2016

Treatment planning and dosimetric verification of cyberknife prostate SBRT (stereotactic body radiation therapy) on an MR-based 3D prostate model imaging insert in a pelvis phantom

https://hdl.handle.net/2144/16805

Boston University
TREATMENT PLANNING AND DOSIMETRIC VERIFICATION OF CYBERKNIFE PROSTATE SBRT (STEREOTACTIC BODY RADIATION THERAPY) ON AN MR-BASED 3D PROSTATE MODEL IMAGING INSERT IN A PELVIS PHANTOM

by

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Submitted in partial fulfillment of the requirements for the degree of Master of Science 2016
ACKNOWLEDGMENTS

It is the end of my thesis; it is not by my effort to be where I am and to achieve all I have. I take this opportunity to thank God for his unending love, grace, and mercy upon my life. He has enabled me to come that long to seeing this last page of my thesis.

I would like to express my honest gratitude and appreciation to my advisor, Dr. B. Nicolas Bloch, for his assistance, patience, and support through my thesis research. His technical and editorial advice was crucial to the fulfillment of this thesis.

I also would like to extend my special gratefulness to Dr. Hong Xiang for providing an invaluable provision, advice, opinions, and the great work environment at the Department of Oncology at Boston Medical Center during the whole collaborate with this thesis.

I am also very thankful to Dr. Kevin C Thomas, who has worked with me and gave me great guidance through my graduate studies. His patience and assistance helped me solving many crisis situations to finish this thesis research.

Most importantly, none of this would have been possible without the love and patience of my family. My immediate family: my mom, brothers and sisters, to whom this dissertation is dedicated to, have been a constant source of love, concern, support and strength all these years. I would like to express my heart-felt gratitude to them.
Purpose of this study was to validate a novel CyberKnife stereotactic body radiotherapy (SBRT) treatment planning on an MRI-based 3D prostate model insert in an anthropomorphic pelvis phantom using Gafchromic EBT3 films to perform dosimetric measurements. The methodology of this study is based on a pelvis phantom and a physical printed 3D model of the prostate with dominant intra-prostatic-lesion and surrounding organs at risk segmented from a patient MR images. Cyberknife prostate treatment planning was performed to have at least 95% the planning target volumes (PTV: prostate expanded with margins of 5 mm in all directions except 3 mm posteriorly) covered by 3625 cGy (725x5) and a simultaneous dose escalation to 4750 cGy on the dominant intra-prostatic-lesion. Plan dosimetry verification was performed using Gafchromic EBT3 films on a Stereotactic Dose Verification Phantom. First, film calibration was done on Gafchromic EBT3 films exposed to various doses of 0-2500 cGy based on a LINAC (Trilogy) and CyberKnife monthly quality assurance (QA) for machine output calibration. Second, absolute dose measurements were taken by using films within the dose range 0-2250 cGy. Third, Gafchromic EBT3 films were placed in coronal and sagittal planes on the standard “blue phantom” or Stereotactic Dose
Verification Phantom (SDVP) on which one fraction of the treatment plan is delivered for verification measurements. Then, on the prostate-pelvis phantom, a dosimetry inserts were used with films through the DIL region. After the calibration, the accuracy of absolute dose measurements with EBT3 was verified to be $\leq 1\%$ in the dose range of interest (500-1500 cGy). On the SDVP phantom, comparison of films vs. plan for the coronal plane yielded $\geq 99.7\%$ passing rates while for sagittal plane yielded $\geq 95.3\%$ passing rates under the gamma criteria of $\leq 2\%$ in dose and $\leq 2$mm in distance to agreement (DTA). This study demonstrated that it is feasible to plan and deliver a SBRT treatment to prostate with a simultaneous dose escalation to the dominant intra-prostatic lesion.

*Keywords*: prostate, SBRT, CyberKnife, quality assurance, pelvis phantom
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LIST OF ABBREVIATIONS

AS ............................................................................................................... Active Surveillance
CTV ........................................................................................................... Clinical Target Volume
DCE ........................................................................................................... Dynamic contrast enhanced
DHT .......................................................................................................... Dihydrotestosterone
DIL ........................................................................................................... Dominant Intraprostatic lesion
EBRT ....................................................................................................... External beam radiation therapy
GFM .......................................................................................................... Gold Fiducial Markers
GTV .......................................................................................................... Gross Tumor Volume
IGRT ......................................................................................................... Image-guided Radiation Therapy
IMRT .......................................................................................................... Intensity modulated radiation therapy
LINAC ...................................................................................................... Linear Accelerator
MU ........................................................................................................... Monitor Unit
OAR .......................................................................................................... Organs At Risk
PTV .......................................................................................................... Planning Target Volume
PSA .......................................................................................................... Prostate-Specific Antigen
QA .......................................................................................................... Quality Assurance
RT ........................................................................................................... Radiation Therapy
RP .......................................................................................................... Radical Prostatectomy
SBRT ....................................................................................................... Stereotactic Body Radiation Therapy
SDVP ...................................................................................................... Stereotactic Dose Verification Phantom
TURP ...................................................................................................... Transurethral Resection of the Prostate
3D-CRT ............................................ Three-dimensional conformal radiation treatment
INTRODUCTION AND BACKGROUND

