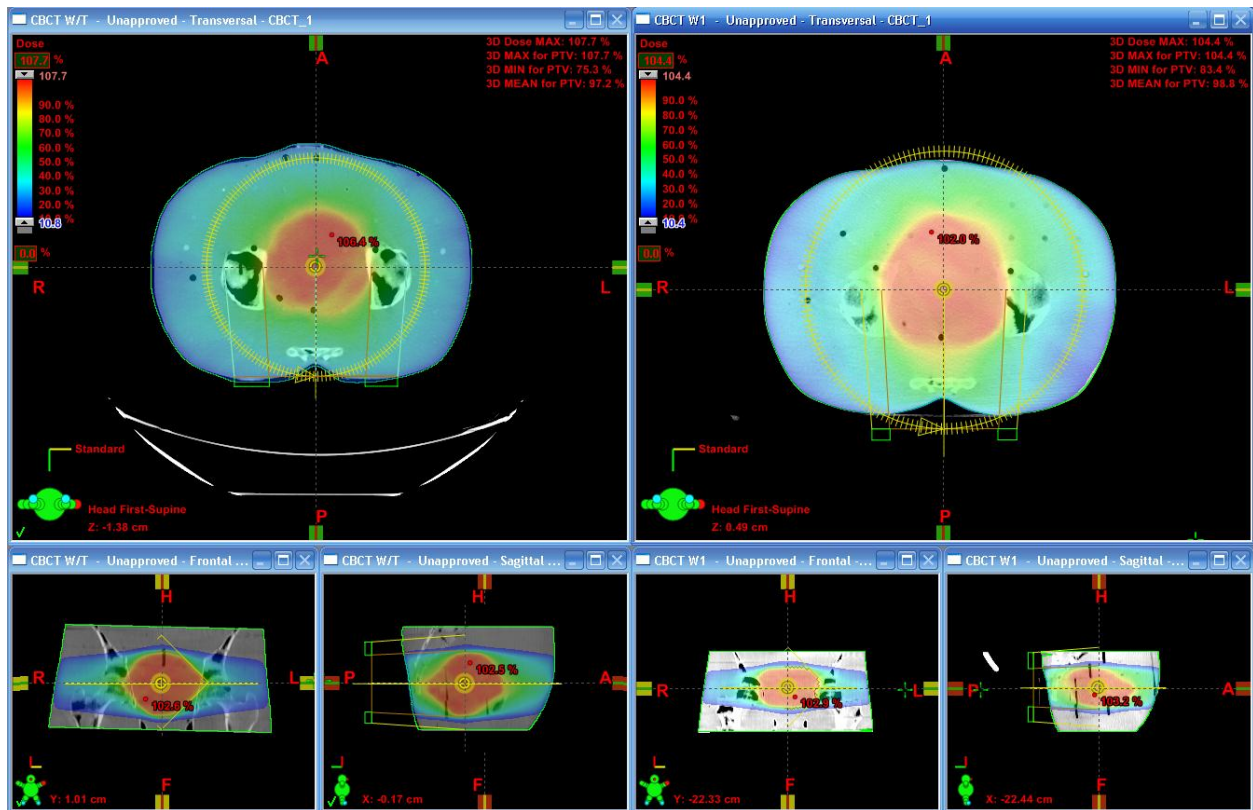


Figure 29: A screenshot of the CBCT dose distributions W/T and W1(participant 1) error (Big T). Top right (Axial slice of CBCT W/T), bottom right (coronal slice of CBCT W/T), bottom middle right (sagittal slice of CBCT W/T), top left (axial slice of CBCT W), bottom middle left (coronal slice of CBCT W) and bottom left (sagittal slice of CBCT W).

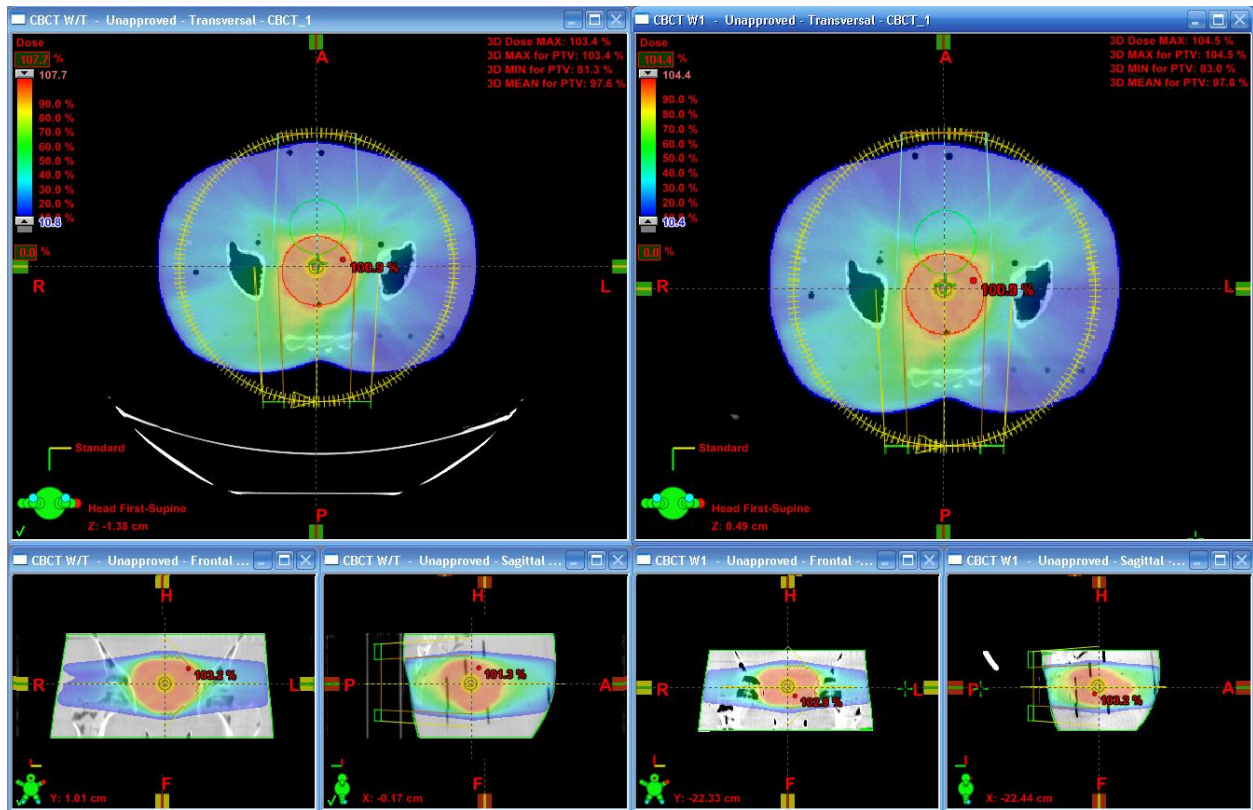


Figure 30: A screenshot of the CBCT dose distributions W/T and W1 error (small T). Top right (Axial slice of CBCT W/T), bottom right (coronal slice of CBCT W/T), bottom middle right (sagittal slice of CBCT W/T), top left (axial slice of CBCT W), bottom middle left (coronal slice of CBCT W) and bottom left (sagittal slice of CBCT W).

