Evaluation of the Three Dimensional Localization Accuracy Using Cone-Beam Computed Tomography in Stereotactic Radiosurgery

By

Tzu-Chi Tseng

Graduate Program in Medical Physics
Duke University

Date: ______________________

Approved:

___________________________
Zhiheng Wang, Supervisor

___________________________
Lei Ren

___________________________
James Dobbins

Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University 2012
ABSTRACT

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Abstract

**Purpose:** Stereotactic Radiosurgery (SRS) indicates a single fraction, large prescription dose, and high dose gradient radiation treatment for intracranial lesions. The stereotactic immobilization and localization techniques assure the submillimeter accuracy which is required for precise target dose delivery and normal tissue sparing during the treatment. The invasive stereotactic frame-based localization system was the gold standard in SRS for many years based on its high reliability; however, the invasive nature has significant disadvantages in causing patient discomfort and increasing clinical burdens. Therefore, based on the development of on-line imaging techniques and the improvement of computer technology, the noninvasive localization system combined with image-guided patient setup correction is currently widely applied in SRS treatments. This work was designed to compare the setup accuracy between the invasive and non-invasive localization system. In addition, the localization and dosimetric accuracy of the treatment after cone beam computed tomography (CBCT) image-guided localization were also evaluated in this work.

**Material and Method:** At Duke University Radiation Oncology Department, SRS treatments are performed with Novalis TX system. Commonly, the invasive BrainLab Headring system is used for patients with trigeminal neuralgia; on the other hand, the non-invasive BrainLab U-frame system with thermoplastic mask immobilization is applied for the patient with other brain lesions. Both 2D kV images and CBCT images are acquired from the on-board imager (OBI) system for patient localization. The couch shift data from 288 patients with 394 brain lesions treated by single fraction SRS were collected to calculate the setup discrepancies of both invasive Headring and
non-invasive U-frame stereotactic localizations. The systematic setup errors were represented by the mean discrepancies in each direction and the corresponding standard deviations were taken as the random errors in patient setup. In addition, the discrepancies in RMS were also calculated in three translational directions as the magnitude of the setup errors. 19 patients with 20 brain lesions immobilized with the noninvasive BrainLab U-frame system and thermoplastic mask were selected to evaluate the localization and dosimetric accuracy of CBCT image-guided SRS by the BrainLab iPlan Phantom Mapping module. The contours of the PTV and critical organ were transferred directly from the planning CT and MR images to the CBCT images after image registrations. The distances between the CBCT isocenter coordinates and the PTV center coordinates after couch shifts applied were considered as the residual errors of image-guided setup correction. Moreover, the delivered dose distributions could be calculated and analyzed by copying the original treatment plans to the CBCT images and assigning the treatment isocenters on the CBCT images according to the couch shifts acquired after planning CT and CBCT image registrations. The CT electron density calibration curve used for original plans was also applied for the CBCT-based planning.

Results: The patient treatment records showed that the radial systematic errors (mean) and the random errors (STD) measured by the OBI system were 1.29±1.36 mm and 1.52±2.28 mm (mean±STD) for the BrainLab Headring system and the U-frame system, respectively. In addition, the radial discrepancies in RMS which represented the magnitude of the shifts were 2.07 mm and 2.73 mm for the BrainLab Headring system and the U-frame system, respectively. The residual errors of the image-guided setup correction evaluated from the distances between CBCT isocenter and the PTV center was 0.49±1.06 mm (mean±STD), and the radial discrepancy in RMS was 1.15
mm. With the dosimetric accuracy of treatment delivery, the average minimum dose, mean dose, and maximum dose in PTV of the original plans and the CBCT-based plans were 95.45% ± 3.80% and 92.88% ± 3.25%, 110.59% ± 1.81% and 110.11%±2.40%, 116.55%±3.11% and 115.93%±2.78%, respectively. In the original plans, the average 100% prescription dose coverage of GTV and PTV were 99.99% and 99.81%, respectively. On the other hand, in the CBCT plans, the average 100% prescription dose coverage of GTV and PTV were 99.90% and 98.20%, respectively. The average conformity index of the original plans and the CBCT plans were 1.846 and 1.863, respectively. Only the difference in average PTV coverage between the two plans was considered statistically significant among all dosimetric parameters.

**Conclusion:** In this study, the invasive BrainLab Headring system demonstrated better localization accuracy than the non-invasive U-frame system. The image-guided system provided larger improvement to the U-frame system than the Headring system in minimizing systematic errors, random errors, and the discrepancies in RMS. In addition, the CBCT-based plans also showed a comparable dosimetric treatment quality relative to the original plans. Only the average PTV coverage in CBCT-based plans was considered poorer than the original plans and the differences was found statistical significant. This deviation may result from the residual discrepancies after image-guided patient localization. However, the treatment goal (100% of GTV covered by 100% prescription dose) can still be achieved by the margin expansions from GTV to PTV. Furthermore, in our work, the rotational image-guided corrections were not considered because of the phantom mapping module limitations. These rotational discrepancies may also cause the degradations in PTV coverage during treatment delivery especially for lesions with irregular shape. Therefore, the future
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1

Introduction and Background

1.1 Stereotactic Radiosurgery

Stereotactic Radiosurgery (SRS), which indicates a single-fraction intracranial radiation delivery, is now widely applied in radiation oncology departments to treat central nervous system pathologies, including: arterialvenous malformations (AVM), brain tumors, trigeminal neuralgia, brain metastases, and others. [1] The term stereotactic describes the use of a stereotactic device to precisely localize the target position. After the target position is determined, a large dose will be administered through multiple noncoplanar fields in order to achieve high dose conformity to the target and, at the same time, spare the nearby non-target structures. [1, 2] As a result, SRS requires highly precise patient immobilization and localization technique combined with concentrated dose delivery to the planning target volume (PTV) and high gradient dose falloff to the external normal tissue area. The effectiveness and feasibility of SRS is demonstrated for a brain lesion less than 4 cm in its maximum diameter. [2] With increasing target size, the volume of the surrounding normal tissue which receives high dose will also increase; therefore, SRS application is limited to small lesions (< 4 cm) to minimize possible normal tissue complications. According to
the AAPM Report No.142, 1 mm is recommended as the requirement for laser target localization accuracy in SRS.

1.2 Stereotactic Radiosurgery Beam Delivery System

The technique of SRS was first developed by neurosurgeon Lars Leksell at Karolinska Institute of Stockholm, Sweden in 1949. [3, 4] By integrating both theoretical and practical aspects of SRS, Leksell executed the first combined use of orthovoltage x-ray and stereotactic frame to treat trigeminal neuralgia in 1951. [3, 4] Later, Leksell used the proton beam generated from cyclotron to irradiate similar brain lesions. After realizing his early work of both proton beam and LINAC based SRS are overly inefficient, Leksell collaborated with Borge Larson to design the first Gamma Knife system in 1968.[5]

In 1995, the AAPM Report of Task Group 42 (TG 42) indicated that the two basic approaches of SRS at the time were (1) the modified linear accelerator (LINAC) combined with tertiary collimator and stereotactic frame system (2) the Gamma Knife system which uses Co-60 source as radiation source. [4] Currently, there are primarily three types of radiation source used in SRS: cobalt-60 gamma rays, mega voltage x-rays, and heavy-charged particles. Among the three, the most widely and commonly used modality is the mega voltage x-rays produced by a clinical linear accelerator (LINAC). It is because that the cost of a LINAC is about ten times less than Gamma Knife unit, and substantially cheaper than a heavy particle accelerator. Also, the LINAC and the heavy particle accelerator used in SRS can also be applied in other radiotherapy procedures; however, a Gamma Knife was mainly designed for SRS application only. [6]
Over the last decades, new beam delivery devices have been invented based on improvements in medical imaging system and computer technology. The SRS beam delivery systems introduced below are the different designed modalities which use one of the three main radiation sources in the treatment: Gamma Knife (Cobalt 60 gamma ray), conventional LINAC (mega voltage x-ray), CyberKnife (mega voltage x-ray), Tomotherapy (mega voltage x-ray), and Proton therapy (heavy-charged particles).

1.2.1 Gamma Knife

A gamma knife system delivers radiation to an intracranial target lesion by simultaneous irradiation with a large number of isocentric γ-ray beams. The original gamma knife unit designed by L. Leksell and B. Larson was composed of 179 cobalt-60 sources arranged symmetrically to irradiate a volume of brain tissue with a diameter approximately 4, 8 or 12 mm. The first commercial Gamma Knife unit was developed by Elekta Corporation (Stockholm, Sweden) in 1987 at the University of Pittsburgh. [5] The modern Gamma Knife system is made up of 201 cobalt-60 radiation sources housed in a hemispherical shield with average activity of 30 Curie (Ci), and the γ-ray beams generated are collimated through circular collimators with various diameters to focus on a single point. [7, 8] The collimator helmet is interchangeable with respect to different lesion sizes- the large collimators are used for large lesions, the smaller collimators are used for lesions with smaller diameter. [8]

1.2.2 LINAC

A LINAC is a device that accelerates electrons to high energy through a high frequency electromagnetic wave generated from a magnetron or a klystron. When the
accelerated electrons strike a high Z target (usually tungsten), bremsstrahlung x-rays with a spectrum of x-ray energies will be produced, and the maximum energy of the spectrum is equal to the incident electron energy. \[7\] Therefore, a LINAC can generate a range of output x-ray energy; however, for SRS, since it is applied to treat intracranial lesions with relatively shallow depths, the 6 MV beam is penetrating enough for such regions and is commonly used in SRS treatment. LINAC-based SRS uses this standard radiation treatment device with the radiation source mounted on the robotic arm rotating around patients to deliver desired radiation dose to patients.

Early LINAC machines were not sophisticated enough to deliver highly accurate dose to intracranial lesions; therefore, it had poor treatment outcomes compared to Gamma Knife system. However, currently, the development of multileaf collimators, inverse treatment planning system (TPS), and image-guided capabilities dramatically improve the LINAC-based SRS accuracy and feasibility. Based on different manufacturers, different LINAC-based SRS systems, such as Novalis (BrainLab, Heimstetten, Germany), Trilogy (Varian, Palo Alto, CA, USA), and X-knife (Radionics, Burlington, MA, USA) are now in clinical application.

1.2.3 CyberKnife

The original CyberKnife system was developed at Stanford University by John Adler, and the first patient was treated in 1994. The CyberKnife combines two main technologies to deliver frameless radiosurgery. First, the Cyberknife consists of a 6MV X-band lightweight linear accelerator which is lighter and smaller than the linear accelerators used in conventional radiation therapy. The small size and light weight allow it to be mounted on a computer-controlled six-axis robotic manipulator which allows a wider range of beam orientation than traditional radiation therapy devices. \[9\] According to the work of M. Murphy, et al. in 1996, the robotic
manipulator can position the LINAC with 1.6 mm of mean radial error and ±0.9 mm of mean positioning error along each coordinate axis. [10] Second, the CyberKnife is an image-guided frameless radiosurgery system which utilizes two orthogonally positioned diagnostic x-ray cameras to acquire patient’s real-time anatomy information during the treatment. By comparing the acquired real-time images with the CT-sim image used in treatment planning, the robotic manipulator can be automatically adjusted to align the beam with the planning target accurately.