1. **Prostate Cancer**

1.1. **Prostate Cancer Cells**

A human body consists of countless living cells. Growth, giving birth to new cells and then die away are the usual order of body cells. The cells reproduce faster in the early phase of human life leading to grow the body. In the adult phase of human life, cells proliferate mostly for replacing dying cells or remedying injuries. When the growth of cells goes beyond the normal rate and becomes uncontrolled, these cells are called cancerous. Cancer has many types, but each of them begins with abnormal proliferation of cells. Cancer cells, unlike normal cells, can grow within other tissues. Excessive growth and growth within other tissues typically characterize cancer cells. When cancer progresses, cancerous cells may infiltrate other parts of the body as well by growing into new tumors instead of normal tissue. The name of this process is metastasis. In this process, free cancer cells are transported in the lymph vessels or bloodstream within our body to distant sites and organs (Vahedifar, 2015).

The prostate gland consists of several different types of cells. The most common generic prostate cell types are epithelial and stromal. Epithelial cells form the prostate glands. The Adenocarcinoma cells are responsible for the most common prostate cancer, which represents more than 99% of prostate cancer. However, there are other types of cancers originating from the prostate such as, small cell carcinomas, transitional cell carcinomas, sarcomas and neuroendocrine tumors (other than small cell carcinomas).
Depending on the cell type and grade, prostate cancers can be aggressive, growing and spreading rapidly, or less aggressive and expanding slowly (Walsh, et al., 2010).

1.2. Prostate Cancer Statistics

American men are found very commonly to have prostate cancer apart from skin cancer. According to the estimation by the American Cancer Society in 2015, there would be 220,800 newly infected prostate cancer cases and 27,540 prostate cancer-related deaths in the United States. Moreover, one man among seven will have the chance of being diagnosed with prostate cancer in his life. The prostate cancer is more prevalent among older men. About 6 cases in 10 are diagnosed in men aged 65 or older with an average age at diagnosis is 66 years while it is very rare in men aged 40 years and younger. Despite prostate cancer is the most popular cancer in American men after lung cancer; prostate cancer will be the cause of death, which is approximately one man out of 38 American men. This means that although many men will be identified with prostate cancer, less than 3% will die of prostate cancer (American Cancer Society’s Statistics Center, 2016).

2. Prostate Cancer Treatment:

2.1. Active Surveillance

Active surveillance (AS) is defined as a management procedure within a chosen group of low-risk prostate cancer patients that includes monitoring of the course of cancer closely.
AS reduces overtreatment, when further clinically relevant prostate cancer is identified, by preventing intervention for inactive tumors and treating mainly (Chung1, et al., 2016). Also, AS has many advantages that involve having a quality of life and regular activities and keeping away the side effects of unnecessary prostate cancer therapy.

2.2. Surgery

Hagan (2014) stated that one of the most standard-of-care treatment choices for prostate cancer is radical prostatectomy (RP) surgery. A number of patients choosing RP has grown during the past decade. During 10 years of the surgery prostate removal, it is approximately 27% and 53% of men will improve a detectable serum PSA level even though the serum prostate-specific antigen (PSA) level should be undetectable after RP (Macdonald, et al., 2004).

2.3. Radiation Therapy for Prostate

Radiation therapy can be divided into two main types, namely, brachytherapy (internal radiation) and external beam and both two are equally capable of curing prostate cancer.

2.3.1. Brachytherapy:

By using advanced computerized treatment planning and image-guided delivery systems, the primary aim of brachytherapy is to deliver high precision and targeted radiotherapy (RT) to the prostate while saving the surrounding organs; such as bladder and bowel, which leads to reducing side effects and possible toxicities. Brachytherapy involves two
different techniques. First, when the prostate tissue has permanently radioactive seeds, low dose rate (LDR) brachytherapy can be used to cure prostate cancer. The second technique is the high-dose rate (HDR), and it is used to treat the prostate cancer when the prostate has the radioactive source for only a short time (Chao, et al., 2015).

2.3.2. External Beam Radiotherapy:
According to (Phak, et al., 2016), external beam radiotherapy (EBRT) is a conventional treatment modality alternative for localized or locally advanced prostate cancer. The following are the types of EBRT:

2.3.2.1 Three-dimensional Conformal Radiation Treatment:
In the 3-dimensional conformal radiotherapy (3D-CRT), the radiation beam is formed to cover the 3-dimensional anatomic configuration of the prostate, involving the seminal vesicles. 3D-CRT provides more enhanced definite delivery of therapy to the target organ. Also, during the recent decade, the effectiveness of 3D-CRT has improved and has substituted conventional EBRT in the treatment of early-stage prostate cancer (Aral, et al. 2015).