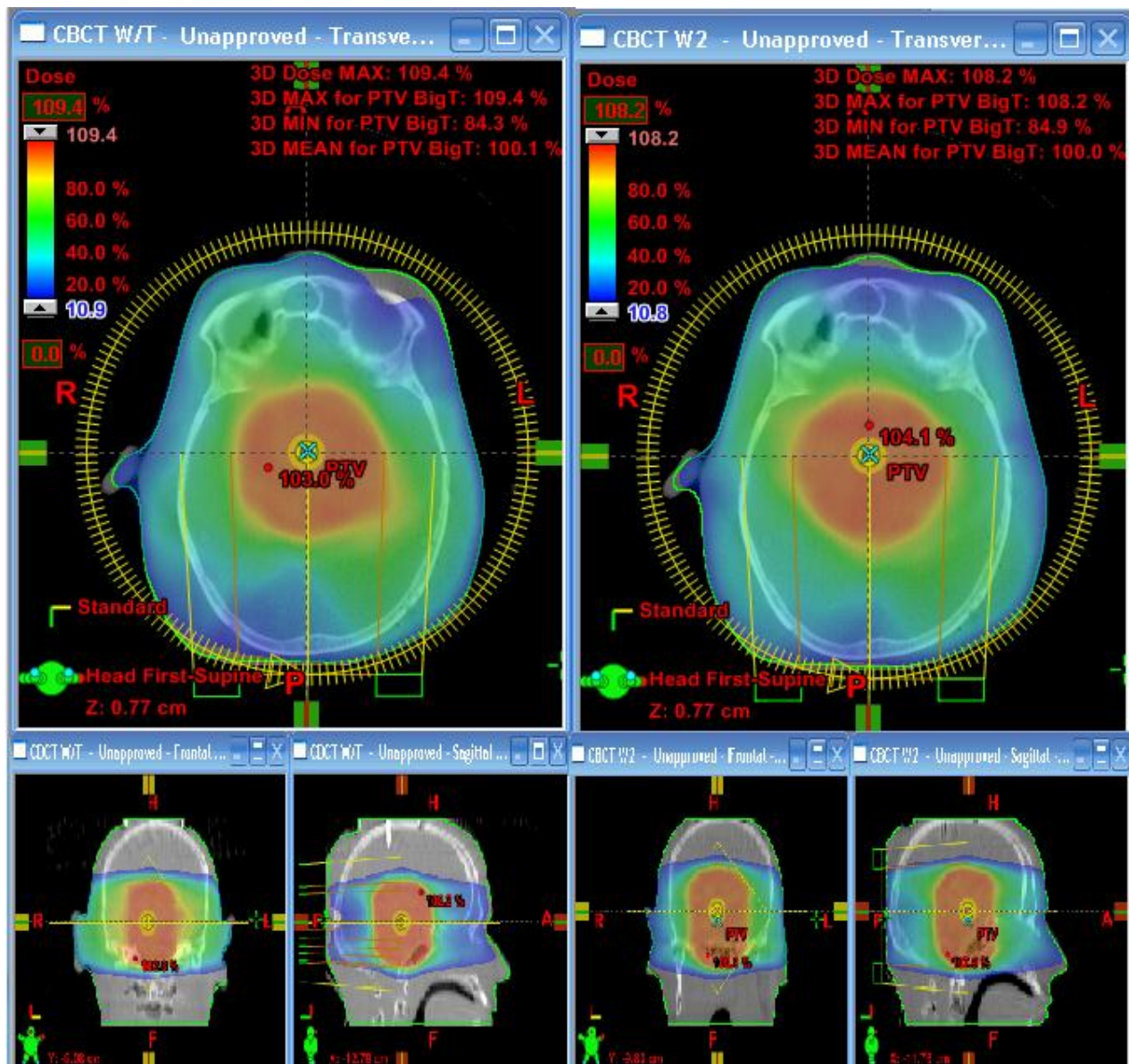


Figure 31: A screenshot of the CBCT dose distributions W/T and W1 error (Big T). Top right (Axial slice of CBCT W/T), bottom right (coronal slice of CBCT W/T), bottom middle right (sagittal slice of CBCT W/T), top left (axial slice of CBCT W), bottom middle left (coronal slice of CBCT W) and bottom left (sagittal slice of CBCT W).

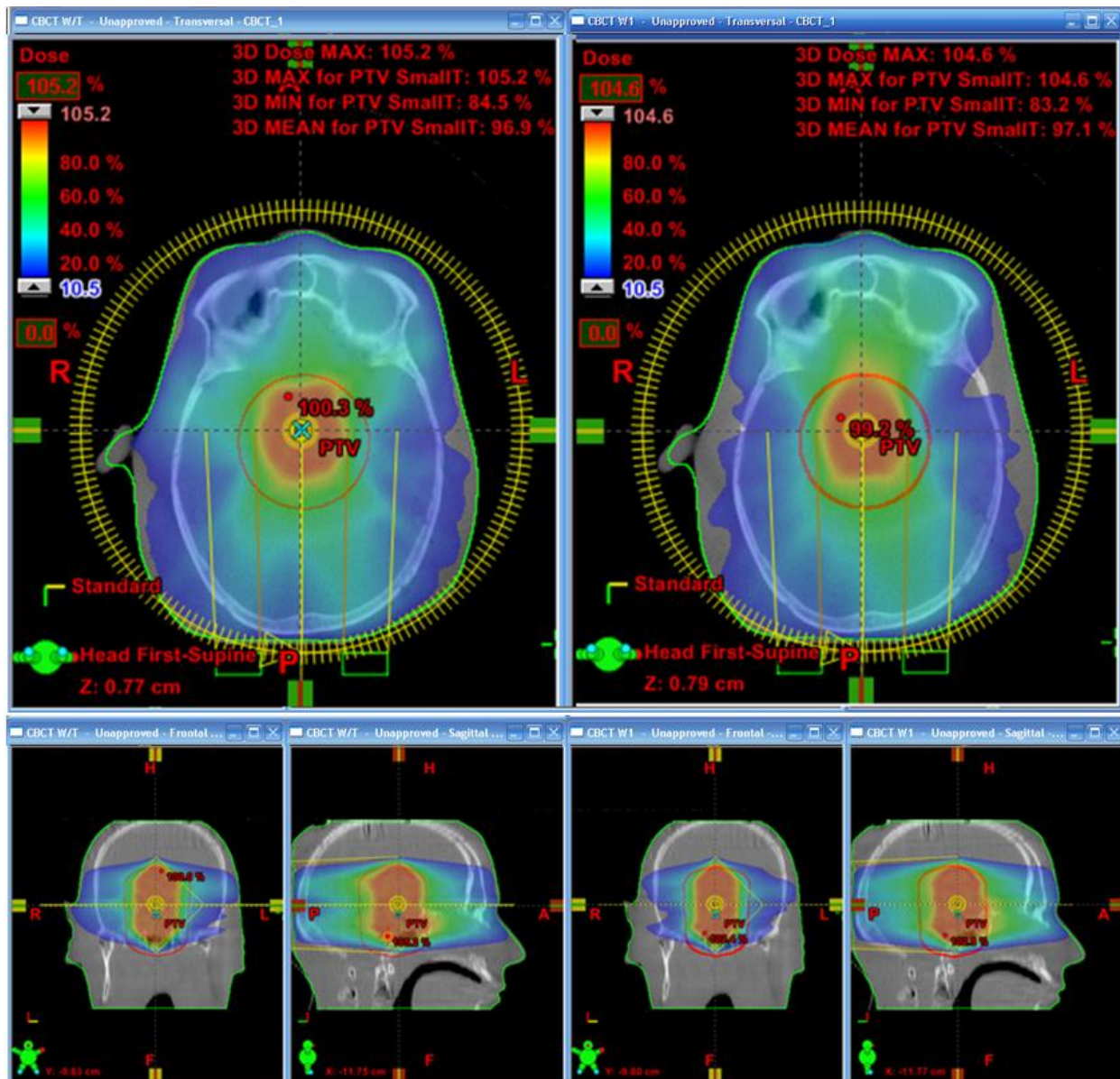


Figure 32: A screenshot of the CBCT dose distributions W/T and W1 error (small T). Top right (Axial slice of CBCT W/T), bottom right (coronal slice of CBCT W/T), bottom middle right (sagittal slice of CBCT W/T), top left (axial slice of CBCT W), bottom middle left (coronal slice of CBCT W) and bottom left (sagittal slice of CBCT W).