1.2.4 Tomotherapy

Tomotherapy is an intensity modulated radiation therapy (IMRT) technique which treats patients slice by slice with intensity modulated beams in a manner analogous to CT imaging. A special collimator was designed to produce intensity modulated beams while the gantry rotates around the longitudinal axis of patients. [7] The tomotherapy technique can be separated into two systems, serial tomotherapy and helical tomotherapy, based on the couch motion during beam delivery. The serial tomotherapy system, developed by the NOMOS Corporation, mounts the multileaf intensity-modulating collimator which consists of a long transverse slit aperture provided with two banks of 20 leaves each to the conventional linear accelerator and the treatment is delivered by multiple fan beams with discrete table increments between each axial gantry arc. According to the study of Carol et al., the potential problem with serial tomotherapy is the possibility of mismatch between adjacent slice pairs. [7]

On the other hand, helical tomotherapy was developed by the medical physics group at University of Wisconsin-Madison. With helical tomotherapy, the patient is translated through the doughnut-shaped aperture as in helical CT scanner, and the IMRT beams are delivered with constant LINAC head and gantry rotation while
couch translating. Consequently, the problem of interslice mismatch is minimized due to the continuous helical motion of the beam around the longitudinal axis of the patient. [7, 11]

1.2.5 Proton Therapy

Proton therapy is a form of radiation therapy that provides more accurate and targeted dose than traditional photon beam therapy. This is because the depth dose distribution of proton beams differs significantly from photon beams. Protons show increasing energy deposition with depth of penetration leading to a maximum called the Bragg-peak that locates near the end of the proton range. That is, in front of the Bragg-peak, the dose deposited is modest as compared to the photon beam, and beyond the Bragg-peak, the dose level is almost zero. Therefore, by choosing the appropriate proton energy, the dose distribution can be controlled to deliver highly concentrated dose to the target volume, and at the same time, spare the surrounding critical structures. [12]

Three types of devices can be used to accelerate protons to high energies: (1) a linear accelerator, (2) a cyclotron, and (3) a synchrotron. However, a conventional LINAC is not suitable for accelerating protons to the high energies required for radiation therapy because of the insufficiency of the electric field in the compact machine. As a result, cyclotron and synchrotron are currently the main accelerators for proton therapy. [7]

In this project, we would like to evaluate the treatment accuracy of the image-guided LINAC-based SRS treatment; therefore, in the following sections, our introduction will be focused on the devices and the techniques used in LINAC-based SRS.
1.3 Immobilization and Localization in LINAC-Based SRS

SRS is the treatment that delivers single-fraction high dose of radiation and produces sharp dose gradient which is required to be located precisely on the margin of the target volume. Therefore, the accuracy of beam delivery in SRS is critically important. Here, the different patient immobilization and localization techniques used to ensure patient positioning accuracy are introduced. The stereotactic immobilization systems can be basically divided into two main categories: the invasive system and the non-invasive system.
1.3.1 Invasive Immobilization System

By applying the specially designed stereotactic frame used in all steps of the SRS process: imaging, target localization, head immobilization, and treatment setup, the accuracy of the treatment can be strictly controlled. The stereotactic frame can be basically separated into two systems: pedestal-mounted frame and couch-mounted frame. The frame includes two parts: the invasive head ring which can be fixed by pins invasively to the patient skull as well as attached to the couch or pedestal and the localizer composed of radiopaque rods which provide a rigidly fixed frame of coordinates for relating the center of imaged target to the center of treatment. [7, 13]

Though the stereotactic frame was the gold standard in SRS immobilization and localization for many years based on its high reliability, it has some significant disadvantages. The invasive nature of the stereotactic frame involves pain and infection risks for patients and it also brings clinical resource burdens to the hospital for additional nurse and physician care requirement. Moreover, the invasive frame-based treatment requires physicians and physicists to finish the treatment plan following the frame placement in order to complete the treatment on the same day. This limits the application of inverse treatment planning, such as IMRT or VMAT, techniques which require pre-treatment QA.

1.3.2 Non-Invasive Immobilization System

Recent developments in image-guided stereotactic localization method using either x-ray based or non-x-ray based systems have provided a foundation for non-invasive patient immobilization stereotactic radiosurgery. Though the non-invasive SRS procedure has generally eliminated the requirement of invasive head ring attachment, a form of head immobilization is still required to limit head
motion. One example of the head immobilization device is the optical-guided frameless system (OFLS) which includes a customized bite block with fiducial markers equipped and an infrared camera system for fiducial detection during the treatment. Another example of the non-invasive patient immobilization is the thermoplastic mask made to conform to patient’s head with non-invasive fixation to the treatment couch through a U-shape frame. [14, 15]

Since the non-invasive patient immobilization devices usually are not as robust as the invasive stereotactic frames, the non-invasive systems should always be used in combination with appropriate image-guidance facility to assure the accuracy of patient setup and target localization. That is, the accuracy of the treatment with non-invasive patient immobilization actually depends on the accuracy of the image-guidance system. Compared with invasive frame-based SRS, the non-invasive patient immobilization system significantly improves patient comfort, provides a more flexible treatment scheme, and reduces the additional requirements of clinical resources. [13, 15]

1.4 Image-Guided Systems in LINAC-Based SRS

The image guidance devices used in radiosurgery provide the patient’s anatomical images before and during the treatment. By registering the images acquired after patient positioning with the planning CT image or the digital reconstructed radiograph (DRR) obtained or reconstructed from the CT simulation procedure, we can analyze the variations in patient setup to ensure the treatment accuracy in SRS. Some imaging systems have been developed that are accessible in the treatment room or mounted directly on the linear accelerator and are called on-board imagers. [7]
1.4.1 Planar Imaging System

The planar imaging system can be separated into two main categories: kilovoltage (kV) x-ray imaging system and megavoltage (MV) x-ray imaging system. The kV on-board imaging system consists of a conventional x-ray tube which can be either mounted on the LINAC gantry with an opposing flat-panel image detector or set up separately from the LINAC (such as the ExacTrac developed by BrainLab™) to acquire a patient’s two dimensional images. On the other hand, the MV imaging system, also known as the electronic portal image device (EPID), directly uses the LINAC MV source and the flat-panel detector to get patient images. [7]

The ability of an x-ray imaging system to differentiate soft tissues is affected by the difference in attenuation coefficient at a given energy between the contrasting objects. For kV CBCT imaging, the contrast changes with energy, because both the photoelectric and Compton effects contribute significantly to attenuation. For MV energies, the Compton Effect is the dominant interaction process, especially for materials with low atomic number, in which case the attenuation coefficient is proportional to electron density and is nearly independent of atomic number. Therefore, the object contrast is constant over a wide range of energies in the MV regime. [16] As a result, the kV imaging systems can obtain images with better contrast than the MV imaging systems. However, both the kV and MV imaging systems do not possess the ability to acquire an image with sufficient quality to visualize soft tissue. In clinical applications, bony structures and the implanted fiducials are usually used to check the accuracy of patient setup and determine the target position. [7]
1.4.2 Cone-Beam Computed Tomography

The 2D images acquired from the planar imaging systems can only provide the images that contain superimposed structures between the radiation source and the image detector. Therefore, the 2D image can only show the areas with large density differences. A cone-beam computed tomography (CBCT) system was developed to obtain volumetric images and provide better soft tissue contrast images.

Similar to the case with planar imaging systems, based on the radiation source used, the CBCT system can be separated into kilovoltage CBCT and megavoltage CBCT. The on-board kilovoltage imaging system, which is mounted on a retractable
arm at 90 degrees with respect to the central axis of the LINAC beam, is capable of radiography, fluoroscopy, and cone-beam computed tomography. By rotating the gantry around the patient for 180 degrees or more and acquiring planar images from multiple directions, three dimensional volumetric images can be reconstructed through a filtered back-projection algorithm. The megavoltage CBCT (MVCBCT) uses the megavoltage therapy beam of the LINAC as the radiation source and the traditional EPID system as image detector. As with the kV CBCT, the volumetric image can be reconstructed through filtered back-projection following a gantry rotation of over 180 degree. [7]

1.5 Treatment Technique for LINAC-Based SRS

Depending on the treatment planning system and the accessibility of different LINAC accessories, several treatment techniques are available for SRS treatment planning.

1.5.1 LINAC-Based SRS with Circular Cones

Non-Coplanar Circular Arc

Initial developments of the LINAC-based SRS treatment technique were based on the use of multiple converging arc treatments delivered with circular collimators. Non-coplanar circular arc treatment uses circular collimators with fix diameters to produce circular fields for radiation delivery. The diameters of the circular collimator can range from 5 mm to 40 mm based on different manufactures. The variety of circular collimator sizes provides more flexibility in treatment than Gamma Knife. The isodose distribution of non-coplanar arcs treatment is spherical, which is similar with the isodose distribution of Gamma Knife. In this kind of treatment technique, the
dose distribution of each isocenter can be optimized by adjusting the number of arcs, the collimator size of each arc, the arc length, the gantry angle, the arc weighting, and the couch angle. [17] The circular arc therapy is useful in treating small spherical lesions in functional radiosurgery. The disadvantage of using a conical field is that it may be necessary to plan several isocenters for a single PTV if the lesion is large. As a result, the dose inside the PTV may not be sufficiently homogeneous. [18]

1.5.2 LINAC-Based SRS with mMLC

3D Conformal Therapy

With the application of micro multileaf collimator (mMLC), SRS treatment can be delivered by a 3D conformal treatment technique. When sufficient conformal fields are applied, the treatment dose distribution quality is comparable to the non-coplanar circular arc therapy with multiple isocenters. More importantly, the 3D conformal therapy only requires one treatment isocenter; as a result, it can significantly improve the dose homogeneity in the target volume. Each of the conformal fields is conformed to the BEV of the target shape with expanded margin; this helps to account for the beam penumbra caused by the mMLCs, which is usually larger than the penumbra of cones. The disadvantage of 3D conformal therapy in SRS treatment is that the ability to spare the critical structures is limited by the limited number of fields. [17]

Non-coplanar Conformal Dynamic Arc Therapy

In contrast to non-coplanar circular arc treatment that has only circular field shape, non-coplanar conformal dynamic arc therapy applies patient-customized blocks or micro multileaf collimator (mMLC) and provides conformal fields for beam delivery. Recently, the mMLC system has replaced the role of customized blocks due to its great convenience in application. As in non-coplanar circular arc treatment, the
weighting of each field, gantry angle, and couch angle can be modified for optimized dose distribution. However, dose calculation in dynamic arc treatment is much more complicated than in traditional arc. This is because the field shapes change while the beam is on, and the planning system has to calculate the dose distribution through a large amount of irregularly shaped fields. Therefore, in dynamic arc treatment, it is very important to choose the angular gap between each field that can balance the treatment dose calculation accuracy with reasonable dose calculation time. [17]

**Intensity-Modulated Radiation Therapy**

The three mentioned treatment techniques above are all forward planning techniques in which the intensity patterns are the same for each field. In contrast, with intensity modulated radiation therapy (IMRT), the optimum goals of the treatment are first set, and then the optimization algorithm is then applied to calculate each treatment parameters to achieve the goals. By dividing the beams into small beamlets, the weight and intensity of each beamlet can be determined to produce the desired intensity pattern in treatment delivery. From each beam direction, the dose delivered to the target is nonuniform. However, all of the beams in combination produce a highly conformal dose distribution. [17]

**Volumetric Modulated Arc Therapy**

The technique of volume modulated arc therapy (VMAT) was proposed by Otto in 2007. This technique is an IMRT based arc delivery which allows the entire modulated dose volume to be delivered through a single 360 degree gantry rotation. Image-guided patient positioning in SRS can potentially increase the total treatment time; traditional IMRT also requires long treatment time due to a large number of beam directions and increased monitor units. Therefore, VMAT is the kind of
technique that is used to increase the efficiency of treatment delivery and achieve high dose conformity at the same time. With VMAT, there are three dynamic parameters that can be changed continuously to achieve better dose conformity to the target volume: the dose rate, the speed of rotation, and the beam shape. Faster treatment is also a major advantage of the VMAT technique, which is not only helpful in reducing the possibility of patient motion during the treatment, but also allows more time for other imaging procedures to be done. [19]

1.6 Research Aim

Intracranial stereotactic radiosurgery (SRS) is now a widely applied treatment technique for different kinds of brain lesion. Several different intracranial stereotactic positioning systems (ISPSs) have been developed and commercialized for patient immobilization and target localization in SRS. These ISPSs provide two main functions in SRS treatment: the first is to establish a coordinate system where a guided therapy can be applied; the second is to provide a method to reapply the coordinate system to the patient such that the coordinates assigned to the patient’s anatomy are identical with the treatment plan coordinates. Therefore, the precision and accuracy of the ISPS used for stereotactically applied radiation is critical for the success and safety of the treatment. [20]

There were two aims in this project. The first aim was to evaluate the patient positioning accuracy of both the invasive BrainLab Headring system, in which a coordinate frame was fixed mechanically to the patient skull, and the BrainLab U-frame system, in which was a noninvasive system with thermoplastic mask fixation. The setup accuracy of the two immobilization systems was measured by the on-board
imager (OBI) system with a set of 2D orthogonal images and a 3D cone-beam CT (CBCT) taken right before the treatment.