2.3.2.2. Intensity Modulated Radiation Therapy:
One of the modern techniques of RT that applies intensity-modulated beams is intensity-modulated radiotherapy (IMRT). Beams can be delivered from any individual beam direction and any different source location for giving multiple intensity levels.
Furthermore, IMRT can avoid the dose limiting of adjacent organs at risk (OAR) and can produce developed tumor control (Bauman, et al., 2012). Comparing to 3D-CRT, IMRT may reach higher RT doses with no addition or even with a lower dose to critical normal structures, such as bowel and bladder (Bruner, et al., 2015).

2.3.2.3. Stereotactic Body Radiation Therapy (SBRT) on CyberKnife:

The practical experience of SBRT in prostate cancer is growing and quickly developing. However, the inadequate number of patients who treated by SBRT throughout the world and the comparatively insufficient follow-up reported in most SBRT experiences causes the SBRT to be in its infancy of being a therapeutic alternative (Arcangeli, et al., 2012). SBRT is a noninvasive highly conformal radiation treatment that could deliver high conformal doses in 3 to 5 fractions of very large doses which can lead to decrease the dose to the rectum, for example. Reducing the dose to the surrounding important normal structures during giving large doses to the target volume is the primary objective of the hypofractionated prostate SBRT. Besides that, according to Arcangeli (2015) in different critical SBRT review, "Minimal clinical target volume (CTV) to planning target volume (PTV) margins, and a daily patient repositioning with correction for the inter- and intra-fraction organ movements are mandatory to improve the treatment accuracy". Additionally, many devices can perform SBRT and with different concentrations. Examples of these devices are CyberKnife®, Varian Trilogy™, TomoTherapy Hi-Art® System, and VERO®.
Radiosurgery has developed as an efficient method for radiation over the past several decades, and its level of precision undoubtedly characterizes it. CyberKnife® (Accuray, Inc., Sunnyvale, CA, USA) remains one of few treatment systems that are being capable of performing a precise efficiency of radiosurgery to tumors throughout the body such as prostate cancers (Hara, et al., 2014). One of the top advantages of CyberKnife in prostate cancer treatment is using a smaller margin around the target and, consequently, the less healthy tissue gets high doses of radiation according to (Higginson, et al., 2010). Stanford provided with the first research on the application of SBRT through CyberKnife to cure prostate cancer, which confirmed the advantage of SBRT treatment planning to the target, bladder, and rectum in comparison to IMRT as identical modalities were tested through both techniques (King, et al., 2003). Moreover, the CyberKnife can identify patient motion and track the target consistently at the time of treatment, and this feature makes the prostate treatment itself more reliable. Additionally, CyberKnife SBRT uses gold fiducial markers (GFM), which are placed within the gland for monitoring real-time organ position through a set of two orthogonal x-ray imaging devices. This intrafractional tracking helps to decrease the amount of the healthy tissue that surrounds the planning target volume.

3. **Role of MRI for Prostate Cancer Treatment**
3.1. **Role of MRI in Guiding Prostate Biopsy**

Prostate cancer diagnosis is fundamentally based on prostate-specific antigen (PSA) screening and transrectal ultrasound (TRUS)-guided prostate biopsy. However, some tumors in the anterior prostate region can be missed because the routine TRUS biopsy is non-targeted and directed toward the peripheral gland (Ahmed, et al. 2009). In this case, another alternative test is needed to examine patients who have a negative initial biopsy while their PSA is growing. Since MRI is the most precise imaging modality for localization of prostate cancer, MRI-guided prostate biopsy gives the chance of more accurate targeting, and it is performed at the time of biopsy. (Bonekamp, et al., 2011). MRI-guided prostate biopsy contains either using MRI individually or the fusion technology between ultrasound and MRI. Furthermore, a combination of ultrasound-guided and MRI-guided prostate biopsy has been shown to be preferred to standard TRUS biopsy in prostate cancer detection (Pinto, at al., 2011).

3.2. **Role of Prostate MRI in Treatment Planning**

By using either 1.5-T or 3-T magnetic field strengths, prostate MRI exams can be performed with using endorectal and pelvic phased-array coils to improve the signal-to-noise ratio. Also, Multi-parametric MRI is the current source method that provides more detailed information about prostate cancer after a biopsy-proven diagnosis (Turkbey, et al. 2011). MRI maps the exact location and boundaries of the dominant intraprostatic lesion (DIL) with approximately 80% sensitivity. With the precise localization of DIL, it
is possible to detect the highly risky zones of extracapsular extension more accurately (Gaya et al. 2015).