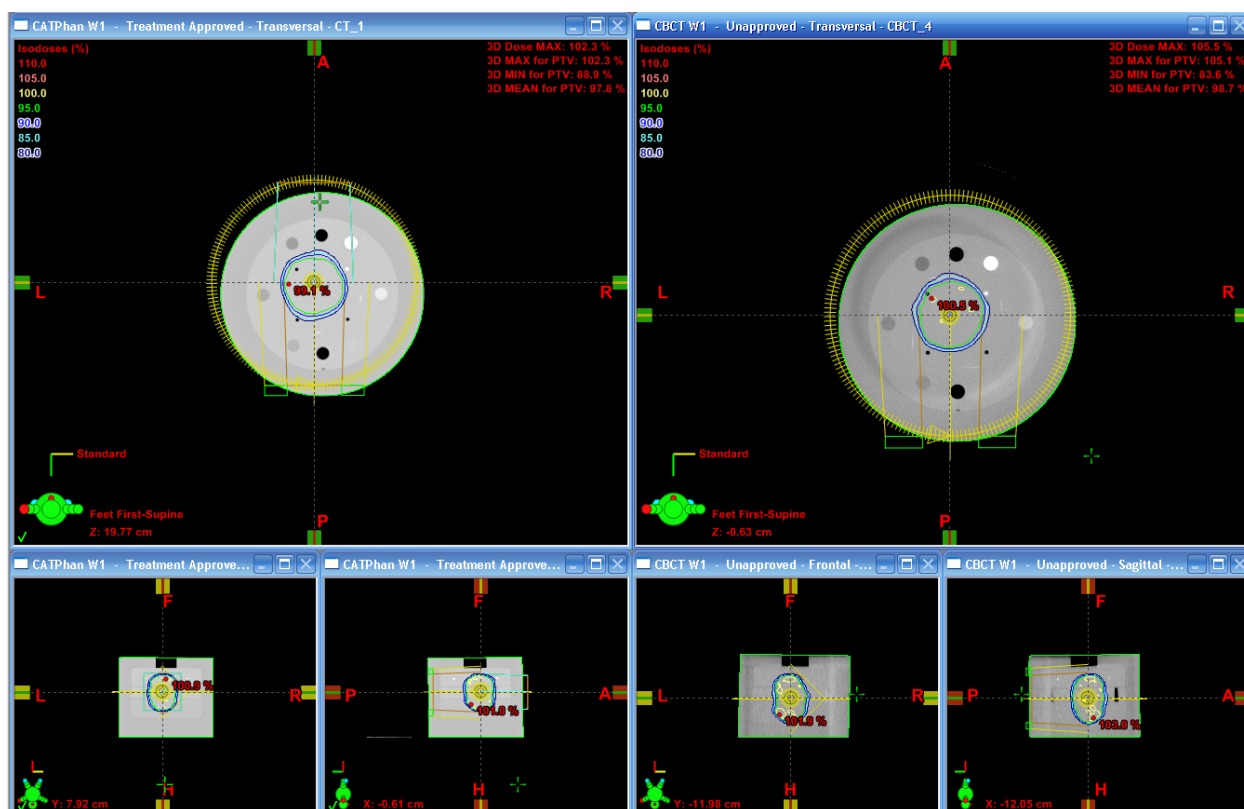


Figure 33: A screenshot of the CBCT dose distributions W/T and W1 error (Big T). Top right (Axial slice of CBCT W/T), bottom right (coronal slice of CBCT W/T), bottom middle right (sagittal slice of CBCT W/T), top left (axial slice of CBCT W), bottom middle left (coronal slice of CBCT W) and bottom left (sagittal slice of CBCT W).

5.4.1. Anthropomorphic phantom (Pelvis: big and small target).

Tables 18 and 19 summarize the homogeneity index, conformity index and conformity number for pelvis plans big target and small target respectively.

Table 18: Summary of indexes for RapidArc pelvis big target

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	90.2	90.2	90.5	89.8	90.3
HI	0.203	0.200	0.166	0.129	0.141
CI	1.160	1.160	1.161	1.062	1.076
CN	1.315	1.308	1.226	1.218	1.232

The HI from big target was found to be more homogenous. CBCT-based plans with deliberate error were more homogenous than the CBCT-based plan without error and pCT-based plan. The cold-spot was more visible on pCT-based and CBCT-based plans without error than CBCT-based plans with error. The CI of pCT-based plans indicated more hotspots as compared to the CBCT-based plans except for participant 1. The CN of pCT-based plans indicated an irradiation of hypothetical healthy tissues as compared to the CBCT-based plans.

Table 19: Summary of indexes for RapidArc pelvis small target

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	90.2	90.2	90.5	89.8	90.4
HI (%)	0.101	0.098	0.134	0.086	0.084
CI (%)	1.064	1.081	1.081	1.042	1.038
CN (%)	1.153	1.213	1.213	1.140	1.140

The HI from small target was found to be more homogenous. CBCT-based plans with deliberate error were more homogenous than the CBCT-based plan without error and pCT-based plan. The cold-spot was more visible on pCT-based and CBCT-based plans without error than CBCT-based plans with error. The CI of pCT-based plans indicated more hotspot as compared to the CBCT-based plans except participant 1. The CN of pCT-based plans indicated an irradiation of hypothetical healthy tissues as compared to the CBCT-based plans.

The calculated dose difference between W/T and W was found to be 0.1%, 0.1% and 0.4% for D_{98} , D_{50} and D_2 respectively for Pelvis big target plans. While the calculated dose difference between W/T and W was found to be 0.1%, 0.3% and 1.4% for D_{98} , D_{50} and D_2 respectively for Pelvis small target plans.

Figures 34 and 35 display the DVHs from RT registered CBCT acquired without deliberate error and with deliberate error for Pelvis big and small target plans respectively.

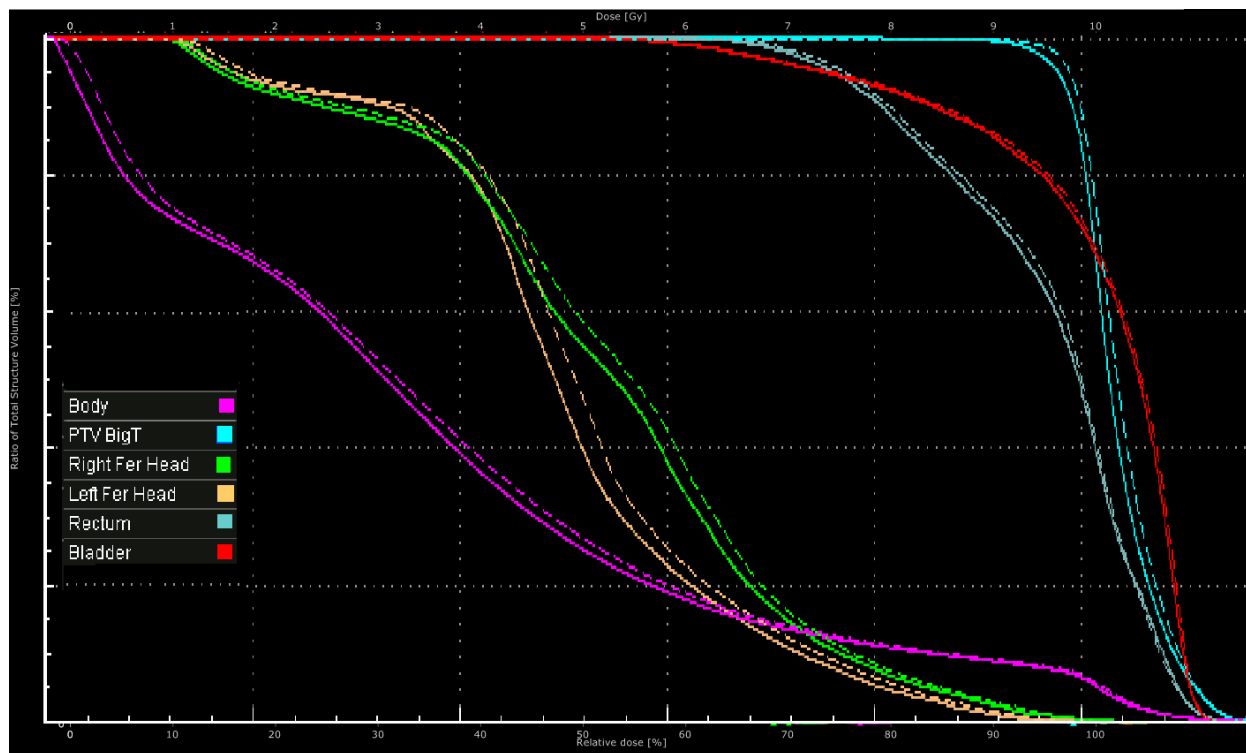


Figure 34: CBCT W/T vs. CBCT W error DVHs (Pelvis- Big T). Dash line is the CBCT W/T and solid line represents the CBCT W.