The second aim of the project was to assess the dosimetric treatment delivery accuracy after 3D CBCT image-guidance patient positioning corrections; the dosimetric treatment delivery accuracy represented the performance of the image-guided system used in patient setups. Several studies had been conducted to evaluate the positioning accuracy of the image-guided localization system. However, most of the studies were done with anthropomorphic phantoms with a designed marker embedded; there were relatively few articles providing patient case studies in estimating image-guidance system accuracy. Therefore, in this project, we conducted patient case studies with institutional review board approval and informed consent in order to evaluate the dosimetric treatment parameters of the mapped treatment plans on the CBCT images obtained after TAPO patient setup in order to assess the positioning accuracy of the CBCT-guided localization.
2

Materials and Methods

2.1 Patient Selection

Between June 2009 and December 2011, 288 patients with 394 lesions were treated with single fraction stereotactic radiosurgery at Duke University Radiation Oncology Department. The couch shifts according to the image-guided system verification were recorded in the SRS treatment checklists by the therapists and physicists. Among these patients, 19 patients with 20 intracranial lesions were selected for further evaluation of the treatment accuracy after image-guided patient setup corrections. These patients were selected by their CBCT image integrity since the dose calculation in the treatment planning system may be influenced if the CBCT image didn’t cover the entire skull, which was caused by the field size limitation of the CBCT imaging system. For example, while the isocenter of the LINAC machine was aligned with the lesion near the skull base, the vertex part of the skull would be out of the imaging field and not be imaged.
2.2 General Treatment Procedure of SRS at Duke

1. **MRI Scan**

   MRI Scans are commonly required for SRS treatment planning procedure based on better soft tissue contrast which is essential for target contouring. It should be scheduled one week before the CT simulation. Since the MRI scans are usually done in the diagnostic imaging department at Duke, the neurosurgeon needs to give clear indication for the technologists that the MRI scans are especially for SRS treatments. Different from other MRI protocols, the MRI scans for SRS should have 0 degree image tilt, and with 3 mm or less contiguous constant slice spacing. Also, the field of view, magnification factor, and matrix size should be kept constant throughout the scan. Usually, T1-weighted scan, T-2 weighted scan, and standard contrast enhanced-scan are ordered, and the contrast enhanced image is the one that shows the lesion clearly, and as a result is often used for GTV contouring during treatment planning.

2. **Patient Immobilization and Localization**

   The patient immobilization devices at Duke University Radiation Oncology Department can be separated into two systems: the invasive system and the non-invasive system. The invasive immobilization system used at Duke is the BrainLab\textsuperscript{TM} Headring system; and, the non-invasive system used is the BrainLab U-frame system. Before CT simulation, the patient will be immobilized with one of these devices to minimize patient motion or head tilt during the scans. Also, a BrainLab localizer is used simultaneously with the immobilization system to provide accurate lesion positions based on the relative coordinate system of the localizer box.
3. **CT simulation**

Before the CT scan, a scout scan is done first to help the dosimetrist and therapists to decide the scan range. Also, the dosimetrists take the responsibility for checking this scout scan to ensure there is no undesired head tilt or rotation prior to the actual CT scan. For SRS, the image field needs to include the entire skull for accurate dose calculation.

4. **Treatment Planning**

A treatment planning process is started with GTV/PTV and critical structures contouring by radiation oncologists and dosimetrist/physicists, respectively. After the treatment area is determined, treatment planners will decide the treatment parameters such as gantry angle, couch angle, beam weight, and treatment accessories based on the treatment technique, prescription dose, and critical structure dose limitation assigned by the radiation oncologists. If the inverse planning technique is applied, pre-treatment quality assurance will be scheduled to verify the plan possesses the same dose distribution (fluence map) as indicated in the treatment planning system. The treatment plan then will be ready for delivery after physician and physicist’s review and approval.

5. **Patient Positioning**

Before the patient gets into the treatment room, the therapists will attach the couch-mounted assembly of the BrainLab immobilization system and check that all devices and couch are level. Then, the BrainLab target positioner (TAPO) will also be put on to check the laser crosshairs on each surface coincident with the marked target isocenter on the printed-out treatment field sheet. With the immobilization device mounted, the gantry and couch angle combinations for each treatment field need to be
checked to assure there is no couch-gantry or patient-gantry collision. If the arc technique is applied, the entire arc length should be check with its relative couch angle to avoid collisions during gantry rotation. When all of the above steps are checked, the therapists will call the patient to enter the treatment room for stereotactic positioning. After the patient is immobilized, the TAPO device will be re-attached to check again the laser-treatment isocenter coincidence.

6. Image-Guidance

A pair of anterior-posterior (AP) and lateral (LAT) 2D kV on-board images (OBI) will be taken directly after patient positioning. By registering these 2D kV images with the digital reconstructed radiographs (DRRs) generated from the CT-sim images and comparing the bony structures in the images, the couch shifts in three orthogonal directions required for accurate target alignment can be obtained and recorded in the treatment checklist. The physicist and the physician will decide whether to apply the 2D couch shifts before the following 3D CBCT imaging procedure. Different from the 2D OBI, the CBCT image can be directly registered with the CT-sim image in vertical, lateral, and longitudinal direction. After verifying the registration accuracy by both the radiation oncologist and the medical physicist, the couch shifts acquired from CBCT-CT match will be applied. If the 3D CBCT couch shift is larger than 2 mm in any direction, a second CBCT image needs to be taken to evaluate the positioning accuracy after the 3D CBCT couch shift. Finally, when the patient position is correctly modified based on the image-guided system, the couch can be locked in the translational direction. And now, the treatment is ready to be delivered.
2.3 Equipment

2.3.1 Stereotactic Immobilization

278 out of the 288 selected patients (383 out of 394 lesions) were immobilized with the BrainLab U-frame System which consists of a U-shaped frame support, a pair of occipital and front thermo-transformable masks (Aquaplast®) conformed to the patient, three reinforcing straps, and a dental support bar (bite block). The three thermoplastic reinforcing straps were used under the mask over the forehead, below the nose, and over the chin to enhance patient immobilization. Furthermore, the dental support was placed in the mouth against the upper dentition to minimize possible head tilt. [15] All these special parts of the system are designed with the expectation to
ensure sub-millimeter repositioning accuracy in all dimensions recommended by the AAPM report.

The other 10 patients selected in this study were the patients with trigeminal neuralgia (TGN). Based on Duke University Radiation Oncology Department’s treatment protocol, these patients were assigned to be immobilized with the BrainLab Headring system. This system uses invasive fixation of the patient skull to fulfill the high accuracy requirement for TGN treatment due to higher dose and smaller treatment field requirement compared to typical SRS.

2.3.2 Stereotactic Localization

During CT simulation (CT-sim) localization, a BrainLab\textsuperscript{TM} (Feldkirchen, Germany) stereotactic localizer was used with both the BrainLab Mask system and the BrainLab\textsuperscript{TM} Headring system in order to provide the three dimensional (3D) stereotactic coordinate system for further treatment planning and delivery. The BrainLab localizer is composed of 6 localizer rods, two of each on the left, right and anterior surface of the localizer box. By detecting the rod points in the reconstructed CT images in the treatment planning system, the exact position of the target can be defined and precisely moved to the LINAC isocenter for radiation beam delivery. Figure 2.2 below displays the BrainLab stereotactic immobilization and localization system used in SRS treatments.

2.3.3 Computed Tomography Simulator

All treatment planning CT-sim scans were done in helical mode on a GE (Milwaukee, Wisconsin) LightSpeed\textsuperscript{®} RT CT simulator with a clinical head scan protocol: slice thickness = 1.25 mm, matrix = 512 x 512, field size= 40 cm x 40 cm.
This setting resulted in an image resolution of 0.78 mm which was suitable for providing submillimeter accuracy for SRS treatment planning.

![Image of BrainLab Mask immobilization System](A)

![Image of BrainLab Headring immobilization system](B)

![Image of BrainLab Localizer](C)

![Image of BrainLab Target Positioner (TAPO)](D)

Figure 2-2 (A) The BrainLab Mask immobilization System. (B) The BrainLab Headring immobilization system. (C) The BrainLab Localizer. (D) The BrainLab Target Positioner (TAPO) (From the BrainLab hardware manual)

### 2.3.4 Treatment Planning System

Treatment plans for SRS were done on the BrainLab iPlan System at Duke. The iPlan RT image 4.1 was majorly used for image registration and structure contouring. MR images were required for SRS treatment planning because of its better soft tissue
contrast, which was critical in target delineation. Generally, the PTVs were usually contoured on the contrast-enhanced T1 weighted MR images, and the critical structures could be contoured on either the MR or CT images based on their visibilities. After the planning target volume (PTV) and the critical structures were defined, further treatment planning would be done on the iPlan RT dose 4.1.1, where the beam orientation, arc length, and couch angle were decided. To give a clear picture for the entire treatment planning process, a brief introduction of the treatment planning flow is introduced below.

**iPlan Image**

After importing the CT-sim and MR images into the iPlan system, the next step is to localize the patient images and contour the PTV and critical structures for treatment planning. This step in the iPlan system is done in the iPlan Image software. The registration step in the iPlan system is automatically done through the least squares error algorithm using the intensity of both images. Users can check the registration and manually adjust it to achieve better results.

After the MR and CT images are registered, the localizer position in the CT image can be used to localize the images. As mentioned above, the BrainLab localizer box has 6 rods embedded on its surfaces and is used to define the rigid coordinate system of the patient anatomy. Theses six rods represents as 6 dots on each slice of the CT image. The iPlan image localization software can detect the 6 dots’ positions and use the calculated distance between each dot pair to determine the relative position of each image slice to the reference coordinate system. Figure 2-3 displays the image localization interface in the BrainLab iPlan Image module. The six green circles indicate the rod positions in each image slice to help defined the coordinates of the delineated target.
The last step of using the iPlan Image module is to contour the PTV and critical structures. In intracranial treatment, the critical structure usually includes the brainstem, the eyes, the optic nerve, the optical track, and the optic chiasm. The contouring is usually done manually for critical structures by the dosimetrist or medical physics. On the other hand, the PTV is manually contoured by radiation oncologists. The PTV is generated by expanding the margin of the gross tumor volume (GTV), which is the actual tumor volume that needs to receive full prescription dose. Based on the SRS treatment plan protocol at Duke, a 1 to 3 mm margin will be expanded from the GTV to generate the PTV. [21]
**iPlan Dose**

The iPlan Dose module is used to decide all the beam parameters and LINAC settings by the treatment planners. The dose calculation, DVH generation, and inverse plan optimization are all done in this software. First, the treatment planner needs to assign a point as the treatment isocenter, which is usually selected as the geometric center point of the PTV. Then the treatment beams are associated with this isocenter. The iPlan Dose can perform treatment plans for conformal techniques, IMRT techniques, and arcs techniques. For SRS at Duke Radiation Oncology Department, the dynamic arc is the most commonly used technique, and usually 3 to 5 arcs are applied. During planning of the dynamic arc technique, the treatment planners will select the optimal arc length and couch kick angle to avoid unnecessary exposure to the surrounded critical structures. Then the system will calculate the leaf position for each combined gantry and couch angle to conform the radiation field to the PTV margin. [21] However, leaf position optimization in the forward treatment planning technique also depends on the OAR type selected. In the iPlan Dose system, there are 3 priority levels can be assigned to each OAR; the level one OARs should be entirely blocked in leaf optimization in order to protect the corresponding areas. However, full block may not be possible because of the PTV positions and the treatment goals; the level two OARs will be blocked during leaf optimization if there is overlapped region of the PTV margin and the OARs in this level; the level three OARs are not taken into consideration during leaf optimization; that is, the OARs will not be blocked when the PTVs overlap with the OARs.