3.2.1. T2-Weighted Imaging:

T2-weighted imaging is applied to define the zonal anatomy and to distinguish the stage of a prostate cancer with excellent details because of the T2 high spatial resolution, superior contrast resolution, multi-planar ability, and large FOV (Claus, et al., 2004). 30% Percent of prostate tumors take place in the central gland, which involves the central zone and the transition zone. However, MRI has the limitation in the detection of tumor in the central gland, which is heterogeneously low in signal intensity on T2-weighted imaging (Choi, et al., 2007)

3.2.2. Dynamic Contrast-Enhanced MRI:

Contrast enhancement in cancerous prostatic tissue is greater than in healthy tissue because of tumor angiogenesis and raised number and permeability of vessels. Dynamic Contrast-Enhanced MRI (DCE-MRI) is one of significant MRI sequences that helps to detect and quantify tumor angiogenesis and provides a direct depiction of tumor vascularity. A rapid set of gradient-echo T1-weighted images is taken directly before, during, and after giving the gadolinium contrast agent. Gadolinium contrast agent reduces the T1 relaxation time of water and provides high signal intensity on T1-weighted imaging (Murphy, et al., 2013). Additionally, DCE-MRI is a quick MRI sequence that examines the entire prostate gland in a few seconds and might prevent using the
endorectal coil (Verma, et al., 2012). DCE-MRI also gives detailed information regarding diagnosis and response to treatment. It is a helpful prognostic marker and indicator of tumor aggressiveness because the degree of angiogenesis correlates with pathologic staging of prostate cancer (Ocak, et al., 2007)

4. **Aim of Study**

To perform dosimetric measurement using Gafchomic EBT3 films for validation of a novel CyberKnife SBRT treatment using a MRI-based prostate model insert in an anthropomorphic pelvis phantom.
1. **CyberKnife Robotic Delivery System**

The CyberKnife System is a robotic, which provides a distinct type of Stereotactic Body Radiation Therapy (SBRT) likewise called radiosurgery (Fig. 1). CyberKnife is the only radiation treatment innovation that follows tumor motion and immediately improves the purpose of the treatment beam when motion is spotted. The CyberKnife Radiosurgery System produces radiation with sub-millimeter precision through using consistent image guidance and robotic movement. Accordingly, the radiation is concentrated to where it counts most, the prostate, and the radiation dosage becomes less steeply around the healthy tissue that surrounds the prostate. The FDA offered clearance for the CyberKnife System in 2001 and over 5,000 males have been treated for the prostate cancer with CyberKnife radiosurgery around the world. (Accuray, 2012).

![Image of CyberKnife Robotic Delivery System](image-url)

**Figure 1: CyberKnife Robotic Delivery System. (P.S. This image was captured by the author during the procedure)**
There are four primary advantages that differentiate the CyberKnife System from other prostate cancer treatments. Initially, the CyberKnife System is a linear accelerator (LINAC) installed to a robotic arm, which is particularly developed to provide stereotactic radiation from numerous various angles (Fig. 2). Second, unlike any other radiation treatment, the CyberKnife System continuously tracks and instantly remedies for the motion of the prostate in actual time. Third, a whole CyberKnife ® treatment plan can be delivered in 4 to 5 sessions. Each treatment session is typically finished in one hour or less. Fourth, the CyberKnife treatment process is entirely non-invasive (Accuray, 2012).

Figure 2: CyberKnife's beam directions: it can provide beams from numerous unique angles around the patient as shown in this image from our novel CyberKnife SBRT treatment that we delivered to anthropomorphic pelvis phantom.
2. Treatment Planning for Early Stage Prostate Cancer

The intent of Treatment Planning in Radiation Oncology is to evaluate medical, physical, and technical aspects of treatment preparation and provide a contemporary variation of the treatment planning procedure. Treatment planning for SBRT typically follows the same process and procedures as IMRT and three-dimensional conformal treatment strategies. Similar to either treatment planning approaches, SBRT preparing identifies the field size(s), gantry angles and other beam characteristics to attain the wanted radiation dosage distribution. SBRT strategies are highly personalized to the target volume(s) and might be geometrically more precise than conventionally fractionated external beam treatment strategies (American Society for Radiation Oncology, 2014).

2.1. CT/ MR scans

CT was the main image platform for treatment planning on the anthropomorphic pelvis phantom in this study. The simulation was carried out in the head-first-supine (HFS) treatment position with the fiducial markers inside the prostate. Axial cuts of 1.5 mm were obtained throughout the hips and prostate from the top of the iliac crests par excellence to the perineum inferiorly.

If not clinically contraindicated, MRI images were acquired previous to the implantation of transponders to figure out the physiological borders of the prostate and they will be fused to the treatment preparation CT. MRI was carried out utilizing a 1.5 T MRI scanner Philips Achieva. The prostate patient imaging involved of T2-weighted (coronal, axial views) images and BLISS (axial view) images for the diagnostics of the
prostate (Philips Healthcare; matrix 200 X 200; field of view, 200 X 200mm; slice thickness 3mm, XL Torso coil positioned over a flat board for immobilization purposes. The images covered the entire penile bulb and seminal vesicle. All GFM show up in T2-images as small black dots and their location was verified.