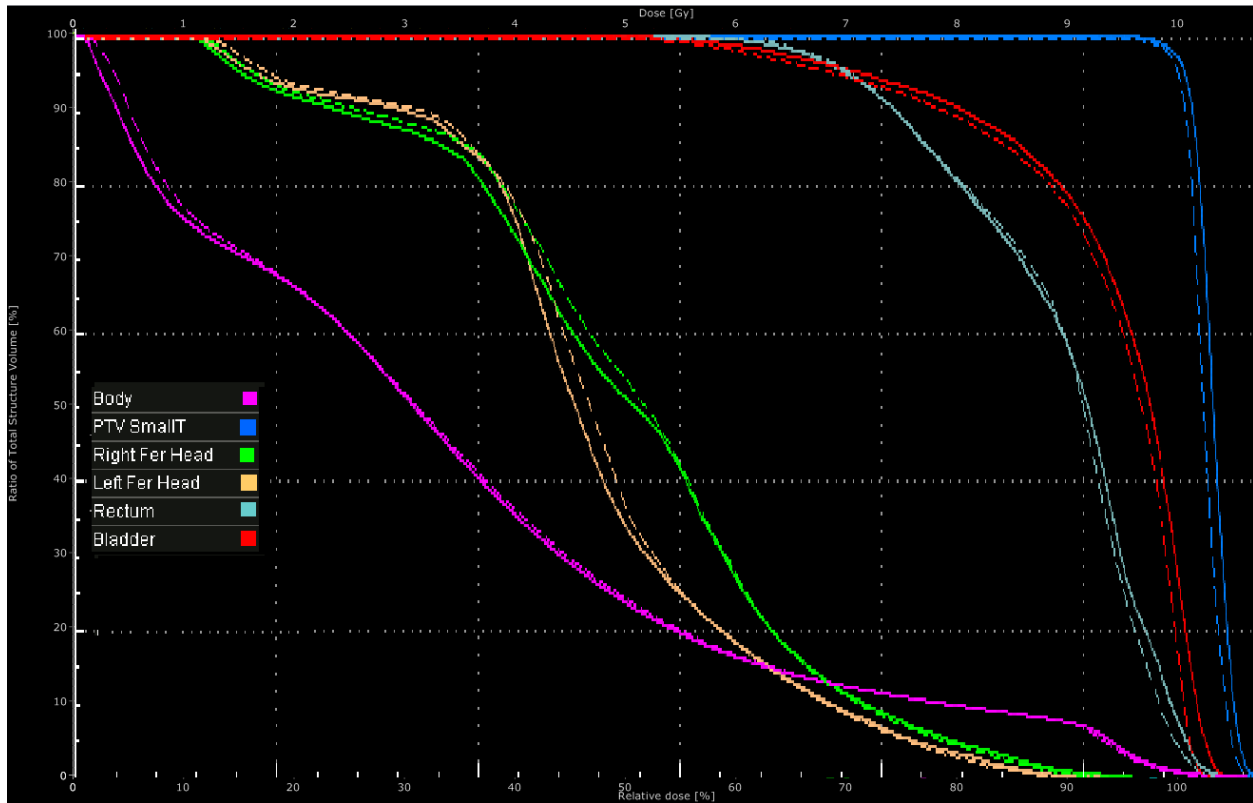


Figure 35: CBCT W/T vs. CBCT W error DVHs (Pelvis- Small T). Dash line is the CBCT W/T and solid line represents the CBCT W.

5.4.2. Anthropomorphic phantom (H & N: big and small target).

Tables 20 and 21 summarize the homogeneity index conformity index and conformity number for H & N big target and small target plans respectively.

Table 20: Summary of indexes for RapidArc H&N big target

	pCT	CBCT without error		CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3	
SSD (cm)	87.8	91.9	92.2	91.6	92.3	
HI	0.193	0.068	0.068	0.065	0.055	
CI	1.167	1.035	1.035	1.033	1.035	
CN	1.286	1.106	1.106	1.102	1.080	

The HI from big target was found to be more homogenous. CBCT-based plans were more homogenous than the pCT-based plan. The cold-spot was more visible on pCT-based plans than

CBCT-based plans. The CI of pCT-based plans indicated more hotspot as compared to the CBCT-based plans which came close to ideal value of 1. The CN of pCT-based plans indicated an irradiation of hypothetical healthy tissues as compared to the CBCT-based plans.

Table 21: Summary of indexes for RapidArc H&N small target

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	87.8	91.9	92.2	91.6	92.3
HI	0.193	0.072	0.072	0.067	0.071
CI	1.167	1.045	1.045	1.043	1.046
CN	1.286	1.105	1.105	1.098	1.105

The HI from small target was found to be more homogenous. CBCT-based plans were more homogenous than the pCT-based plan. The cold-spot was more visible on pCT-based plans than CBCT-based plans. The CI of pCT-based plans indicated more hotspot as compared to the CBCT-based plans which came close to ideal value of 1. The CN of pCT-based plans indicated an irradiation of hypothetical healthy tissues as compared to the CBCT-based plans.

The calculated dose difference between W/T and W was found to be 0.7%, 1.0% and 2.0% for D_{98} , D_{50} and D_2 respectively for H & N big target plans. While the calculated dose difference between W/T and W was found to be 0.6%, 1.7% and 3.1% for D_{98} , D_{50} and D_2 respectively for H & N small target plans.

Figures 36 and 37 displays the DVHs from RT registered CBCT acquired without deliberate error and with deliberate error for H & N big and small target plans respectively.

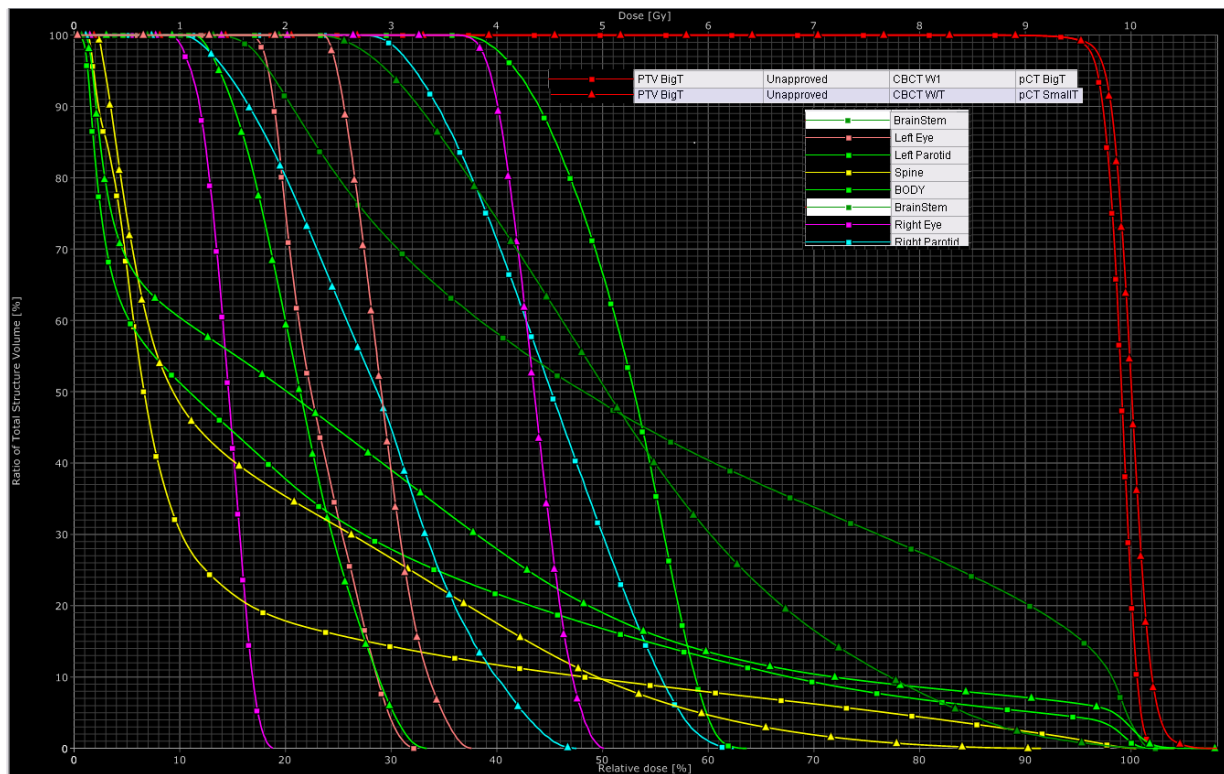


Figure 36: CBCT without deliberate vs. CBCT with deliberate error DVHs (H & N-Big T). The triangle represents CBCT W/T and square represents the CBCT W.