At Duke, the OARs in SRS treatments are all set as level three OARs to assure proper PTV coverage and dose distribution. After entering the prescription dose and the dose constraint for the PTV (usually set the hard constraint as: 99.0% to 99.8%
PTV volume needs to receive 100% of prescription dose), the MU for each arc will be calculated and the users can check the dose distribution from the DVHs and the isodose lines. For a small target volume as in SRS, the dose calculation grid size is usually selected as 1 mm for better accuracy.

**Phantom Mapping**

The iPlan treatment planning system provides the Phantom Mapping software for treatment verification before actual treatment delivery. The treatment plan dose distribution can be directly exported by clicking the “dose export button” in the iPlan Dose; however, the purpose of phantom mapping is to calculate a new dose distribution based on the phantom configuration, which is different from the patient’s shape in the treatment plan. As a result, the phantom mapping module in the iPlan treatment planning system should be able to re-calculate the dose distribution based on the phantom shape so that it can be used to compare with the film measurement or ion-chamber measurement. By getting the phantom 3D image from a CT simulator, any existing treatment plan can be exported to the Phantom Mapping module and obtain its dose distribution on the phantom CT-sim image.[21]

2.3.5 **Linear Accelerator**

At Duke University Medical Center, all the SRS patients are treated on Novalis TX (Varian Medical System, Palo Alto, CA; BrainLab, Feldkirchen, Germany). The Novalis TX is a megavoltage treatment unit with 3 energy options for the photon beam: 6 MV, 15 MV, and 6 MV in radiosurgery mode of 1000MU/min dose rate. The system is also equipped with the ExacTrac Robotics system (BrainLab, Feldkirchen, Germany) and kV on-board imager with both 2D and 3D CBCT imaging capabilities.
that can help to improve the image-guided stereotactic radiosurgery accuracy by combining the use of a high definition multileaf collimator (HDMLC). [15, 22]

**HDMLC**

The HDMLC consists of 120 leaves, which includes 2x32 of 2.5 mm central leaves and 2x28 of 5 mm peripheral leaves. The major difference between the Novalis TX system and the conventional Novalis stereotactic units is the 6 MV SRS mode with HDMLC. [15, 22]

**ExacTrac Robotics System**

The Novalis ExacTrac x-ray system consists of two floor-mounted x-ray tubes and two ceiling-mounted amorphous silicon (aSi) flat panel detectors. The ExacTrac system generates two orthogonal x-ray images through the LINAC isocenter. Then the system generates the digital reconstructed radiograph (DRR) from the planning CT image to simulate the 2D planar image with the same projection angle as the ExacTrac x-ray system. By comparing the bony structures or air cavities in the x-ray images and its corresponding DRRs, the patient alignment accuracy can be verified. After determining the manually desirable translation and rotation parameter for patient position correction, the robotic couch can be moved to reposition the patient and correct the setup error by pressing the robotic enable bar of the control pendent. [15, 23]

**kV On-Board Imager (OBI)**

The Varian OBI system consists of a kV x-ray source and an opposed kV amorphous silicon (aSi) detector with sensitive area of 30x40 cm$^2$. Both the x-ray source and the detector are mounted orthogonally to the treatment beam direction on
the LINAC using robotic arms. The OBI system provides three image acquisition modes: 2D radiograph acquisition, 2D fluoroscope image acquisition, and 3D cone-beam CT image acquisition. Though the 2D radiograph acquisition mode can be used to acquire 2D planar images at any projection angles with selected source-to-image distance, generally, the anterior-posterior projection and the lateral projection are taken to localize the target position. As with the ExacTrac system, the 2D images obtained from the OBI system can be registered and compared with the DRR images generated by the Varian Aria Off-line review software. Then the position deviation can be recorded for couch shift or further evaluation. [15, 24]

The 3D CBCT images are generated from 360 to 655 projections acquired over certain range of gantry rotation. There are six kinds of CBCT acquisition modes in the Varian system: low-dose head, standard-dose head, high quality head, pelvis spotlight, pelvis, and low-dose thorax. The first four modes are scanned with full-fan acquisition, where 360 projections are acquired over 200 degrees of gantry rotation. The last two modes are scanned with half-fan acquisition, where 655 projections are acquired over a complete gantry rotation. The full-fan acquisition means that the kV image is centered and can see the entire object to be reconstructed in every projection, and the maximum reconstruction diameter is 25 cm; the half-fan acquisition indicates that the kV image is offset laterally and can see only part of the object to be reconstructed in every projection, and this method increases the reconstruction diameter of the image to 45 cm. As a result, generally, the full-fan technique is usually used to image small diameter anatomic sites such as brain, while the half-fan technique is commonly used for large diameter anatomic sites such as thorax and pelvis. Furthermore, for each acquisition mode, the reconstructed slice thickness can be chosen from 1mm to 2.5 mm. In this work, the full-fan CBCT acquisition technique with 1 mm reconstructed
slice thickness was selected. After obtaining the 3D CBCT image, it could be directly registered to the planning CT image to evaluate the patient setup deviation for further couch shift or verification. [15, 24]

2.4 Daily Quality Assurance

Quality assurance in radiation therapy is the procedure that ensures the consistency of medical prescription and the radiation delivery during treatment. It can also monitor the safe fulfillment of that prescription, including dose to the target volume, dose to the surrounding critical structures, to determine the end result of the treatment. [25]

2.4.1 Output Constancy and Laser Alignment

The AAPM TG 142 recommends the deviation of daily output for the IMRT stereotactic machines to be no more than 3% and the tolerance of laser localization to be 1 mm for stereotactic machines. At Duke University Radiation Oncology Department, machine laser alignment and the daily output of the LINAC for photon and electron beams with different energy are checked by the daily QA3 device developed by Sun Nuclear (Melbourne, Florida). This device utilizes 25 specially designed detectors, both diodes and ion-chambers, to obtain a real-time optimized result, and simultaneously checks beam output, beam flatness, beam symmetry, radiation field size, and beam energy.

During machine output QA, the daily QA3 device is positioned on the table top, aligned with the central axis (CAX) at 100 cm source-to-surface distance (SSD). There is no buildup requirement for the QA3 device. Then the laser alignment is checked by verifying that the lasers touch the surface of the daily QA3 device within the side notches. There are a total of 4 lasers that need to be checked: the left
and right vertical lasers, the left and right horizontal lasers, the sagittal laser, and the ceiling laser.

For beam output consistency check, 100 monitor unit (MU) is delivered with 20x20 cm MLC field for both the photon and electron beam energy: 6 MV and 15 MV photon beam; 6 MeV, 9 MeV, 16 MeV electron beam. When testing the 6 MV photon beams, which is the energy used in SRS, the dose rate is set to 1000 MU/min relative to the others with 400 MU/min.

2.4.2 Mechanical and Radiation Isocenter Coincidence

Since the margin expanded from gross tumor volume (GTV) to planning target volume (PTV) is tight for SRS compared to other treatment techniques, the coincidence of the mechanical and radiation isocenter of the LINAC machine needs to be verified, typically using a Winston-Lutz test. With the BrainLab stereotactic system, a 5 mm tungsten ball imbedded in the Winston-Lutz pointer is mounted on the BrainLab immobilization device base and positioned at the machine isocenter based on the in-room lasers. Then, a level device is positioned on the couch and the mounting system to check that the whole setup is level. If there is fine adjustment needed for the pointer location, the knobs under the couch can be used to manually adjust the couch in roll, yaw and pitch direction. After the pointer is moved to the mechanical isocenter, a 7.5 mm radiosurgery circular collimator is mounted on the LINAC head, and the ball is imaged with 1500 MU delivery by radiochromic films for different gantry/couch angle combination: (C:0, G:180); (C:0, G:90); (C:0, G: 0); (C:0, G:210); (C:270, G:0); (C:45, G:0); (C:315, G:0); (C:90, G:0). For each exposure, the film records two circular regions, one with lower dose created by the ball and another with higher dose created by the circular collimator. The mechanical setup and
an example of Winston-Luz result are shown in Figure 2-4 and Figure 2-5, respectively. [15, 23, 26]

The deviation of the center for both circular regions indicates the deviation of the mechanical and radiation isocenter. Based on the AAPM recommendation, the deviation of the two isocenters should be within 1 mm. If test results exceed the 1 mm limitation, further laser adjustment needs be made to ensure the accuracy of beam delivery while the patients are set up by the in-room laser alignment. [15, 23]

Figure 2-4 (A) BrainLab Winston Lutz test equipment (Couch-mounted adaptor; Winston Lutz phantom pointer; and field collimator), (B) Winston Lutz phantom pointer, (C) Ideal adjustment of the circular radiation field and the target ball position (From the BrainLab hardware manual).
2.4.3 **OBI System Accuracy**

**CBCT Imaging Isocenter Accuracy - 3D/3D Analysis**

After the Winston-Lutz test for the mechanical and radiation isocenter coincidence is passed, the same setup can be used to verify the accuracy of the 2D and 3D OBI imaging system. When the Winston-Lutz test is passed, the center of the embedded tungsten ball can be considered as the isocenter of the radiation field. Then a volumetric CBCT scan is acquired in the full-fan CBCT Mode with 25 cm FOV coverage: 512x512 matrix size, 17 cm axial dimension coverage, and 1 mm slice thickness. By matching the tungsten ball image generated by the CBCT with the reference plan CT image generated by the multislice CT simulator, the difference between the CBCT and LINAC isocenter can be obtained. The difference should be within 1 mm. [15, 27]

**Couch Shift Accuracy - 3D/3D Analysis**

To verify the couch shift accuracy, we remotely shift the couch position by 0.5 cm in the vertical direction, 2.0 cm in the longitudinal direction, and 1.0 cm in the lateral direction, and this planned shift and the new couch position are recorded. Then, the CBCT image is taken for the off-center tungsten ball. After the image is acquired, the CBCT image is manually matched with the reference plan CT image, and the shift
The agreement between the two shifts should be less than 1 mm.