2.2. **CT/ MR Registrations**

We used the RT image processing software application with a high-quality screen (MIM 5.4, MIM Software Inc., Cleveland, OH, USA) for the co-registration of the CT and T2 images. Overall, the registration of planning CT and the MR scans are done in MIM software using a point-based registration technique that utilizes the well-identified 4 fiducials in both CT and the MR (BLISS) scan. Based on the midpoint of GFM locations, both CT and the T2 images were lined up together. The margins of the prostate capsule were examined in 3 airplanes, to guarantee exact anatomical superimposition. The T2 series contains ideal exposure of prostate and urethra; the T1 series assists identify the fiducial markers, which produce a small signal in the T2-weighed images. A Little adjustment of co-registration was applied if the margins of the prostate in the CT and T2 images did not overlap because the possible seed displacement. The rotation angles of co-registration, along with the movement of the midpoint of seeds in the CT and T2 images were determined. However, during treatment delivery on CyberKnife, DRRs generated from CT image were used to assess the fiducial markers alignment between planned prostate position and the live treatment position in the anthropomorphic pelvis phantom (Fig.3).
2.3. *Treatment Planning/Target Volumes*

a. The Gross Tumor Volume (GTV): it was specified by the physician as all understood condition as defined by the preparation CT and MR (when readily available) collectively with scientific aspects. The GTV for this study was the prostate only.

b. The clinical target volume (CTV): it was similar to the GTV and included the prostate without the seminal vesicles as defined by non-contrast axial CT scan.

c. The planning target volume (PTV): it was specified as the CTV with additionally a 3 mm margin in the posterior side and 5 mm in all other dimensions.

2.4. *Contouring*

The regular tissue volume that has to be contoured was included the bladder (which was contoured from its base to the dome), rectum, bilateral thigh (which was covered until the
ischial tuberosity's level), influential blisters, penile bulb, skin, and urethra. The typical tissues were contoured and thought about as solid organs instead of contouring the bladder and rectal walls.

The anus was contoured from the rectum for a length of 15cm or to the rectosigmoid flexure. This commonly is placed below the base of the sacroiliac joints. The tissue within the skin and external all other vital regular structures and PTVs were indicated as indefinite tissue (Fig.4).

![Image of normal tissue contouring](image)

**Figure 4: Pelvic normal tissue contouring: Axial (left), coronal (middle), and sagittal (right) slices.**

2.5. **Plan Objectives/Constraints**

Inverse planning utilizing the CyberKnife ® MultiPlan treatment planning system will be used. The treatment plan used for each patient will be based on an analysis of the volumetric dose consisting of dose-volume histogram chart (DVH) analyzes (Fig.5) of the PTV and critical regular structures. Any beams going into through a hip prosthesis on their way to the planning target volume will be shut off.
For this study, we followed the treatment planning guidelines of RTOG-0938 to give 725x5 (3625 cGy) to the prostate PTV, and complied with all the dose volume constraints for organs at risk (OARs), including rectum, bladder, penile bulb, urethra and femur heads. In addition, we placed a simultaneous dose boost to 950x5 (4750 cGy) to the dominant intra-prostatic lesion.

![Dose-volume histogram (DVH) comparison for prostate.](image)

**Figure 5: Dose-volume histogram (DVH) comparison for prostate.**

2.6. *Plan Optimizations*

In this research study, the plan generation was done by a method called sequential optimization. This approach flexibly makes it possible for resolving preparation problems and optimizes numerous confliction goals, which might influence clinicians' choices. The
sequential optimization separately attends to every objective in a predefined order. In many radiosurgery treatments, the possibility of the option is retained after each step by using a particular user-defined value in order to enhance the preparing quality at the next action. In this experiment, the application of CyberKnife sequential technique was attained on the same day of the target contouring. The relaxation specification was only used to the last action in the sequential chain, and this significantly helped planners to avoid major enhancements in plan quality after the 2nd action. According to previous scientific studies, the sequential optimization technique has the right characteristics for scripting. Scripts are known as plan templates, which efficiently reduce the irregularity of various treatment preparation strategies and help to improve the changes amongst comparable plans. The sequential optimization was run to satisfy the RTOG 0938 dose constraints requirements and to accomplish the following scientific goals: First, to cover at least 95% of PTV with 100% of the prescription dose (3625 cGy). Second, to meet all OAR (organ-at-risk) dose-volume constraints, including: a). Urethra: maximum dose below 3878 cGy (107% prescription dose); b). Rectum: volume receiving 3806 cGy below 1 cc, volume receiving 3440 cGy below 3 cc, volume receiving 90%, 80% and 50% of the prescription dose below 10%, 20% and 50%; c). Bladder: volume receiving 3806 cGy below 1 cc, volume receiving 90% and 50% of the prescription dose below 10% and 50%; d). Penile Bulb: maximum dose below 3625 cGy and volume receiving ≥ 20 cGy below 3 cc. e). Femur heads (both left and right): volume receiving 20 cGy below 10 cc.  f). Skin: no area of skin receiving dose above 3000 cGy. Finally, to get a dosage distribution extremely conformal around the target (conformity index below 1.2 or below
1-2-1.5), without any hot spots of (over 107% beyond prescription dose) in the overlap normal OAR tissue (Fig.6). After an optimized plan of acceptable quality was achieved, the beam and time decrease tools were used to finalize the plan to reach a deliverable that is both dosimetrically optimized and also delivery efficient.
Figure 6: Treatment planning for prostate and critical organs: axial (top), coronal (middle), and sagittal (bottom).
3. Film QA for Plan Verification

3.1. **Blue Phantom (Standard Imaging)**

The Stereotactic Dose Verification Phantom provides dosage measurements for commissioning treatment systems, such as Accuray CyberKnife®, and certain plan dosage confirmation. With simply one phantom, usage film, ion chambers and the distinct SRS Dosimetric QA Slab to carry out quick and precise system examination.