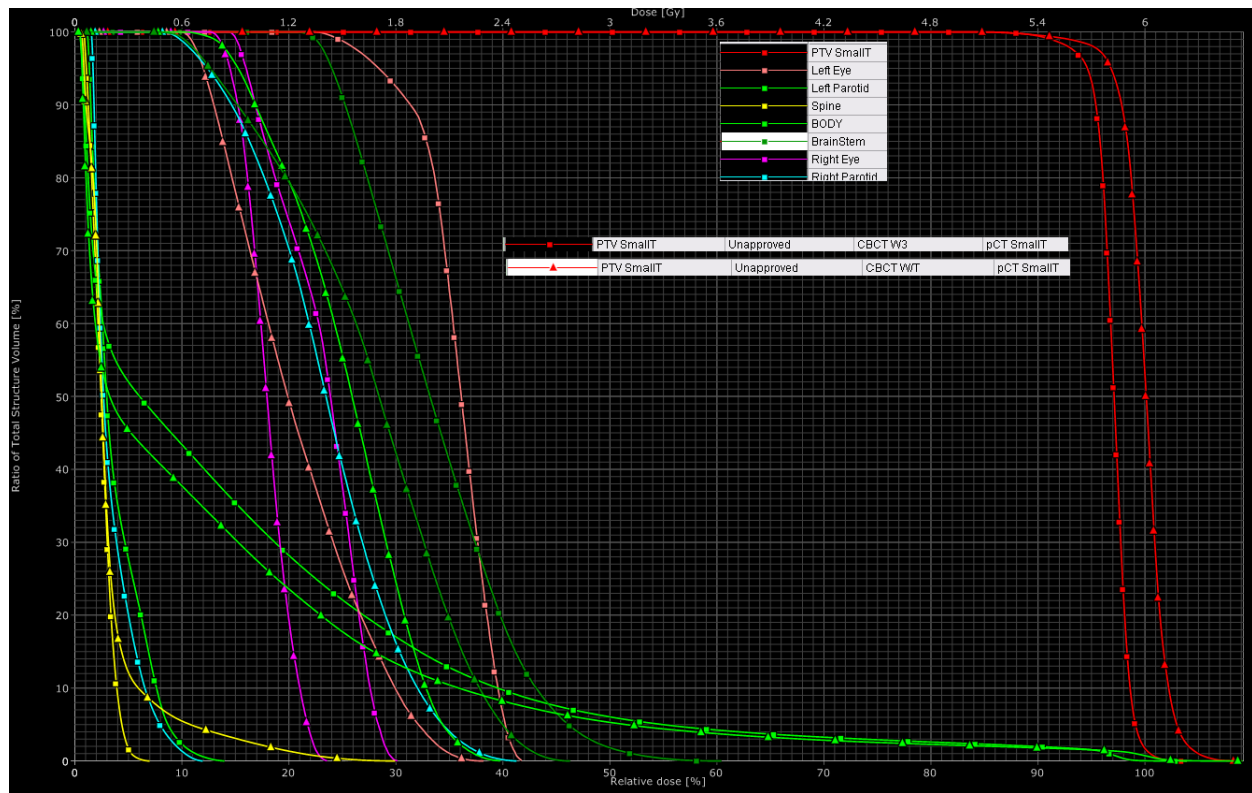


Figure 37: CBCT without deliberate vs. CBCT with deliberate error DVHs (H & N-Small T). The triangle represents CBCT W/T and square represents the CBCT W.

5.4.3. Catphan (R) phantom.

Table 22 summarizes the homogeneity index, conformity index and conformity number for Catphan® plans.

Table 22: Summary of indexes for RapidArc Catphan® phantom plan

	pCT	CBCT without error	CBCT with 3mm error		
		Physicist	Participant 1	Participant 2	Participant 3
SSD (cm)	88.8	91.1	91.4	90.8	91.2
HI	0.048	0.051	0.059	0.044	0.058
CI	1.027	1.028	1.031	1.025	1.033
CN	1.072	1.078	1.091	1.067	1.088

The HI for all plans was found to be more homogenous. The CI of all plans came close to ideal value of 1. The CN of all plans indicated that the irradiation of healthy tissue was close to none.

The calculated dose difference between W/T and W was found to be 0.2%, 0.3% and 0.4% for D_{98} , D_{50} and D_2 respectively for Catphan® plans.

Figure 43 displays the DVH from RT registered CBCT acquired without deliberate error and with deliberate error for Catphan® plan.

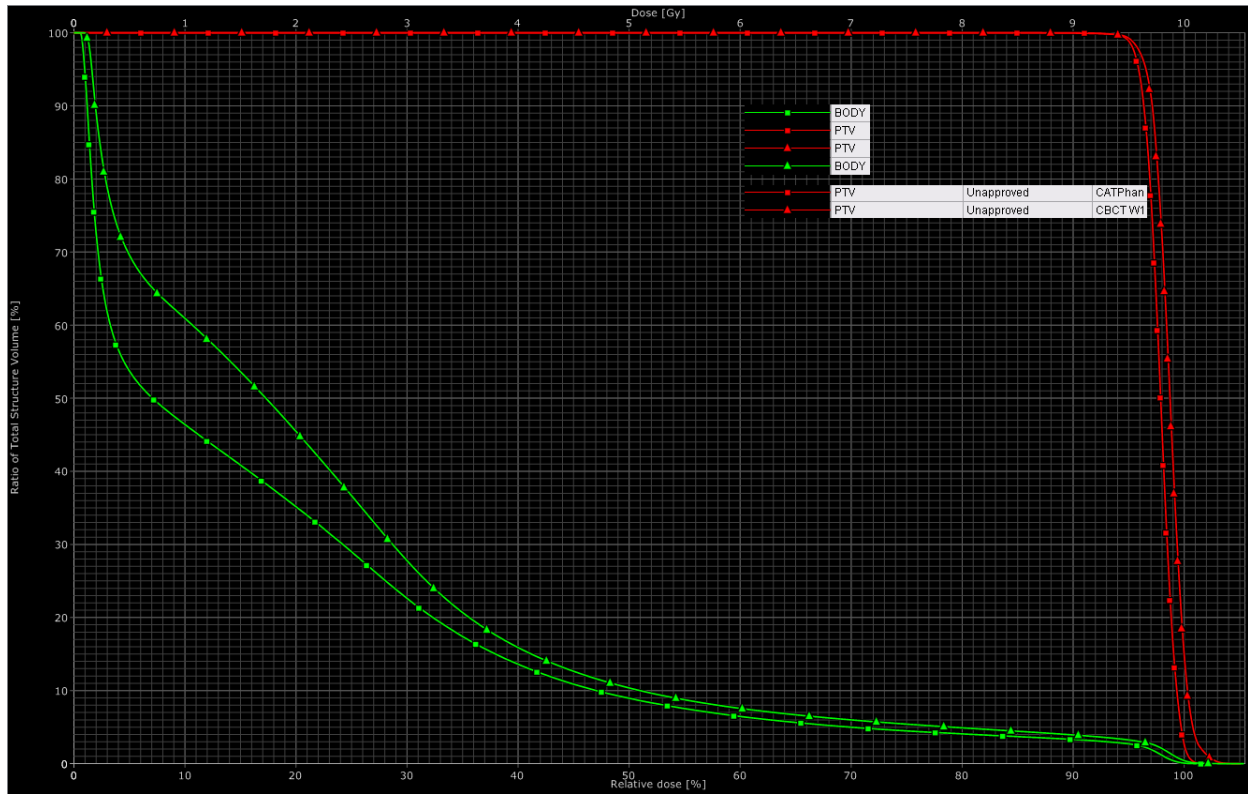


Figure 38: CBCT without deliberate vs. CBCT with deliberate error DVHs (Catphan®). In the DVH, red represents PTV and green the phantom body. The square represents CBCT W/T and triangle represents the CBCT W.

The figure 39 depicts the DVH comparison between the pCT and CBCT W/T error for the H & N small target. As reported by Qian (2010) that the reconstructed dose showed no sufficient difference between the original pCT-based plan and original CBCT-based plan in the absence of setup errors. Lee (2008) also concluded that there was no significant difference in the calibrations noted over the range of HUs, and the CBCT and pCT HU profiles were in agreement to within 10% except that the CBCT showed a larger fluctuation of HU and reduced HUs at the periphery of the phantom. Figure 44 is in agreement with Qian (2010) and Lee (2008) for both

the pCT and CBCT-based plan, and the deviation between the CBCT and pCT on the eyes could be attributed to a large fluctuation of HU since the organs are on the periphery of the body.

The calculated dose difference between pCT- and CBCT-based plans was found to be 3.4%, 3.4% and 3.7% for D_{98} , D_{50} and D_2 respectively for Pelvis big target plans. The calculated dose difference between pCT- and CBCT-based plans was found to be 4.8%, 5.6% and 5.1% for D_{98} , D_{50} and D_2 respectively for Pelvis small target plans.

The calculated dose difference between pCT- and CBCT-based plans was found to be 13.0%, 0.7% and 1.9% for D_{98} , D_{50} and D_2 respectively for H & N big target plans. The calculated dose difference between pCT- and CBCT-based plans was found to be 9.0%, 1.3% and 2.3% for D_{98} , D_{50} and D_2 respectively for H & N small target plans.