After the CBCT image is taken for the off-center tungsten ball, we manually shift the couch so that the lasers align with the center marker of the Winston-Lutz pointer. The differences between this manually shift of laser-aligned couch position and the previous remotely shift couch position is also be recorded. After subtracting the planned shift from the laser aligned couch position, the discrepancy with the remotely shift of couch position should also be within 1 mm. [15, 23, 27]

**kV Imaging Isocenter Accuracy - 2D/2D Analysis**

Also, by using the same Winston-Lutz Setup, two orthogonal images are taken at anterior-posterior (AP) and right lateral (RLAT) orientations with source to imager distance of 150cm. The radiologic setting for both views follows the standard parameters for Head-Lateral imaging: tube voltage (kV) = 70; tube current (mA) = 200; exposure time (ms) = 25. The accuracy of the kV imaging system isocenter then can be obtained by measuring the distance between the tungsten ball center in the image and the digital graticule. The deviation should be within 1 mm. [27]

**2.4.4 ExacTrac Calibration**

**ExacTrac System Isocenter Calibration**

The isocenter calibration is performed with the isocenter calibration phantom, which is a 10x10x2 cm³ solid block with 5 infrared markers attached on its anterior surface. This phantom is visually aligned with the lasers by the crosshairs marked on each phantom surface. Then the ceiling-mounted infrared camera can detect the position of the 5 infrared markers, and set the laser isocenter (mechanical isocenter) as
the origin of the infrared coordinate system. This procedure provides the basis for further x-ray calibration of the ExacTrac system. [23]

**ExacTrac System x-ray Calibration**

For the ExacTrac system x-ray calibration, a BrainLab x-ray calibration phantom is used. Based on the infrared markers on the surface of the x-ray calibration phantom, the user can be guided to position the phantom onto the previously calibrated infrared isocenter. After the phantom is correctly positioned, two orthogonal oblique x-ray images are taken to capture the radiopaque disks inside the phantom, and a marker detection algorithm is performed to locate the marker onto the two images. The locations of these markers are used to determine the mapping projection parameters, which are used to map from 3D objects to 2D projections. [23]

### 2.5 Setup Accuracy Analysis

In this project, 394 brain lesions from 288 patients who received stereotactic radiosurgery were studied to assess the immobilization and localization accuracy of the BrainLab patient positioning system. Among the selected patients, 10 were immobilized with the invasive BrainLab Headring system; and, the other 278 were immobilized with the reloadable BrainLab mask system. All the patients were simulated with the stereotactic immobilization device and CT localizer. Their CT images were then imported to the BrainLab iPlan system for treatment planning. After the plans were done, four overlays (A, B, C, and D) were printed from the treatment plans that indicated the position of the treatment isocenter. On the treatment day, the overlays were then attached to the target positioner (TAPO) where the cross hairs on the overlays were aligned with the room lasers. This made the couch to be initially
positioned close to the location where the PTV center is positioned at the treatment isocenter. [28]

After TAPO setup, a set of 2D AP/Lateral images and a 3D CBCT image were taken by the OBI system. By registering the 2D images with the DRRs and the 3D CBCT with the CT-sim image, the required shift in anterior-posterior (AP), superior-inferior (SI), right-left (RL) direction can be measured. Based on the clinical protocol and the physician’s evaluation, some patients cases (141/394) had the 2D shifts applied, and the others (253/394) had only the 3D shifts applied. When 2D shifts were applied, the CBCT images would be taken after the couch shift. In this project, the TAPO setup accuracy was evaluated by analyzing the shifts required after TAPO positioning, which were the discrepancies between TAPO and image-guided setup. Therefore, for patients that had both 2D and 3D matching shift applied, the 2D and 3D matching shift should be added up to obtain the total discrepancy between the two setups; however, for patients with only 3D matching shift applied, the 3D matching shift was the total discrepancy, and the 2D matching shift measurement could be ignored. In this project, the systematic setup discrepancies were evaluated by the mean value of couch shifts and the corresponding standard deviations represented the random error of patient setup; the magnitudes of the setup discrepancy were evaluated by the root mean square (RMS) among the collected data. The radial discrepancies were calculated based on equation (1).

\[
\text{Radial Discrepancy} = \sqrt{AP^2 + SI^2 + RL^2},
\]

where AP, SI, and RL are the shift distances required from the image-guided system.
2.6 CBCT Treatment Plan Evaluation

In this project, 20 patients immobilized with the noninvasive BrainLab U-frame system and thermoplastic mask were selected to evaluate the dosimetric accuracy of CBCT image-guided SRS by the BrainLab iPlan Phantom Mapping module. The contours of the PTV and critical organ were transferred directly from the planning CT and MR images to the CBCT images after image registrations. The delivered dose distributions could be calculated and analyzed by copying the original treatment plans to the CBCT images and assigning the treatment isocenters on the CBCT images according to the couch shifts acquired after planning CT and CBCT image registrations. Figure 2-6 below shows the flow chart which indicates the procedure of evaluating the dosimetric accuracy on the CBCT-based treatment planning.

Figure 2-6 The flow chart of the procedure in evaluating the dosimetric accuracy of CBCT patient localization.
2.6.1 Contour Transferring

In this work, the CBCT images acquired before patient treatments for image-guided setup corrections were imported to the phantom mapping system as the phantom images. Before importing, in order to obtain exactly the same PTV and critical structures contour, the CBCT images were first registered with the MR and CT images in the iPlan Image module and the contours were directly transferred onto these images. Figure 2-7 below shows the interface of image registration between the CBCT and MR images in the BrainLab iPlan image module. The bony structure alignment in both images could be used to evaluate the registration accuracy and then manually modified any misalignment.

Figure 2-7 The MR image and the CBCT image registration through BrainLab iPlan Image module. By matching the bony area in both images, the registration accuracy can be checked and modified. After image registration, the original contour on the MR image can be directly transferred to the CBCT image.
2.6.2 CBCT Coordinate System

In the iPlan Phantom Mapping system, the default treatment isocenter was selected as the CBCT isocenter, which was ideally the radiation isocenter as well. However, because the couch shift after CBCT/CT registration was applied after the CBCT image acquisition, the treatment isocenter in the CBCT coordinate system actually changed after the shift. Therefore, the treatment isocenter in the Phantom Mapping module needed to be modified with the shift by directly adding up the shift distances in each translational direction.

The origin of the CBCT coordinate system was located at the left posterior vertex of the central reconstructed slice; also, the positive directions of x, y, z coordinates correspond to the right, anterior, superior anatomic direction as shown in Figure 2.8 (A). The reconstructed slice thickness was 1 mm. Therefore, the isocenter of the OBI system, which was also the isocenter of the LINACs is at the coordinates (125, 125, -0.5) of the CBCT coordinate system. On the other hand, the in-room LINAC coordinate system followed the DICOM coordinate system in which the x-axis pointed to the right when facing the gantry, the y-axis pointed toward the floor, and the z-axis pointed toward the gantry as shown in Figure 2.8 (B). By referring to the two separate coordinate systems, the positive vertical, longitudinal, lateral couch shifts in the in-room LINAC coordinate system were associated with the couch shifts in negative y, positive z, and negative x directions in the CBCT coordinate system.

There was one thing had to be kept in mind in this project: during the Phantom Mapping process, the treatment isocenter in the CBCT coordinates changed to the opposite directions as the couch shifts. For example, when the couch required a vertical shift in the positive y direction in the LINAC coordinate, the treatment isocenter in the CBCT actually moved toward the negative y direction in the LINAC
coordinate system, which was also the positive y direction in the CBCT coordinate system. This idea was critical since it decided the treatment isocenter location, which was the key factor regarding to the entire treatment dose distribution when evaluating the dosimetric treatment accuracy by the Phantom Mapping module.

![Diagram](image)

Figure 2-8 (A) The CBCT coordinate system. The CBCT/radiation isocenter coordinates is (125, 125, -0.5) relative to the CBCT coordinate system origin. The positive directions of x, y, z coordinate correspond to the right, anterior, superior anatomic direction. The total scan length is 25 cm in x, y direction, and 17 cm in z direction; (B) The in-room LINAC coordinate system (DICOM Coordinate System).
2.6.3 **CBCT-image guided Setup Accuracy Analysis**

Since, the ultimate goal of patient localization was aligning the PTV center with the treatment delivery isocenter, after correctly modifying the treatment isocenter in the CBCT image coordinate system, the residual error of image-guided patient localization could be evaluate through measuring the distances between the treatment isocenter coordinates and the PTV center coordinates in the CBCT image coordinate system.

2.6.4 **Target Coverage**

Quantitative target coverage has two different definitions: the dose coverage definition and the volumetric coverage definition. The dose coverage is defined in the 1993 Radiation Therapy Oncology Group (RTOG) radiosurgery guideline as the ratio of minimum dose in the target volume to the prescription dose. The dose coverage definition is shown in equation (2).

\[
\text{Coverage}_{\text{RTOG}} = \frac{\text{Minimum dose in the target volume}}{\text{prescription dose}} \quad (2)
\]

A value of 1.0 (no underdosage in the target) is ideal, 0.9-1.0 is per protocol, 0.8-0.9 represents a minor deviation, and coverage < 0.8 is considered a major deviation from the desired protocol. [29]

On the other hand, the volumetric coverage definition is usually preferred as the coverage analysis in SRS. This is because that the SRS treatment plans require a steep dose fall off near the target boundary; thus the dose may fall to 80% of the prescription dose within 0.5 or 1 mm. If the target is located near a critical structure, it may be necessary to underdose a small volume of the target, but this volume of underdosage needs to be kept to a minimum. Therefore, the volume coverage definition
which clearly shows the percentage of the target volume covered by prescription dose is useful for this evaluation. [29] The volume coverage definition was shown in equation (3)

\[ \text{Target Coverage (Volumetric)} = \frac{V_{p,T,P_i}}{V_T} \times 100\%, \quad (3) \]

where \( V_{p,T,P_i} \) is the target volume that receive the prescription dose or greater, and \( V_T \) is the target volume. [29]

In this project, we applied the RTOG dose coverage for PTV coverage analysis and the volumetric target coverage for both PTV and GTV coverage analysis. Typically, for SRS treatment plans, the PTV volumetric coverage is set in the constraint to ensure that over 99% of the target volume is covered by 100% of the prescription dose; on the other hand, 100% volume coverage for GTV is desired. Through evaluating the dose and volume coverage in both the original plan and the CBCT plan, the dosimetric treatment accuracy based on the image-guided shift system can be verified.

2.6.5 Conformity Index

Besides the coverage of prescription dose to the target volume, how the volume of dose distribution matches the size and shape of the target volume is also important. It is because the dose received by the surrounding normal tissue is another consideration for treatment planning. The BrainLab iPlan Dose module provides the calculated conformity index shown in the DVH window. The conformity index definition is calculated by the following equation:

\[ \text{Conformity Index (CI)} = \frac{V_{p_i}}{V_{PTV_{p_i}}} = 1 + \frac{V_{\text{Normal Tissue}_{p_i}}}{V_{PTV_{p_i}}}, \quad (4) \]
where $V_{pi}$ is the total tissue volume receiving the indicated dose, $V_{PTV,pi}$ is the volume of planning target volume receiving the indicated dose, and $V_{Normal~Tissue,pi}$ is the normal tissue volume receiving the indicated dose as shown in Figure 2.9.

The value for the conformity index ranges from 1 to infinity. A value of 1 indicates a perfect conformation of the treatment dose; a value between 1 and 2 indicates that the plan is per protocol; $2 < CI < 2.5$ indicates a minor deviation, and $CI > 2.5$ indicates a major deviation.

![Figure 2-9 Definition of the volumes used in coverage and conformity parameters. The solid line is the target volume, $V_T$; the dotted line is the prescription isodose, $pi$; the shaded area is the total volume that receives at least the prescription dose, $V_{pi}$; and the hatched area is the volume of the target volume that receives at least the prescription dose. (Lomax et al.)](image)

### 2.6.6 Statistical Hypothesis test

The paired student t-test was used in this project to analyze the differences in dose, coverage, and conformity index between the original treatment plans and the CBCT-based treatment plans. Statistical significance was considered at $p < 0.05$. 
3

Results

3.1 Setup Discrepancy

*BrainLab Headring Patient Immobilization*

Figure 3.1 displays the histogram that recorded the frequencies of couch shifts required after image registrations in the vertical (AP), longitudinal (SI), and lateral (RL) directions for each patient case of BrainLab Headring immobilization. As can be seen, the discrepancies were mainly distributed between ±2 mm in all three translational directions. Figure 3.2 shows the systematic errors calculated from the mean of the couch shifts and its corresponding standard deviations, which represented the random errors of the TAPO setup with BrainLab Headring immobilization. In vertical (AP), longitudinal (SI), and lateral (RL) directions, the systematic errors were 1.09 mm, 1.18 mm, and 0 mm, respectively, and the random errors were 0.70 mm, 0.98 mm, and 0.63 mm, respectively. The overall radial systematic error and random error were 1.29 mm and 1.36 mm, respectively. On the other hand, in Figure 3.3, the discrepancies in RMS were 1.28 mm in the vertical (AP) direction, 1.51 mm in the
longitudinal (SI) direction, and 0.60 mm in the lateral (RL) direction. The overall radial discrepancy in RMS was 2.07 mm.

Figure 3-1 The discrepancies between TAPO setup and image-guided setup for patients with BrainLab Headring immobilizations: (A) the discrepancies in vertical (AP) direction, (B) longitudinal direction (SI), and (C) lateral direction (RL).
Figure 3-2 The systematic errors (mean) and the random errors (STD) between TAPO patient setup and image-guided setup in each direction for patients with BrainLab Headring immobilization.