The size of the conventional phantom is 20 x 20 x 10 cm, comprised of 2 4 cm top and bottom build-up slabs, and 2 identical 2 cm test inserts in the center. Optional inserts involve the SRS Dosimetric QA Slab and Stereotactic Dose Verification Phantom (SDVP) Heterogeneity insert. Stiff positioning posts make sure phantom setups are exactly repositioned, and thumb or flat-head screws protect the phantom together for repeatable outcomes. The Stereotactic Dose Verification Phantom is built of Blue Water material and extra pieces are readily available in lots of densities for increased accumulation.

One of the blue phantom advantages is the having the laser positioning lines, which are offered to place precisely the phantom for both computed tomography scans and also for planning treatment. GFM are inserted entirely inside the phantom for extra orientation and locating precision. Distance ranges within the CT scanning and TPS can be verified with confidence.

Five water similar Blue Water pieces provide film to be placed 2 mm separated for dosage profile analyses of tiny SRS analyzes (Fig.7). A hole in each slab sites a 2.5 x 2.5-inch film in the middle. (Standard Imaging Inc, 2014).
3.2. **Gafchromic EBT3 Films**

The radiochromic film (Ashland Incorporated, USA) has ended up being a crucial tool to confirm dosage distributions in extremely conformal radiation therapy such as SBRT. Recently, a brand-new generation of these films, EBT3, has appeared. EBT3 has the same structure and density of the delicate layer of the previous EBT2 films. However, its symmetric layer setup permits the user to eliminate side orientation dependence, which is reported for EBT2 films. The most crucial EBT3 qualities have been investigated, such as reaction at high-dose levels, sensitivity to scanner orientation and post-irradiation
pigmentation, energy and dosage rate dependence, and orientation reliance on film side (Borca, et al., 2012).

3.3. *FilmQA Pro software (Analysis tool)*

FilmQA Pro 3.0 software is an advanced, quantitative analysis tool specifically created to streamline and enhance the intensity-modulated radiation treatment quality control (IMRT QA). Our software is also reliable for the QA of SRS, SBRT and VMAT procedures. It enables you to scan or open pictures of exposed film and compute the optimized dosage maps.

FilmQA Pro 3.0 software application utilizes exclusive multi-channel dosimetry, which eliminates or alleviates film and scanner artifacts by discovering whether errors are being made during scanning. In addition, the current version now enables one-scan analysis, integrating calibration and strategy confirmation in a single scan. This is a brand-new method needing just the patient film, a reference spot and an unexposed spot. This procedure removes mistake sources such as interscan irregularity, allowing you to lower errors to below 1 percent (Ashland, 2016).

3.4. *Monthly accelerator QA for CyberKnife and Trilogy*

The dosage output, energy constancy, and the consistency of the beam shape and beam proportion ought to be inspected month-to-month and compared to values gotten throughout commissioning. Typically, the biggest collimator (60 mm) was used for this
check. Simultaneous reference dosage measurement utilizing a PTW Farmer chamber type 30013 was carried out for all film irradiations. This ion chamber is a water resistant requirement chamber for outright photon and electron dosimetry with therapy dosimeters to be utilized in water or solid-state product (PTW-Freiburg, Germany). DQA test delivery was done on the basic CyberKnife BallCube2 Phantom (Accuray). For Trilogy QA, the distance from the source to the ion chamber was 100 cm (99 cm to the ion chamber’s layer surface) with (10x10 cm2) beam field. We delivered 3 different photon energies and read the results through an advanced therapy dosimetry machine regarding the measurement of the Trilogy output. For CyberKnife QA, the distance from the source to the ion chamber was 80 cm (and exactly 79 cm to the ion chamber’s layer surface) as shown in (Fig.8). The distance was taken after we used the water cup technique to make the beam vertically straight by spotting the reflection point of the beam light through the manual controller. We gave 200 desired MU three times to take the measurement of the CyberKnife output. We put 2 layers 5cm depth for each at the bottom of the ion chamber’s layer for back scattering and 2 more layers above the ion chamber’s layer too. Measuring the temperature (by two general purpose lab thermometers) and pressure (from Logan Airport website) was necessary for each QA measurement at the moment of doing the procedure.
Figure 8: Distance measurement tool for CyberKnife: measuring the distance manually between the source of to the ion chamber’s layer. (P.S. This image was captured during the procedure).