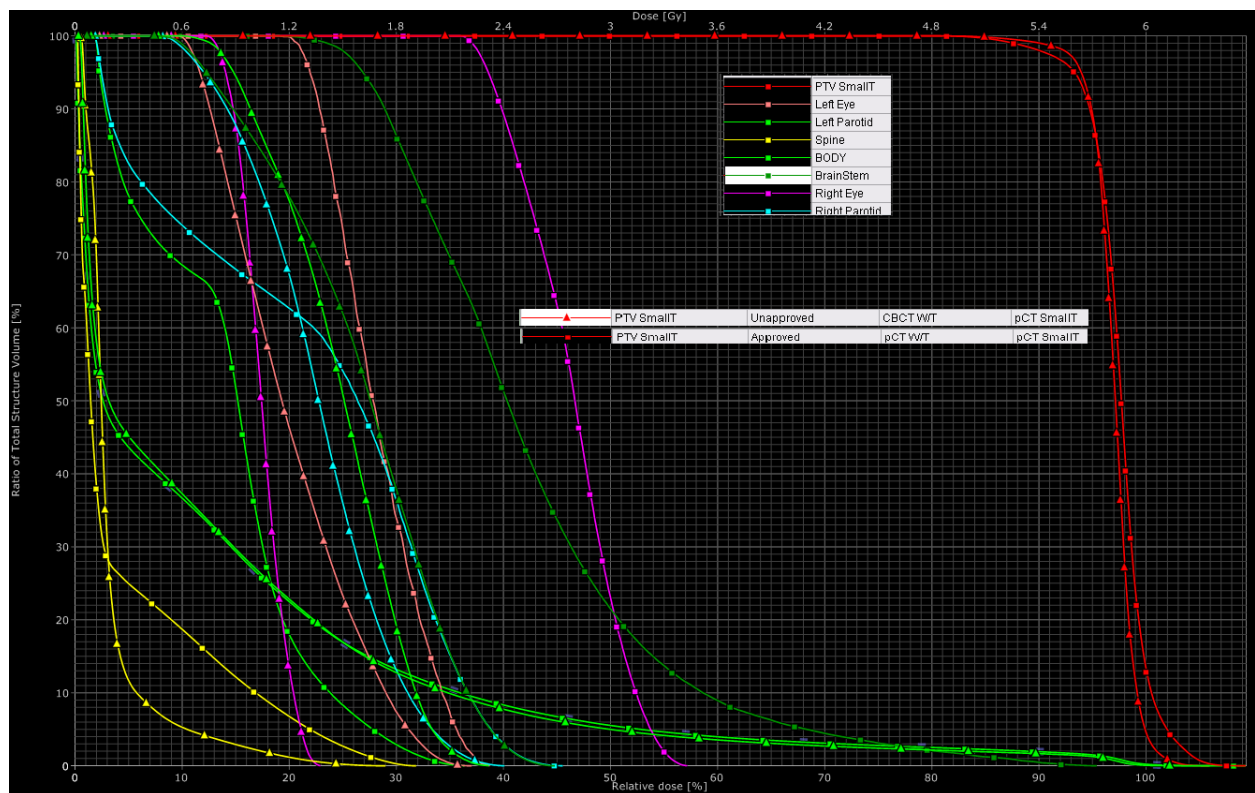


Figure 39: pCT vs. CBCT without deliberate error DVHs (Small T). The triangle represents CBCT W/T and square represents the pCT W/T.

The calculated dose difference between the pCT- and CBCT-based plans was found to be 0.3%, 0.4% and 0.6% for D_{98} , D_{50} and D_2 respectively for Catphan® plan.

Figure 40 depicts the DVH comparison between the CBCT-based plan with increased ($W1\uparrow$) deliberate error from CBCT-based plan without deliberate error by the 1st participant and the CBCT-based plan with increased ($W3\uparrow$) deliberate error from the CBCT-based plan without deliberate error by the 3rd participant for H & N small target. Since participants were increasing the error in the same direction, the HUs fluctuations affected both in the same magnitude but right eye was less affected with minimal statistical difference. The PTV gave no statistical difference and was accepted.

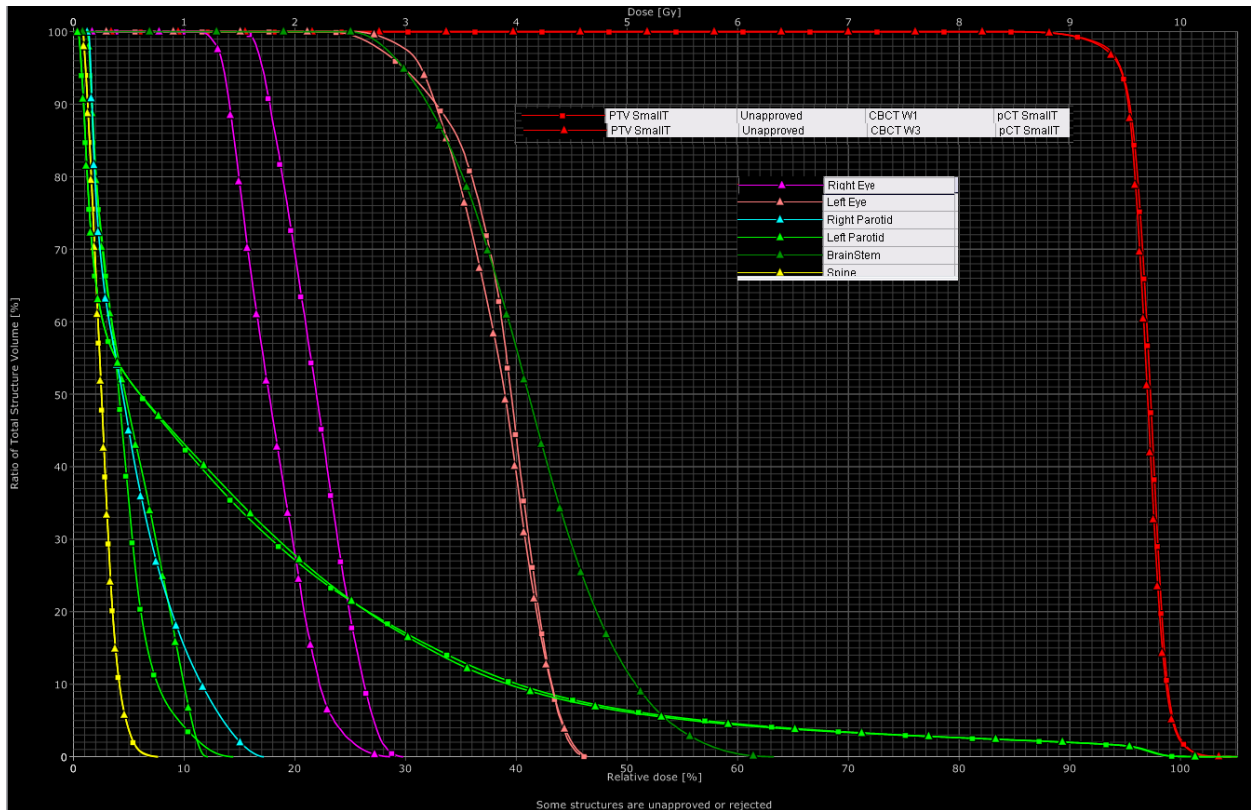


Figure 40: CBCT $W1\uparrow$ vs. CBCT $W3\uparrow$ deliberate error DVHs (Small T). The triangle represents CBCT $W3$ and square represents the CBCT $W1$.

Figure 41 depict the DVH comparison between the CBCT-based plan with increased (W2↓) deliberate error from the CBCT-based plan without deliberate error by the 2nd participant and the CBCT-based plan with increased (W3↑) deliberate error from the CBCT-based plan without deliberate error by the 3rd participant for H & N small target. Since the participants were increasing the error in the opposite directions, the HUs fluctuations affected the organs in the periphery and both eyes were within the clinical acceptable dose constraints. The PTV gave negligible statistical difference in the D₂ and could not be quantified but accepted.