Figure 3-3 The discrepancies in RMS between TAPO patient setup and image-guided setup in each direction for patients with BrainLab Headring immobilization.
U-frame Patient Immobilization

Figure 3.4 displays the frequency of patient setup discrepancies between the TAPO and image-guided setup in the vertical (AP), longitudinal (SI), and lateral (RL) directions for patients immobilized with the BrainLab U-frame system. As can be seen, the discrepancies were mainly distributed between ±3 mm in all three translational directions. However, a few cases with setup discrepancies up to ±6 mm were detected. The systematic errors in the vertical (AP), longitudinal (SI), and lateral (RL) directions were 1.17 mm, 0.94 mm, and -0.23 mm, respectively, and the random errors were 1.14 mm, 1.66 mm, and 1.06 mm, respectively, as shown in Figure 3.5. The overall radial systematic error and random error were 1.52 mm and 2.28 mm, respectively. The discrepancies in RMS shown in Figure 3.6 were 1.63 mm in the vertical (AP) direction, 1.91 mm in the longitudinal (SI) direction, and 1.08 mm in the lateral (RL) direction. The overall radial discrepancy in RMS was 2.73 mm. Table 3.1 below compares the systematic errors, random errors, and discrepancies in RMS for both the BrainLab Headring and U-frame patient immobilization system.
Figure 3-4 The discrepancies between TAPO setup and image-guided setup for patients with the non-invasive BrainLab U-frame immobilizations: (A) the discrepancies in vertical (AP) direction, (B) longitudinal (SI) direction, and (C) lateral (RL) direction.
Figure 3-5 The systematic errors (mean) and the random errors (STD) between TAPO patient setup and image-guided setup in each direction for patients with the non-invasive BrainLab U-frame immobilization.

Figure 3-6 The discrepancies in RMS between TAPO patient setup and image-guided setup in each direction for patients with the non-invasive BrainLab U-frame immobilization.
Table 3-1 Systematic errors, random errors, and setup discrepancies in RMS for both BrainLab Headring and U-frame patient immobilization system.

<table>
<thead>
<tr>
<th></th>
<th>BrainLab Headring</th>
<th>BrainLab U-frame</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systematic Error (mm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Random Error (mm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Discrepancy in RMS (mm)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.2 Treatment Accuracy Evaluation

3.2.1 *Mechanical Setup Accuracy for the 20 selected cases*

As mentioned in section 2.3.4, the treatment isocenter coordinates in the CBCT coordinate system are (125, 125, -0.5). Therefore besides the discrepancies acquired from image fusion of CT and CBCT images, the TAPO setup discrepancies could also be evaluated by the distances between the contoured PTV center and the treatment isocenter in the CBCT coordinate system. The distances between the PTV center and the treatment isocenter for these 20 selected patients were listed in Table 3.2. In addition, Figure 3.5 shows the discrepancies between the PTV center and the treatment isocenter in a space distribution plot. In ideal patient setup conditions, the contoured target centers in the CBCT images should be located at the treatment isocenter for accurate dose delivery. However, the target center positions of these 20 patients had the mean discrepancies from the treatment isocenter of -0.17 mm in AP, -1.30 mm in SI, and 0.06 mm in the RL, and the corresponding STD were 0.82 mm, 1.31 mm and 1.65 mm, respectively. The radial systematic and random error was 1.31 mm and 2.26, respectively. Also, the discrepancies in RMS were calculated in AP, SI,
and RL directions with the results of 1.28 mm, 2.06 mm, and 0.78 mm, respectively. The radial discrepancy in RMS was 2.55 mm.

![Figure 3-7](image)

Figure 3-7 The spatial distribution of the planning target volume (PTV) center positions in the CBCT coordinate system. The treatment isocenter coordinates were (125, 125, -0.5) and was shown as the blue circular marker in the plot. The relative distance between the PTV center and the treatment isocenter can be taken as the TAPO setup inaccuracy.
Table 3-2 The PTV center coordinates for each patient case and their corresponding distances to the treatment isocenter (125, 125, -0.5) before couch shift in the CBCT coordinate system.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>PTV center coordinates (mm)</th>
<th>Distance to the isocenter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X (RL)</td>
<td>Y (AP)</td>
</tr>
<tr>
<td>1</td>
<td>124.3</td>
<td>127.5</td>
</tr>
<tr>
<td>2</td>
<td>124.2</td>
<td>128.2</td>
</tr>
<tr>
<td>3</td>
<td>123.4</td>
<td>125.9</td>
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<td>124.4</td>
<td>127.4</td>
</tr>
<tr>
<td>5</td>
<td>126</td>
<td>123.8</td>
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<td>124.3</td>
<td>126.8</td>
</tr>
<tr>
<td>7</td>
<td>124.6</td>
<td>124.2</td>
</tr>
<tr>
<td>8</td>
<td>126.8</td>
<td>124.9</td>
</tr>
<tr>
<td>9</td>
<td>125.5</td>
<td>124.2</td>
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<td>124.7</td>
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<td>124.6</td>
</tr>
<tr>
<td>13</td>
<td>124.8</td>
<td>123.8</td>
</tr>
<tr>
<td>14</td>
<td>125.8</td>
<td>125.3</td>
</tr>
<tr>
<td>15</td>
<td>124.6</td>
<td>124.8</td>
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<td>124.4</td>
</tr>
<tr>
<td>20</td>
<td>124.9</td>
<td>124.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>X (RL)</th>
<th>Y (AP)</th>
<th>Z (SI)</th>
<th>Radial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic Error (Mean of discrepancies)</td>
<td>0.06</td>
<td>-0.17</td>
<td>-1.30</td>
<td>1.31</td>
</tr>
<tr>
<td>Random Error (Standard deviation)</td>
<td>0.82</td>
<td>1.31</td>
<td>1.65</td>
<td>2.26</td>
</tr>
<tr>
<td>Discrepancies in RMS</td>
<td>0.78</td>
<td>1.28</td>
<td>2.06</td>
<td>2.55</td>
</tr>
</tbody>
</table>
3.2.2 Image-guided Setup Accuracy

In the previous section, the TAPO setup accuracy was evaluated through the distances between the PTV center position and the treatment isocenter in the CBCT coordinate system. For U-frame SRS immobilization, after TAPO setup, further image-guidance was required to correct the discrepancies by image registrations between the OBI images and the planning CT image or its corresponding DRR to ensure the translational accuracy is within 1 mm in each direction. In Table 3.3, the translational couch shifts after planning CT and CBCT/DRR registration were recorded. After applying the required shifts for each patient, the treatment isocenters in the CBCT coordinate system were moved with the same distances in the opposite directions as couch shifts. The treatment isocenters after CT and CBCT/DRR image registration were also listed in Table 3.3.

For ideal image-guided patient positioning, the PTV center in the CBCT image should be positioned at the treatment isocenter after applied the corresponding shift indicated by image-guided system. That is, after modifying the treatment isocenter to the position after couch shifts, the coordinates of this new treatment isocenter should be coincident with the PTV center coordinates. Therefore, the displacements between the treatment isocenter coordinates after couch shifts and the PTV center coordinates could be used as a quantitative measurement for CBCT patient setup accuracy evaluation. As illustrated in Table 3.4, the systematic errors in AP, SI, and RL directions were -0.08 mm, -0.48 mm, and 0.01 mm, respectively, and the random errors were 0.62 mm, 0.72 mm, and 0.48 mm, respectively. The overall radial systematic error and random error were 0.49 mm and 1.06 mm, respectively. In addition, the differences in RMS between the coordinates of treatment isocenter after couch shift and the coordinates of PTV center were 0.47 mm in RL, 0.61 mm in AP,
and 0.85 mm in SI. The overall radial discrepancy in RMS was 1.15 mm. In general, the systematic errors, the random errors and the discrepancies in RMS were all less than 1 mm in each direction. This shown an improvement of setup accuracy compared with the TAPO setup for both Headring and U-frame immobilization.

Table 3-3 The first column shows the shifts acquired from CT and CBCT/DRR image registrations (based on LINAC coordinate system). The second column is the treatment isocenter after the couch was shifted (in the CBCT coordinate system). The third column indicates the PTV center positions in the CBCT coordinate system, which were expected to locate at the treatment isocenter after the couch shifts for accurate treatment delivery.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>CT and CBCT/DRR registration shift (mm)</th>
<th>Treatment isocenter after couch shift (mm)</th>
<th>PTV center coordinates (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RL  AP  SI</td>
<td>RL  AP  SI</td>
<td>RL  AP  SI</td>
</tr>
<tr>
<td>1</td>
<td>0   2   0</td>
<td>125 127 -0.5</td>
<td>124.3  127.5 -0.8</td>
</tr>
<tr>
<td>2</td>
<td>-1  2   3</td>
<td>124 127 -3.5</td>
<td>124.2  128.2 -4.5</td>
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<td>3</td>
<td>-1  1   3</td>
<td>124 126 -3.5</td>
<td>123.4  125.9 -2.6</td>
</tr>
<tr>
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<td>0   2   4</td>
<td>125 127 -4.5</td>
<td>124.4  127.4 -5.3</td>
</tr>
<tr>
<td>5</td>
<td>0   0   1</td>
<td>125 125 -1.5</td>
<td>126  123.8 -3.2</td>
</tr>
<tr>
<td>6</td>
<td>1   2   0</td>
<td>124 127 -0.5</td>
<td>124.3  126.8 -1.2</td>
</tr>
<tr>
<td>7</td>
<td>0   0   1</td>
<td>125 125 -1.5</td>
<td>124.6  124.2 -3.7</td>
</tr>
<tr>
<td>8</td>
<td>1   0   1</td>
<td>126 125 -1.5</td>
<td>126.8  124.9 -2.0</td>
</tr>
<tr>
<td>9</td>
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<td>125 124 -0.5</td>
<td>125.5  124.2 -0.4</td>
</tr>
<tr>
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<td>126 125 -0.5</td>
<td>126.2  124.7 -0.6</td>
</tr>
<tr>
<td>11</td>
<td>0   0   1</td>
<td>125 125 -1.5</td>
<td>125  125 -2.5</td>
</tr>
<tr>
<td>12</td>
<td>1   0   1</td>
<td>126 125 -1.5</td>
<td>125.8  124.6 -1.3</td>
</tr>
<tr>
<td>13</td>
<td>0   1   1</td>
<td>125 124 0.5</td>
<td>124.8  123.8 0.2</td>
</tr>
<tr>
<td>14</td>
<td>1   0   0</td>
<td>126 125 -0.5</td>
<td>125.8  125.3 -0.9</td>
</tr>
<tr>
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<td>0   1   0</td>
<td>125 124 -0.5</td>
<td>124.6  124.8 -0.6</td>
</tr>
<tr>
<td>16</td>
<td>0   0   2</td>
<td>125 125 1.5</td>
<td>124.8  123.9 1.3</td>
</tr>
<tr>
<td>17</td>
<td>0   1   0</td>
<td>125 126 -0.5</td>
<td>125.6  125.3 -0.5</td>
</tr>
<tr>
<td>18</td>
<td>0   -1  0</td>
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<td>124.7  124.5 -1.0</td>
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<tr>
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<td>0   0   1</td>
<td>125 125 -1.5</td>
<td>125.5  124.4 -1.2</td>
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<tr>
<td>20</td>
<td>0   -1  0</td>
<td>125 124 -0.5</td>
<td>124.9  124.2 -1.8</td>
</tr>
</tbody>
</table>
3.2.3 Phantom Mapping-CBCT Based Planning

Minimum, Mean, and Maximum Dose in PTV

To evaluate the dosimetric treatment accuracy after image-guided patient setup, the CBCT images with transferred contours from original plans were imported to the BrainLab iPlan phantom mapping module as the phantom images, and the original plans were loaded and copied onto the CBCT images to evaluate the dose distribution on these CBCT images. Figure 3.8 shows the treatment planning interface of the original treatment plan in the BrainLab iPlan Dose module and mapped plan in the iPlan Phantom Mapping module, respectively.