3.5. Film Dose Calibration

Radiochromic film measurement is the current approach of option both for regular QA as well as certain validation of patient treatment for the CyberKnife system. The EBT3 film can decrease the uncertainties in film-based quality assurance, which were used for this purpose in this study (Fig.9). In this study, we did two film dose calibrations on both Trilogy and CyberKnife by following the same technique of the monthly QA with the same distance to the films. However, we added only 1.5 cm layer above the film with 2 more layers at the bottom for Trilogy and 3 layers (5cm, 5cm, and 2cm) for the CyberKnife.
3.6. **Absolute Dose Measurements Using Films**

To rapidly perform film calibration and prevent manual robot setup, dedicated treatment strategies with various prescription doses, each with a single vertical beam 60 mm (the largest collimator) were used for this check. Absolute Dose Measurements was done also on the very same basic CyberKnife BallCube2 Phantom (Accuray) with specifically cut radiochromic EBT3 films (Ashland). To specify the film calibration curve, we utilized 6 to 8 dosage levels (variety 0-20 Gy). All films were positioned at 1.5 cm depth ($D_{\text{Max}}$) (See Fig.10). To specify the film calibration curve, we made use of six to 8 dosage levels (variety 0-20 Gy).
Figure 10: CyberKnife and Trilogy film calibration and absolute dose measurements. The film was placed at $D_{\text{Max}}$ 1.5cm at source axis distance of 80cm. (It was drawn by the author)

3.7. Measurement of Delivered Dose and Comparison with Planned Dose

Gafchromic EBT3 films were placed in coronal and sagittal planes through DIL region for the specific QA plan on the blue phantom (SDVP). The dose was delivered based on the novel CyberKnife SBRT treatment of the prostate, which is different than the standard care plan. The following figures show the specific QA plan results for coronal and sagittal planes with their DVH (Fig.11 and 12).
Figure 11: Specific QA plan (Coronal) with DVH

Figure 12: Specific QA Plan (Sagittal) with DVH
RESULTS AND DISCUSSION

1. Film Dose Calibration for Trilogy

Roughly after 24 hours of exposing the EBT3 films for Trilogy calibration, we did a completed calibration for EBT3 films by FilmQA Pro for various known doses (0, 250, 500, 750, 1000, 1250, 1500, 2000, 2500 cGy), we got tabulated and graphical calibration data for each color channel along with the color reciprocal linear vs. dose fitting function and coefficients relating measured film response to each dose (Fig.13).

Figure 13: Calibration curve generated in FilmQA Pro: it shows the dose-response data for each color channel for Trilogy film dose calibration
In Table 1, it shows also a calibration table for the same various doses (0-2500 cGy) that we used for the film dose calibration method with a statistics table that was generated for the chosen region of interest in the middle of each EBT3 film.

**Table 1: Response percentage of calibration films on Trilogy was exported by FilmQA Pro software that show the reponse for each color: Red, Green, and Blue.**

<table>
<thead>
<tr>
<th>Absorbed dose (cGy)</th>
<th>Red (%)</th>
<th>Green (%)</th>
<th>Blue (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2500.0</td>
<td>7.7</td>
<td>11.7</td>
<td>15.5</td>
</tr>
<tr>
<td>2000.0</td>
<td>9.2</td>
<td>14.3</td>
<td>17.5</td>
</tr>
<tr>
<td>1500.0</td>
<td>12.4</td>
<td>19.3</td>
<td>20.4</td>
</tr>
<tr>
<td>1250.0</td>
<td>14.3</td>
<td>22.0</td>
<td>21.9</td>
</tr>
<tr>
<td>1000.0</td>
<td>16.3</td>
<td>25.3</td>
<td>23.7</td>
</tr>
<tr>
<td>750.0</td>
<td>20.6</td>
<td>26.9</td>
<td>25.9</td>
</tr>
<tr>
<td>500.0</td>
<td>26.6</td>
<td>36.0</td>
<td>28.8</td>
</tr>
<tr>
<td>250.0</td>
<td>37.2</td>
<td>45.7</td>
<td>32.5</td>
</tr>
<tr>
<td>0.0</td>
<td>64.6</td>
<td>62.7</td>
<td>37.8</td>
</tr>
</tbody>
</table>

2. Dose map (single scan) for CyberKnife

After we had the statistics table and calibration curve for the CyberKnife film dose calibration and after the same amount of time we had for exposing the EBT3 calibration films, we generated a dose map (single scan) in FilmQA Pro based on the absolute dose films which are (0, 100, 300, 600, 900, 1200 cGy) followed by a certain statistics (average and standard deviation) that was taken for each color: Red, Green and Blue (see Table.2).
**Table 2: Measurement CyberKnife Dose:** it shows that in the high dose region (700cGy – 1200 cGy) the dose measurement accuracy is at ± 1.0% (P.S. Roughly 725 cGy is the prescription dose for prostate and 950 cGy for the lesion).