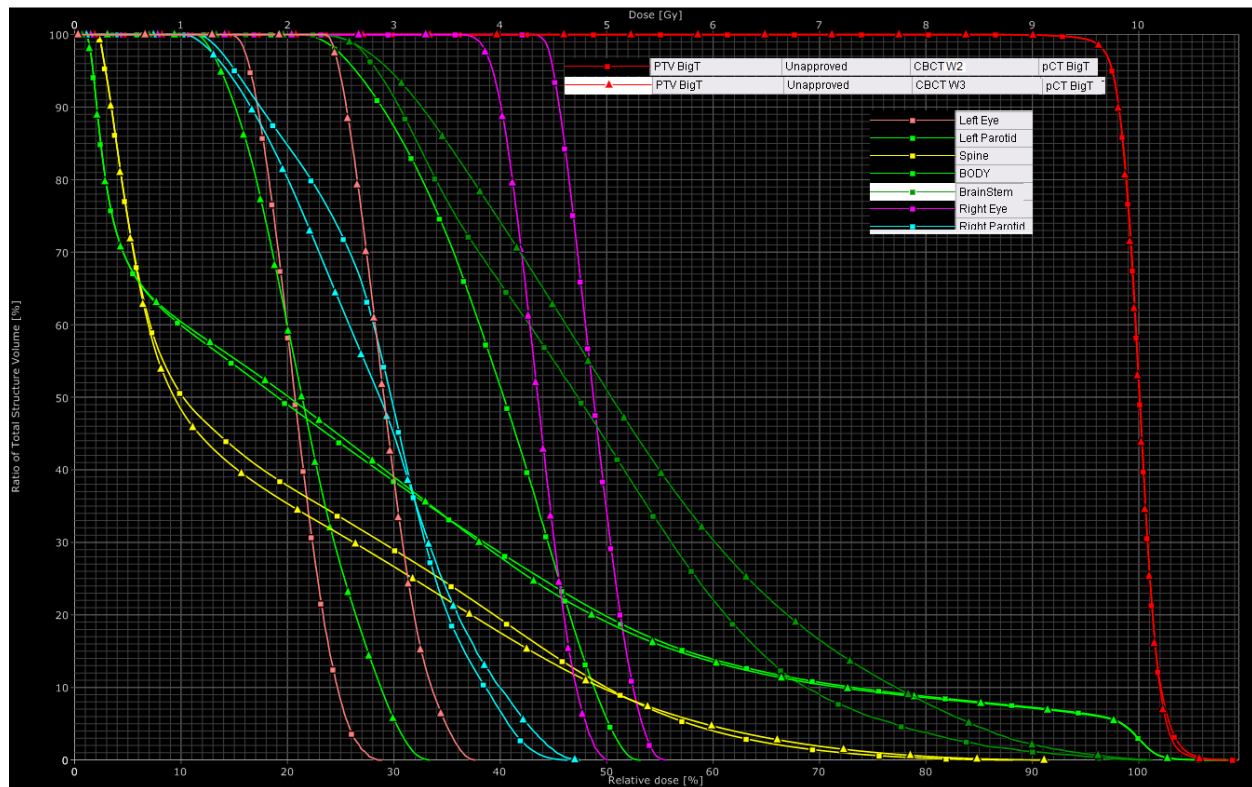


Figure 41: CBCT W2↓ vs. CBCT W3↑ deliberate error DVHs (Big T). The square is the CBCT W2 and rectangle represents the CBCT W3

The correlation coefficients between the participants' CI and the D₉₈ were summarized in Figures 42 to 46 and all participants (e.g., Obs.W1 represent participant 1) were in good agreement, except the H & N big target plan that was calculated to be 0.738.

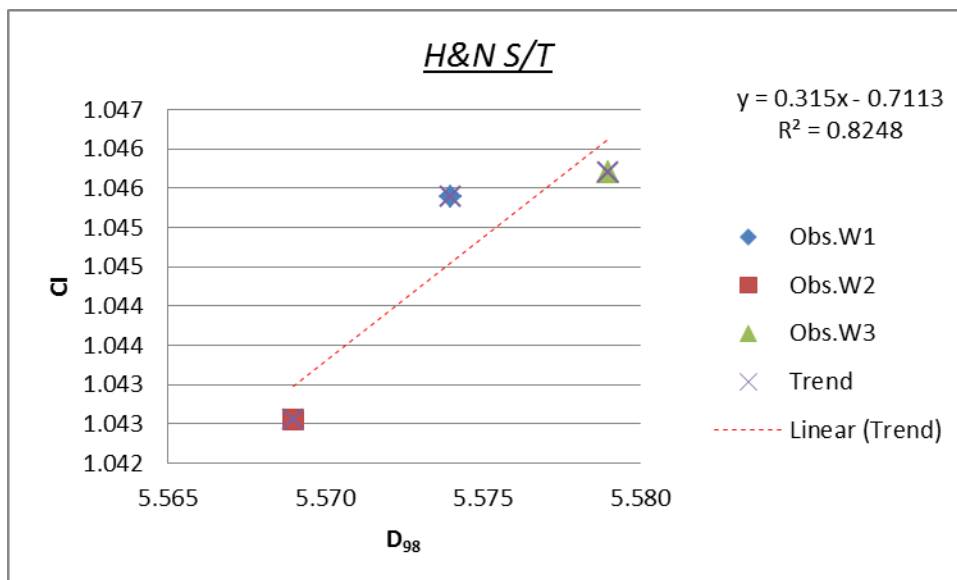


Figure 42. H & N small target scatter graph of the conformity index as a function of near minimum dose between inter-participant correlations.

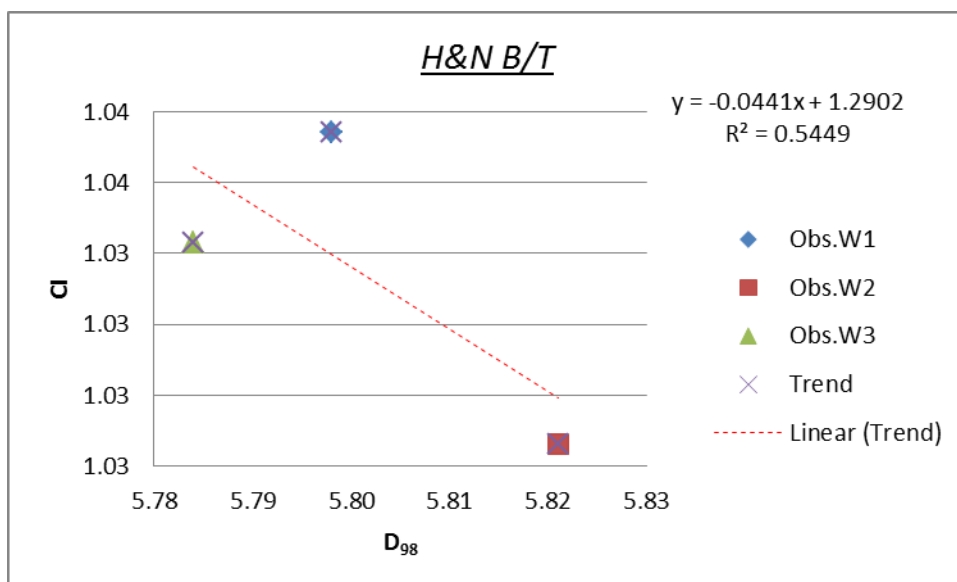


Figure 43. H & N big target scatter graph of the conformity index as a function of near minimum dose between inter-participant correlations

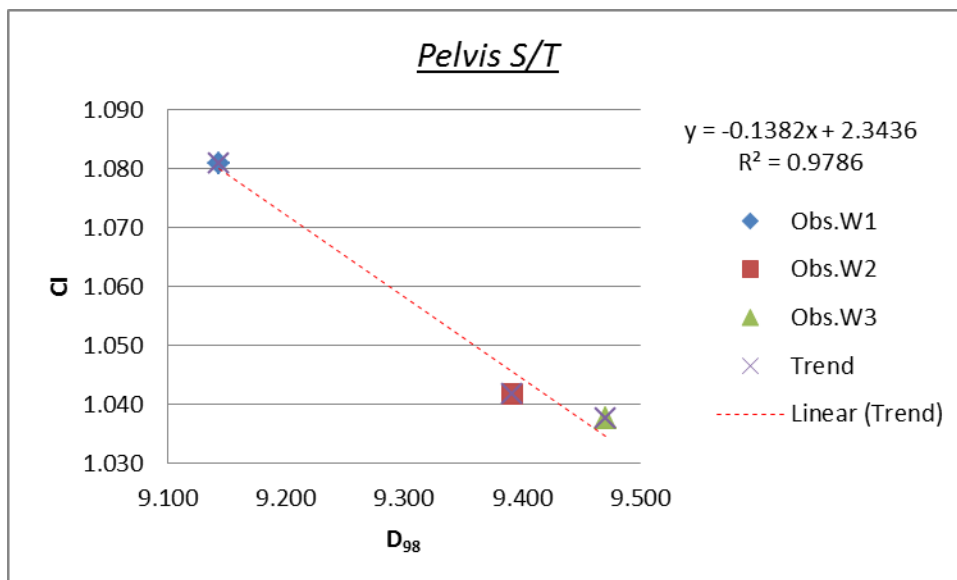


Figure 44. Pelvis small target scatter graph of the conformity index as a function of near minimum dose between inter-participant correlations