| PTV Center and Treatment Isocenter Discrepency after CBCT image-guided shift (mm) |
|---|---|---|---|---|---|---|---|---|---|
| Case | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| RL | -0.7 | 0.2 | -0.6 | -0.6 | 1 | 0.3 | -0.4 | 0.8 |
| AP | 0.5 | 1.2 | -0.1 | 0.4 | -1.2 | -0.2 | -0.8 | -0.1 |
| SI | 0.3 | -1 | 0.9 | -0.8 | -1.7 | -0.7 | -2.2 | -0.5 |
| Case | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
| RL | 0.5 | 0.2 | 0 | -0.2 | -0.2 | -0.2 | -0.4 | -0.2 |
| AP | 0.2 | -0.3 | 0 | -0.4 | -0.2 | 0.3 | 0.8 | -1.1 |
| SI | 0.1 | -0.1 | -1 | 0.2 | -0.3 | -0.4 | -0.1 | -0.2 |
| Case | 17 | 18 | 19 | 20 |
| RL | 0.6 | -0.3 | 0.5 | -0.1 |
| AP | -0.7 | 0.5 | -0.6 | 0.2 |
| SI | 0 | -0.5 | 0.3 | -1.3 |
| Mean | RL= 0.01 mm | AP= -0.08 mm | SI= -0.48 mm | Radial= 0.49 mm |
| STDV | RL= 0.48 mm | AP= 0.62 mm | SI= 0.72 mm | Radial=1.06 mm |
| RMS | RL= 0.47 mm | AP= 0.61 mm | SI= 0.85 mm | Radial=1.15mm |
Figure 3-8 The interface of (A) original treatment plan in the BrainLab iPlan Dose module, (B) corresponding evaluation in the BrainLab iPlan Phantom Mapping module.
Instead of assigning the PTV centers as the treatment plan isocenters, the copied plan isocenters on the CBCT images were manually adjusted to the position of the new treatment isocenters in the CBCT coordinate system after the corresponding couch shifts indicated by CT and CBCT registrations. Table 3.5 illustrates the minimum doses, mean doses, and maximum doses received by the PTVs for both the original plans and the CBCT-based plans. For the 20 original treatment plans, it ranged between 83.58% and 98.87%, 107.4% and 115.06%, 111.8% and 124.66% for the minimum dose, the mean dose, and the maximum dose, respectively. Similarly, in their corresponding CBCT-based plans, the minimum dose, the mean dose, and the maximum ranged between 84.69% and 96.6%, 105.4% and 114.56%, 110.3% and 122%, respectively. The histogram in Figure 3.9 clearly displays the differences in these dose values between the two plans. The average minimum dose, mean dose, and maximum dose were 95.45%, 110.59%, and 116.55% for the original treatment plans, and were 92.88%, 110.11%, and 115.93% for corresponding CBCT-based plans. The average differences between the two plans were listed in Table 3.6; generally, the CBCT-based plans which represented the actual treatment delivery dose distribution indicated a 2.57% lower minimum dose (p=0.218), 0.48% lower mean dose (p=0.053), and 0.62% lower maximum dose (p=0.098) compared with the original treatment plans. These differences between the two plans, which were also the differences between the treatment plans and delivered treatments, were not considered statistical significant. That is, the results of actual treatment delivery were comparable with the original treatment plans.
Table 3-5 The prescription doses for each patient case. Also, the minimum, mean, and maximum dose in the PTV for both the original CT-based treatment plans and the CBCT-based plans were listed. (CT= Original CT-based Plan; CBCT= CBCT-based plans)

| Case No. | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|          | CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT| CT  | CBCT|
| Prescription Dose | 20 Gy | 16 Gy | 20 Gy | 20 Gy | 15 Gy | 15 Gy | 20 Gy | 20 Gy | 18 Gy | 15 Gy | 12 Gy | 20 Gy | 18 Gy | 20 Gy | 16 Gy | 15 Gy | 18 Gy | 15 Gy |
| Minimum Dose | 93.15% | 89% | 89.88% | 84.69% | 96.8% | 96.4% | 98.55 | 89.75% | 96.53% | 93.51% | 98.15% | 99.4% | 99.58% | 95.2% | 95.4% | 98.8% | 95.2% | 97.39% | 93.33% |
| Mean Dose | 110.45% | 110.2% | 115.06% | 114.56% | 111.95% | 110.45% | 107.4% | 105.4% | 110.13% | 114.44% | 110.13% | 112.17% | 112.08% | 108.55% | 108.5% | 124.66% | 117.4% | 118.83% | 119.11% |
| Maximum Dose | 115.45% | 115.3% | 122% | 122% | 117.2% | 116% | 111.8% | 110.3% | 117.33% | 116.6% | 112.67% | 111.47% | 113.85% | 118.43% | 120% | 118.3% | 119.11% | 115.27% | 114.87% | 124.66% |

Table continued...
Figure 3-9 The histograms correspond to the data listed in Table 3.4: (A) the minimum dose; (B) the mean dose; and (C) the maximum dose in PTV of both original and phantom mapping plans.
Table 3-6 The mean value and the standard deviation of the minimum, mean, and maximum dose in PTV for both the original CT-based plans and CBCT-based plans. The differences between the two were calculated by subtracting the original plan measurements from the phantom mapping measurements.

<table>
<thead>
<tr>
<th></th>
<th>Mean, SD</th>
<th>Differences</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Original CT-based Plan</td>
<td>CBCT-based Plan</td>
<td></td>
</tr>
<tr>
<td>Minimum Dose</td>
<td>95.45%±0.04</td>
<td>92.88%±0.03</td>
<td>-2.57%</td>
</tr>
<tr>
<td>Mean Dose</td>
<td>110.59%±0.02</td>
<td>110.11%±0.02</td>
<td>-0.48%</td>
</tr>
<tr>
<td>Maximum Dose</td>
<td>116.55%±0.03</td>
<td>115.93%±0.03</td>
<td>-0.62%</td>
</tr>
</tbody>
</table>

PTV Coverage

From the minimum dose percentages shown in Table 3.6, the RTOG definition of the target coverage can be evaluated. The average RTOG target coverage was 0.9545 and 0.9288 for the original CT-based plans and the CBCT-based plans, respectively. Although the original CT-based treatment plans had higher average RTOG coverage, both of them were over 0.9, which indicated per protocol treatment qualities. In addition, the differences between the two plans were not found statistical significant in our study (p=0.218).

On the other hand, the volumetric target coverage results, which represented by the percentage of the target volume covered by 100% prescription dose, were listed in Table 3.7. Both the GTV and PTV volumetric coverage were calculated for each patient case. The average GTV and PTV coverage were 99.99% and 99.81%, respectively for the original CT-based plans, and were 99.90% and 98.20%, respectively for the CBCT-based plans. The differences between the two plans were not found statistical significant in GTV volumetric coverage (p=0.122); however, in PTV volumetric coverage, the differences were considered statistically significant (p=0.016). The histogram in Figure 3.10 displays a clear comparison of the PTV volumetric coverage for both plans in each patient case. Generally, in the original
treatment planning process, the clinical protocol aimed to provide 100% of GTV coverage and over 99% of PTV coverage; besides 1 of the original treatment plans, the other 19 cases achieved these goals successfully. In contrast, the CBCT-based plans showed a minor deviation to the treatment goals. In one of the CBCT-based plans, the PTV dose coverage was only 88.10%, which indicated a 10.9% deviation to the 99% coverage goal. This Case will be further discussed in the next chapter.

Table 3-7 The volumetric target coverage results for both GTV and PTV with 100% prescription dose in the original CT-based plans and the CBCT-based plans.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>GTV 100% Dose Coverage</th>
<th>PTV 100% Dose Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT</td>
<td>CBCT</td>
</tr>
<tr>
<td>1</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>2</td>
<td>100%</td>
<td>99.70%</td>
</tr>
<tr>
<td>3</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>4</td>
<td>100%</td>
<td>99.95%</td>
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<tr>
<td>5</td>
<td>100%</td>
<td>99.75%</td>
</tr>
<tr>
<td>6</td>
<td>100%</td>
<td>99.10%</td>
</tr>
<tr>
<td>7</td>
<td>100%</td>
<td>99.55%</td>
</tr>
<tr>
<td>8</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>9</td>
<td>100%</td>
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</tr>
<tr>
<td>10</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>11</td>
<td>99.77%</td>
<td>100%</td>
</tr>
<tr>
<td>12</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>13</td>
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</tr>
<tr>
<td>16</td>
<td>100%</td>
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</tr>
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<td>17</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>18</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>19</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>20</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Mean, STD  
99.99%±0.05  99.90%±0.23  99.81%±0.16  98.20%±2.66

Differences  
-0.09%  -1.61%

p-value  
0.122  0.016
Figure 3-10 The histogram that shows the comparison of volumetric coverage for (A) GTV with 100% prescription dose coverage; (B) PTV with 100% prescription dose coverage between the original CT-based plans and the CBCT-based plans.
**Conformity Index**

Conformity index is a parameter calculated from the information of the prescription dose level in the dose volume histogram (DVH) as mentioned in the previous chapter. In this project, the treatment plan conformity indexes were obtained from the BrainLab conformity index definition as shown in equation (4). Table 3.8 shows that the conformity indexes ranged from 1.44 to 2.26 for the original CT-based treatment plans; in contrast, for the CBCT-based plans, the conformity indexes range from 1.41 to 2.42. In average, the original treatment plans had the conformity index of 1.85±0.23 relative to the phantom mapping plans which had the conformity index of 1.86±0.28. The difference between the two plans in conformity index was 0.018, which was not considered statistically significant (p=0.649).

![Figure 3-11](image)

Figure 3-11 The histogram of the conformity indexes in 100% prescription dose level for both the original CT-based plans and CBCT-based plans.
Table 3-8 The Conformity Indexes (CI) of the original CT-based and CBCT-based plans and the corresponding differences.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Original CT-Based Plan</th>
<th>CBCT-Based Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.760</td>
<td>1.790</td>
</tr>
<tr>
<td>2</td>
<td>1.880</td>
<td>1.922</td>
</tr>
<tr>
<td>3</td>
<td>1.885</td>
<td>2.100</td>
</tr>
<tr>
<td>4</td>
<td>1.950</td>
<td>1.551</td>
</tr>
<tr>
<td>5</td>
<td>1.570</td>
<td>1.548</td>
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<tr>
<td>6</td>
<td>1.815</td>
<td>1.759</td>
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<td>1.953</td>
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<td>8</td>
<td>1.735</td>
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<td>2.070</td>
<td>2.406</td>
</tr>
<tr>
<td>10</td>
<td>2.260</td>
<td>2.420</td>
</tr>
<tr>
<td>11</td>
<td>1.690</td>
<td>1.412</td>
</tr>
<tr>
<td>12</td>
<td>2.265</td>
<td>2.048</td>
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<tr>
<td>13</td>
<td>1.675</td>
<td>1.709</td>
</tr>
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<td>14</td>
<td>1.535</td>
<td>1.558</td>
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<tr>
<td>15</td>
<td>1.760</td>
<td>1.762</td>
</tr>
<tr>
<td>16</td>
<td>1.440</td>
<td>1.528</td>
</tr>
<tr>
<td>17</td>
<td>2.125</td>
<td>2.090</td>
</tr>
<tr>
<td>18</td>
<td>1.665</td>
<td>1.796</td>
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<tr>
<td>19</td>
<td>2.065</td>
<td>1.993</td>
</tr>
<tr>
<td>20</td>
<td>1.920</td>
<td>2.043</td>
</tr>
</tbody>
</table>

Mean, STD  \(1.85 \pm 0.23\)  \(1.86 \pm 0.28\)
Differences 0.018
p-value 0.649
4 Discussion

4.1 Patient Localization Accuracy in SRS

4.1.1 Mechanical Setup Accuracy

The results of this work indicated that the non-invasive U-frame immobilization system had larger radial systematic and random setup errors relative to the invasive Headring immobilization system. Although the systematic error of the Headring system in the SI direction was slightly larger than the U-frame system, the standard deviation demonstrated significantly larger random errors for the U-frame system in that direction. The discrepancies in RMS which represented the magnitudes of the setup displacement also pointed out that the Headring system had better accuracy compared to the U-frame system in the three translational directions. Moreover, the maximum TAPO setup discrepancies evaluated by the OBI system were 6 mm for patients with U-frame immobilization. Compared to the 2 mm maximum TAPO setup discrepancies for patients with Headring immobilization, the TAPO setups had relatively considerable displacements when the U-frame immobilization system was applied. Therefore, we considered that the invasive Headring immobilization system
possesses better mechanical localization accuracy compared to the non-invasive U-frame system.