<table>
<thead>
<tr>
<th>Known Dose (cGy)</th>
<th>Red</th>
<th>SD</th>
<th>Green</th>
<th>SD</th>
<th>Blue</th>
<th>SD</th>
<th>Average</th>
<th>SD</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>120.2</td>
<td>0.9</td>
<td>127.5</td>
<td>1.5</td>
<td>123.2</td>
<td>1.1</td>
<td>123.6</td>
<td>1.2</td>
<td>23.6%</td>
</tr>
<tr>
<td>300</td>
<td>349.6</td>
<td>4.6</td>
<td>348.7</td>
<td>4.2</td>
<td>349.2</td>
<td>4.2</td>
<td>349.2</td>
<td>4.3</td>
<td>16.4%</td>
</tr>
<tr>
<td>600</td>
<td>593.4</td>
<td>8.1</td>
<td>594.2</td>
<td>7.7</td>
<td>593.8</td>
<td>7.6</td>
<td>593.8</td>
<td>7.8</td>
<td>-1.0%</td>
</tr>
<tr>
<td>900</td>
<td>918.4</td>
<td>16.7</td>
<td>900.3</td>
<td>13.1</td>
<td>907.6</td>
<td>14</td>
<td>908.8</td>
<td>14.6</td>
<td>1.0%</td>
</tr>
<tr>
<td>1200</td>
<td>1200.4</td>
<td>23.5</td>
<td>1185.4</td>
<td>20.2</td>
<td>1190.5</td>
<td>20.6</td>
<td>1192.1</td>
<td>21.4</td>
<td>-0.7%</td>
</tr>
</tbody>
</table>

3. Film dose vs. plan dose (Blue phantom)

The use of the blue phantom makes the overlay of Treatment Plans accurate as compared to overlays on other phantoms.

3.1. **Coronal Plane**

3.1.1 Coronal Isodose:

After we had adjusted the rotational and translational position of the measurements relative to the plan, we generated the isodose maps for the coronal plane that shows an overlay of the isodose lines between the treatment plan and dose map and to show a clear visible tool to decide if the two plans are precisely aligned (Fig.14).
3.1.2. Coronal Profile:

Regarding evaluating the dosimetry films of the blue phantom, we applied appropriate calibration function to convert the resulting image into dose space by the quantitative analysis tool of FilmQA Pro. Figure 15 shows both vertical and horizontal dose profiles for the coronal plane, which are necessary illustration tools that used to represent the measured and computed dose along a line and helpful for assessing areas with high and low dose gradients, respectively with a 10 pixels wide for the treatment plan (thick line) overlaid with the measured profile from the dose map (thin line).
3.1.3. Coronal Gamma Criteria:

After the calibration, the accuracy of absolute dose measurements with EBT3 was verified to be $\leq$ in the dose range of interest (5-15 Gy). On the SDVP (blue) phantom, comparison of films vs. plan for the coronal plane yielded $\geq 99.7\%$ passing rates under the gamma criteria of $\leq 2\%$ in dose and $\leq 2\text{mm}$ in distance to agreement (DTA) for all pixels which is typically considered for a perfect comparison and one of the most significant parts a leading physicist should do in fixing up CyberKnife QA plan.

**Figure 15: Coronal Dose profiles:** (Vertical, left) and (Horizontal, right).
3.2.  *Sagittal Plane*

3.2.1. Sagittal Isodose:

We generated the isodose maps for sagittal plane that shows an overlay of the isodose lines between the treatment plan and dose map after we adjusted the rotational and translational position of the measurements relative to the plan (Fig.16)

![Figure 16: Sagittal isodose map: Delivered Dose (thin lines) vs. Planned Dose (thick lines)](image)

3.2.2. Sagittal Profile:

Regarding evaluating the dosimetry films of the blue phantom, we applied appropriate calibration function to convert the resulting image into dose space by the quantitative
analysis tool of FilmQA Pro. Figure 17 shows both vertical and horizontal dose profiles for the sagittal plane respectively with a 10 pixels wide for the treatment plan (thick line) overlaid with the measured profile from the dose map (thin line).

**Figure 17: Sagittal dose profiles:** (Vertical, left) and (Horizontal, right).

3.3.3. Sagittal Gamma Criteria:
After the calibration, the accuracy of absolute dose measurements with EBT3 was verified to be $\leq$ in the dose range of interest (5-15 Gy). On the SDVP (blue) phantom, gamma index criteria of comparison of films vs. plan for the sagittal plane are $\leq 2\%$ dose difference and $\leq 2\text{mm} \ DTA$ for all pixels with a pass-rate above 95.3.0\%.
3.3. **Further Work**

After completing the first major step of validating the novel plan, a limitation to this study was not having done the other major step and the most realistic measurement which involves a special dosimetry insert because currently it is not optimal and not entirely designed which needs more improvement and it would require further investigation.
CONCLUSION

In this study, the EBT3 film is shown to provide an accurate method for verifying the patient specific SBRT plan dose delivery in comparison to treatment planning. Besides that, robotic SBRT with simultaneous integrated dose escalation to the dominant intra-prostatic lesion was designed and planned under currently accepted OAR dose-volume constraints and can be accurately delivered. Such dose escalation needs more precise MR-based target delineation and reliable prostate tracking. Potentially, this additional refined design of SBRT may assist to decrease the local recurrence related to under-dose to the sub-volume including a dominant intra-prostatic lesion.
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