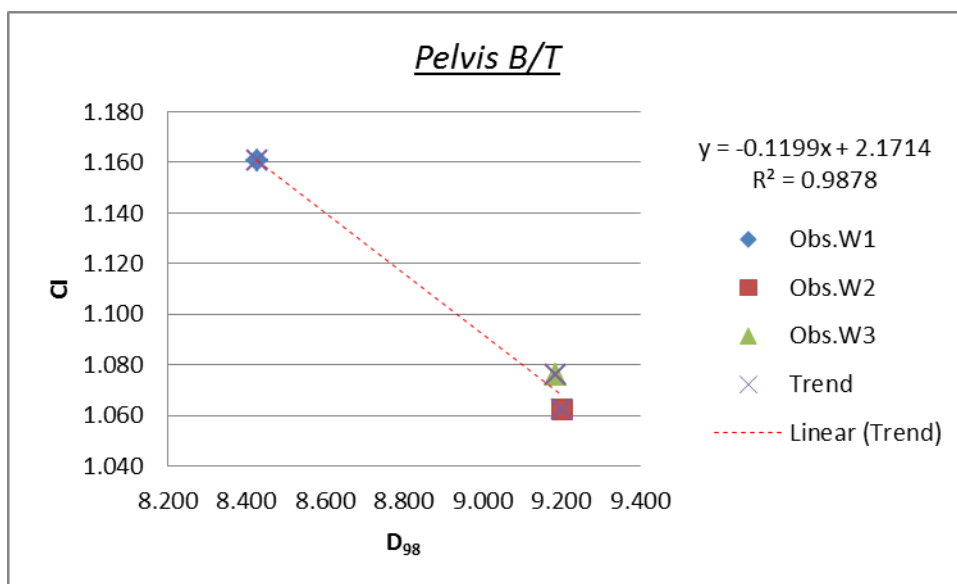


Figure 45. Pelvis small target scatter graph of the conformity index as a function of near minimum dose between inter-participant correlations

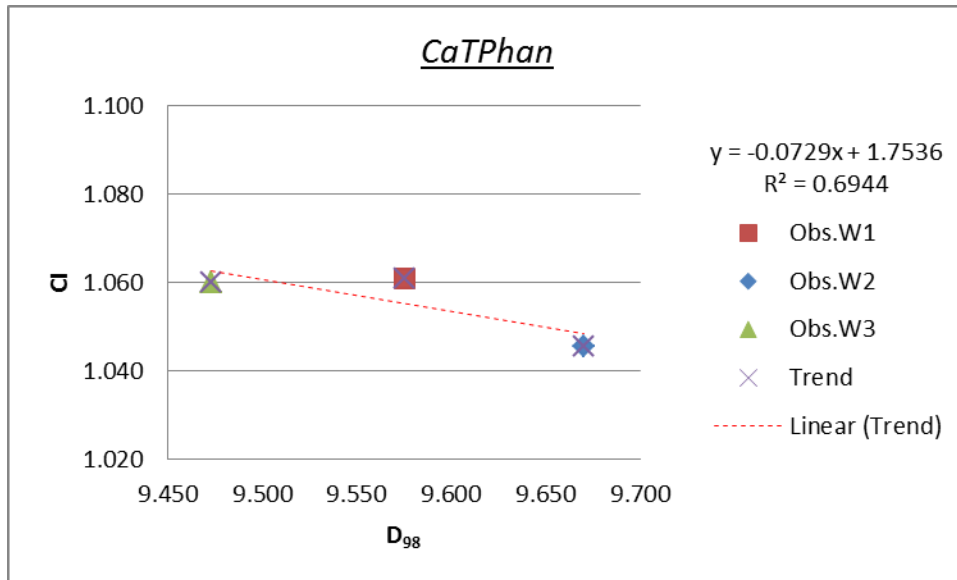


Figure 46. Catphan® scatter graph of the conformity index as a function of near minimum dose between inter-participant correlations

The correlation coefficients between the participants' CI were found to be 0.994, 0.989, 0.908, 0.738 and 0.833 for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans respectively.

Chapter 6 Conclusions and recommendations

6.1 *End to End testing*

End-to-end testing at 3 institutions was carried out successfully for a variety of modern Radiotherapy treatment techniques. The measured and planned doses for both 2D array phantoms and water phantom measurements were comparable and acceptable.

ADH and Grey's Hospital used the same dosimetric and treatment equipment type. Even though DVH based dose measurement processing software was not available at Grey's Hospital, the OmniPro I'mRT point dose measurement results were within 9% and 2.5% for the 2D array and water phantoms respectively.

The maximum D_2 difference was found to be $-2.2\pm0.6\%$, $-1.3\pm0.5\%$, $-3.6\pm0.3\%$ and $-4.6\pm0.6\%$ for the 3D-CRT, ssIMRT, dIMRT and RapidArc plans respectively with the 2D array for ADH. The maximum dose (D_2) difference was found to be $4.7\pm0.2\%$, $8.2\pm0.5\%$, $9.3\pm0.1\%$ for 3D-CRT, ssIMRT and dIMRT plans respectively with the 2D array for Greys. The maximum dose (D_2) difference was found to be $-0.4\pm0.8\%$, $-1.0\pm0.2\%$, $-1.9\pm0.6\%$ and $-2.3\pm0.4\%$ for the 3D-CRT, ssIMRT, dIMRT and VMAT plans respectively with the 2D array for IALCH.

The DD in water measured at an isocenter with a Farmer ionization chamber was found to be $1.4\pm0.4\%$, $2.9\pm0.7\%$, $3.3\pm0.3\%$ and $1.4\pm0.4\%$ for the 3D-CRT, ssIMRT, dIMRT and RapidArc plans respectively for ADH. The dose difference in water measured at an isocenter with a Farmer ionization chamber was found to be $0.2\pm0.2\%$, $1.4\pm0.5\%$, and $2.3\pm0.1\%$ for 3D-CRT, ssIMRT and dIMRT respectively for Greys. The dose difference in water measured at the isocenter with a Farmer ionization chamber was found to be $1.3\pm0.5\%$, $6.5\pm0.2\%$, $6.6\pm0.3\%$ and $14.7\pm0.1\%$ for the 3D-CRT, ssIMRT, dIMRT and VMAT respectively for IALCH.

The 2D detectors' sampling time and the 7.6 mm and 7.02 mm resolutions of the MatriXX^{Evolution} and OCTAVIUS 4D 1500 respectively, contributed to high dose differences in the dIMRT and

RapidArc/VMAT techniques. The high dose difference with the Farmer ionization chamber for IALCH (as high as 14.7%), might be attributed to the dose calculation algorithm which was the Monte Carlo algorithm.

The entire end to end testing accuracy was determined and the sources of the high dose discrepancies were not investigated in this study.

6.2 *Factors influencing IMRT and RapidArc*

The factors influencing the calculation speed and accuracy in the IMRT and RapidArc planning were determined. All treatment techniques indicated some degree of agreement with varying grid size, except that the calculation time was completely different for RapidArc because the calculation time is affected by the number of control point (177 control points) to be calculated over the entire arc.

6.3 *CBCT based IGRT assessment of set-up error.*

CBCT based IGRT assessment of set-up error and systematic errors at ADH was carried out successfully for a RapidArc treatment technique. The reference pCT images and acquired CBCT images were matched and reviewed online and offline.

The *pre-treatment* setup errors were found to be less than 6 mm for the Pelvis big target, Pelvis small target, head and neck (H&N) big target, H & N small target and Catphan® plans. The *post-correction* setup errors were found to be less than 5 mm for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans. The *post-delivery* setup errors were found to be less than 4 mm for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans.

6.4 *Dosimetric impact of dose delivered with deliberate offset.*

The introduction of a known error indicated a significant impact on the dose distribution differences. The dose difference was minimal in simple plans while on more complex plans like the H & N, it was as high as 3.1% for an offset of 3mm.

The maximum dose (D_{98}) difference between doses delivered without and with the 3 mm known offset were found to be -0.1%, -0.1%, 0.7%, 0.6% and 0.2% for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans respectively.

The maximum dose (D_{50}) difference between dose delivered without and with the 3 mm known offset were found to be 0.1%, -0.3%, 1.0%, 1.7% and 0.3% for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans respectively.

The maximum dose (D_2) difference between dose delivered without and with the 3 mm known offset were found to be -0.4%, -1.4%, 2.0%, 3.1% and 0.4% for the Pelvis big target, Pelvis small target, H & N big target, H & N small target and Catphan® plans respectively.

The over/underestimation of the pCT by the CBCT can be attributed to HU mapping. Complex treatments were delivered with deliberate offsets and the offset was found to have a significant impact on the dose delivered to the target, especially in H & N plans.

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