The mechanical setup accuracy was evaluated in this work by registering the 2D images with DRRs reconstructed from the CT-sim images and the 3D images with the CT-sim images. The shifts calculated from image registration represented the variation in patient setup. The systematic errors in mechanical setup with a different patient immobilization system result from different source errors that include: (1) systematic error associated with each immobilization system, (2) systematic error of the BrainLab localizer and target positioner (TAPO), (3) OBI systematic error, and (4) alignment of room laser with the radiation isocenter. [28] The OBI systematic error and the laser alignment error were both ensured to be lower than 1 mm in each translational direction every day before treatments.

On the other hand, the random errors were mainly from the position change of the patient head relative to the frame because of frame slippage in the Headring or patient motion in the U-frame based localization. Since we assumed that the patient head position relative to the U-frame is the same for treatment and simulation, the position change of the patient would influence the treatment accuracy and need to be verified before treatment delivery. Personnel judgment in patient setup with the stereotactic immobilization and localization system and image registration with the bony structures alignment would also cause random setup errors. In addition, the limited treatment couch increment resolution was another random error source. The suggested table shifts of the CBCT registration software, and the linear accelerator console parameters, were all presented in centimeters, and the finest resolution is 1 millimeter. Therefore, submillimeter corrections are rounded up or down. This ±0.5 mm may have caused the increased standard deviations of the couch shifts acquired from the OBI system.
4.1.2 CBCT Image-Guided Setup Accuracy

From the measured data in Table 3.4, improvements in both the systematic errors and the random errors were discovered for the TAPO setup with Headring immobilization or U-frame immobilization when using CBCT image-guided setup correction. For TAPO setup with Headring immobilization, the systematic error was minimized for 1.01 mm in AP, 0.7 mm in SI, and was comparable in RL. The radial systematic error decreased from 1.29 mm to 0.49 mm, with 0.8 mm improvement. Also, for the TAPO setup with U-frame immobilization, the systematic error was minimized for 1.09 mm in AP, 0.46 mm in SI, and 0.22 mm in RL. The radial systematic error decreased from 1.52 mm to 0.49 mm, with 1.03 mm improvement. The image-guided setup also decreased the random errors in both systems. The improvements of 0.08 mm, 0.26 mm, and 0.15 mm of random errors in AP, SI, RL direction, respectively were found for the Headring immobilization system; and the improvements of 0.52 mm, 0.94 mm, and 0.58 mm were found for the U-frame immobilization system.

On the other hand, the discrepancy in RMS for the TAPO setup with Headring immobilization was reduced 0.67 mm in AP, 0.66 mm in SI, and was comparable in RL direction when having CBCT image-guided setup correction; and for U-frame immobilization, it was reduced 1.02 mm in AP, 1.06 mm in SI, and 0.61 mm in RL The improvement of the radial setup accuracy in RMS was 0.92 mm and 1.58 mm for Headring and U-frame immobilization, respectively. Figure 4.1 displays the systematic errors, random errors, and the discrepancies in RMS for different patient localization methods in radial and three translational directions.

In addition, the CBCT positioning accuracy results of the Novalis TX system in
this work agreed with the study of Kim et al. [30] done in 2011, which measured the setup discrepancies from an anthropomorphic phantom. His results showed that the setup errors (mean±STD) in the RL, AP, and SI directions were 0.5±0.7 mm, 0.6±0.5 mm, and 0±0.5 mm, respectively. Both the works indicated submillimeter isocenter positioning accuracy. Compared to the application accuracy assessments done by Maciunas et al. which showed that the radial setup discrepancy of the Leksell frame used with the Gamma Knife was 1.7 mm ± 1.0 mm (mean±SD) and the BRW frame was 1.9 mm ± 1.0 mm (mean±SD) [31], the image-guided setup accuracy was highly comparable to these typical invasive immobilization and localization systems. The residual setup discrepancy could be partially compensated by the PTV margins which were expanded from the GTV delineations by 1 to 3 mm. The expanded margin helped to ensure that the GTV had received the full amount of the prescription dose. The results in this study and in different literatures concluded that the image-guided SRS performed by the OBI system with on-line position correction is essential to guarantee the efficacy of non-invasive patient immobilization for SRS treatment. [32]

Figure 4-1 The histograms show the systematic errors (SE), random errors (RE), and setup discrepancies in RMS for TAPO setup with Headring or U-frame immobilization and image-guided setup in radial and three translational directions and radial.
Many studies had adopted the conclusion that image-guidance with on-line correction can in principle completely replace the role of stereotactic positioning with external coordinate system.[32] Our results also indicated a tolerable residual positioning error for patients immobilized with a non-invasive system and corrected by shifting the couch after OBI guidance. Although the invasive patient setup is still useful in avoiding large rotation errors compared to non-invasive system, the simplification that can be provided by image-guided non-invasive patient positioning is also critically important in the clinical practice.[32]

4.2 Dosimetric Accuracy Evaluation for Image-guided SRS

The CBCT-based treatment plans in this project were used to evaluate the dosimetric treatment delivery accuracy for the SRS treatment with image-guided patient localization. These results, including DVH and isodose distribution, were taken as the actual treatment delivery conditions, and were compared with the original plan data to see the differences between treatment plans and treatment deliveries.

4.2.1 Feasibility of Using CBCT Images for Treatment Planning

This study investigated the dosimetric accuracy of the treatment deliveries with CBCT image-guided localization by copying the original treatment plans onto the CBCT images which were taken right before treatment deliveries. The dosimetric feasibility of the CBCT-based treatment planning was evaluated by Sua Yoo et al. in the paper ‘Accuracy and feasibility of cone-beam computed tomography for stereotactic radiosurgery setup’. Although this study indicated that the HU values in the CBCT images of patients were lower than those in CT images, the discrepancies of the corresponding dosimetric consequences were actually small and less than 1% for the homogeneous head phantoms. In addition, the results of the study suggested
that the CBCT-based treatment planning results are comparable to the results of CT-based treatment plans. [33] Also, in the work of Padamanaban, Sriram et al., the isodose distribution calculated based on CT and CBCT for a single direct field and a wedged field agreed to within 1%. Only for the thorax plans which had more tissue heterogeneity, pronounced dose discrepancies of 3% were discovered. [34] Therefore, in this project, we assumed the CBCT-based treatment plans generated in the BrainLab Phantom Mapping module were comparable in dosimetric aspect to the original CT-based treatment plans, and the differences between the two plans in DVH and isodose distribution were mainly caused by the CBCT positioning inaccuracy.

4.2.2 CBCT-based Treatment Plans

The CBCT-based treatment plans can be taken as a further evaluation for the image-guided system accuracy besides the residual errors measurement after couch shift corrections. When comparing the original CT-based treatment plans and the corresponding CBCT-based plans, the average dosimetric parameters in the CBCT-based plans showed a minor deviation from the original treatment plans. This indicated that the actual treatment delivery outcomes had smaller minimum dose, mean dose, maximum dose, PTV RTOG coverage, GTV volumetric coverage, PTV volumetric coverage, and larger conformity index compared to the original plans. However, the statistical analysis results demonstrated the differences were actually minor and were not considered statistically significant except for the PTV volumetric coverage. With PTV volumetric coverage, if we removed the outlier data of 88.10%, its average would become 98.73% instead of 98.20%, and this brought down the differences to 1% between the two plans’ average. Therefore, in our opinion, the SRS treatments with image-guided patient setup corrections possess a good treatment quality based on its precision in target localization especially for the GTV. The PTV
coverage deviations may result from the residual setup discrepancies after image-guidance localization, which may be caused by image registration inaccuracy and mechanical uncertainty of the OBI system.

The case with the outlier data in PTV coverage was further evaluated in this study. By assessing the registered image from the Aria Offline Review module, discrepancies between the CT image and the CBCT image was detected. As a result, we assumed that the deviation of the PTV coverage form the original plan was caused by the image registration inaccuracy. However, the GTV coverage of this case was 99.55%, which didn’t show significant deviation from the original plan. This demonstrated that the margin expanded from the GTV to PTV was essential for compensating the residual errors of patient positioning and maintaining dose coverage for GTV.

4.2.3 The Sources of Dosimetric Treatment Quality Deviation from the Original Treatment Plans

OBI and LINAC Isocenter Coincidence

When manually modified the treatment isocenters in the CBCT images to the LINAC isocenters according to the couch shift amount acquired after image registration between CBCT and CT-sim images, we took the CBCT image center coordinates (125, 125, -0.5) as the LINAC isocenter coordinates before the couch shift. Therefore, the coincidence of the two isocenters would influence the accuracy of the dosimetric results we got to evaluate the actual treatment delivery condition. However, from the daily QA procedures, the deviations between the two were kept within 1 mm.
**Image Registration Error**

The CBCT image slice thickness was 1 mm in this study, and that of the simulation CT was 1.25 mm. The differences in slice thickness between two images could have caused additional image registration error. The PTV and critical organ contours were transferred directly from the simulation CT images onto the CBCT image after image registration. As a result, the registration error would cause inaccuracy of the transferred contour locations, and would influence the dosimetric results we acquired in this study.

**Rotational Correction**

In our study, the image-guided patient setup after image registrations were only considered and corrected for translational discrepancies. However, the Novalis TX system actually provides the 4 degree of freedom (DOF) and the 6-DOF CBCT image guidance ability, and the techniques are routinely applied in clinical SRS treatments. In 4-DOF correction, the CBCT image can be registered with the CT-sim image in the three translational directions and one rotational direction (yaw); and, the 6-DOF technique further allows the corrections in the other two rotational directions (pitch and raw). When the 6-DOF technique is applied, based on the discrepancies in each direction, the couch position can be corrected using the robotic couch motion.

At Duke University Radiation Oncology department, the image-guided SRS treatments were mostly done through 4-DOF couch position correction, which included the yaw direction corrections. The corrections in rotational directions should not be ignored especially for lesions with irregular shape. This is because for the lesions with irregular shape, without adequate rotational discrepancy corrections the target dose coverage may be compromised and the surrounding normal tissue may
receive more dose than what the planner expected. [15] However, in this project, the rotational discrepancies were difficult correct in the BrainLab Phantom Mapping module, and were ignored when comparing the two plan results. Therefore, this might be a source that influenced the comparison between the original treatments and the real treatment deliveries.
5

Conclusion

The results of this work agreed with the conclusions of previous studies that the image-guided patient positioning combined with the BrainLab U-frame immobilization offers the necessary target localization accuracy in SRS treatment. In addition, it also demonstrated that image-guidance is essential for U-frame patient immobilization since it provides significant accuracy improvement in patient positioning and target localization.

The CBCT-based treatment plans demonstrated that the dosimetric result of actual treatment delivery condition was similar to the original CT-based treatment plans in isodose distribution, GTV coverage, and dose conformity. A minor deviation in PTV coverage which may be caused by the residual localization error of the CBCT image-guided localization was discovered. However, the rotational discrepancy corrections which might influence the Phantom Mapping results were not considered in this work. Therefore, the future work can be focused on designing a comprehensive evaluation method which can also take the rotation discrepancy corrections into consideration.
Bibliography


