

A QA Analysis of a Contrast Localized Linac-Based Technique for Hypo-Fractionated Partial Breast Radiotherapy

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ABSTRACT

AIM: Partial-Breast Radiotherapy following lumpectomy is an effective treatment for women with early stage breast cancer, with the technique of either brachytherapy or external beam treatment broadly being implemented in clinics. However, the current popular brachytherapy treatments are still limited to treating somewhat regularly shaped targets, with an additional limitation defined by the skin and rib radiation tolerances. A linac-based method that utilizes frame fixation, a contrast enhanced cavity/fiducial location approach, image localization guided treatment techniques, and special immobilization techniques was demonstrated to be accurate method to deliver radiotherapy to a site in the breast, a task that has challenged clinicians for decades.

METHODS: A prospective study of ten patients (six Left Breasts and four Right Breasts) had placed three internal gold-seed markers inside the surgical bed post-surgery (provided by CIVCO Corporation)/prior to planning and six external markers (made by Beckley). (Two sets of three fiducials) were placed in an axial plane above and below the surgery site) Prior to the Computerized Tomography (CT) scan performed for planning, contrast is introduced into the cavity to allow localization of the breast cavity during planning. A simulation was performed in a large-bore 3rd generation scanner with a patient's breast affixed using an Electa Body frame to improve localization and to control breathing variances. The planning was performed on an Eclipse treatment planning system, and the treatment was performed using a Varian CD Linear accelerator.

RESULTS: Small volumes field sizes, sometimes as small as 4×4 , and Mutli-Leaf Collimators (MLCs) were required to deliver patient dose verification. This process was performed prior to treatment using diodes (including planar isodose to evaluate the MLCs required to deliver compared to the plan verification when using Map Check. (Diode Array Radiation Dosimeter made by Sun Nuclear Corporation)

CONCLUSIONS: A Quality Analysis (QA) was performed. Five to seven fields were used, indicating good statistical and clinical agreement in these 10 cases. All fields were imaged daily prior to treatment using 2 Dimensional (2D) MV portal imaging and correlated and evaluated by the Radiation Oncologist using the Acculoc patient positioning system.

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Key words: Breast Cancer; Partial; Hypo-Fractionated; High Dose Rate; Brachytherapy; Radiotherapy; Quality Assurance; Megavoltage; Computerized Tomography; Magnetic Resonance; Planned Target Volume; Clinical Target Volume; Gross Target Volume; Stereotactic Body Frame; 3 Dimensional; 2 Dimensional; Defined Field of View; Sterio-Tactic; Intensity Modulated Radiation Therapy; Digitally Reconstructed Radiographs.

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INTRODUCTION

The Center for Disease Control (CDC) reports that "breast cancer is the most common form of cancer in women"^[1]. Breast cancer is the number one cause of death in Hispanic women and is the second most common cause of death in other ethnic populations of women. In 2006, it was reported that 191,419 American women were

diagnosed with breast cancer, with 40,820 deaths. It is thought that one in eight women will eventually develop breast cancer.

Accelerator-based partial breast irradiation, either using High-Dose Rate (HDR) brachytherapy or external beam radiotherapy, continues to gain popularity as a means of treatment for appropriate breast cancer patients^[2]. There is a growing interest by clinicians to implementing partial breast treatment techniques with such irradiation.

Hypo-fractionated dose regimens using a linac-based system are performed in departments that do not have an HDR unit. In a recent 2009 American Society of Oncology (ASCO) meeting, Nick Mulcahy (Moderator for ASCO) stated that “even though partial breast irradiation remains in the investigational phase, it was found not to diminish survival”^[3].

Additionally, concerns of a changing health care environment suggest that future capital budget requests for technological upgrades in radiotherapy equipment will be constrained. Upgrading to new equipment or purchasing new capital equipment to perform radiotherapy procedures can be costly, so considerations of retrofitting existing equipment to perform these procedures could be a cost-saving alternative. It has also been suggested that the software and hardware to perform these procedures would need to be evaluated prior to purchase to determine if this equipment meets the recommendations of the manufacturer, including mechanical/imaging specifications. It is for these reasons we began to develop a simple, low-cost method of delivering hypo-fractionated linac-based treatment to deliver radiation to the partial breast (for early stage disease) and began evaluating the physical results of such treatment.

Furthermore, there have been significant advances in the localization for breast cancer patients and the measurements of the positioning of the lumpectomy cavity that enable targeting a radiotherapy hypo-fractionated regimen with a delivery of a high degree of accuracy. In these recent studies the use of either breast surface markers or surgical clips as surrogates for the cavity were reported to provide improved localization in most patients compared to using bony landmarks alone as image guidance for improved accuracy of daily radiation treatment^[4]. Historically, the breast has always been one of the most challenging sites for implementing radiotherapy due to the irregularity of the shape of the structure and to the mobility of the breast itself.

Planning can also be a challenge when determining the target in external hypofractionated partial breast irradiation, especially when determining the Planning Target Volume (PTV). Traditionally, CT was used to determine the PTV^[5]. Studies have indicated that introduction of a contrast media can improve visualization of the surgical cavity during planning. A number of immobilization devices have been used to duplicate the breast position for daily treatment, with some improvement in the reproducibility of the breast position for daily radiation treatment. The following is a schema of this prospective phase II trial to access the feasibility and clinical results of this study of employing 3Dimensional (3D)-Conformal techniques and Magnetic resonance Imaging (MRI)/Computerized Tomography (CT) fusion for Accelerated Partial Breast Radiotherapy of Breast cancer.

MATERIALS AND METHODS

Prior to the CT planning session, candidates for this prospective phase II trial hypo-fractionated partial breast irradiation had three gold fiducials (1.2 by 3 mm found to be more visible on Megavoltage (MV) imaging than Platinum with similar cost) by placed into surgical bed

post-surgery (1-2 days); in addition, six markers were placed at the time of simulation externally on the skin defining two axial planes, one superior and the other inferior to the surgery site.

Contrast media for localization was placed in the cavity during the time of fiducial placement. Using similar technique to Vicini^[6]. The patient was positioned supine in a stereotactic Electa Stereotactic Body Frame (SBR) body frame utilizing a diaphragmatic plunger to reduce/control breathing variances and, to some degree, immobilize the breast itself. A large bore Phillips-Model AcQSim CT 3rd generation scanner was used for all patients. The technical settings for the CT for simulation were Defined Field of View (DFOV) 550 mm, 130Kilovoltage (kV), 250Milliamps (mA), scan slice thickness/spacing 2-3 mm (similar protocol for partial breast planning for HDR), and Computerized Tomography Dose Index (CTDI) Vol: 1394 mGy. An Electa frame is used to immobilize the breast of interest in addition to vac-lock system for treatment planning CT. A system of six gold seeds (three in each plane) above/below the tumor bed of the area centered for treatment. There were a total of nine seeds used for CT per patient^[7] during the simulation; four points were marked on the patient's skin surface using the laser on the SBR frame. An amorphous phantom is used to illustrate the treatment process in this paper. The planning CT was then sent to a Varian Eclipse Planning system software version 6.5 with critical structures/target structures outlined, including the breasts themselves, lungs, heart, cavity, Clinical Target Volume (CTV), and PTV. The CTV was generated by expanding the expansion cavity by 15 mm in all directions, with the CTV not to be closer than 7 mm to the skin surface.

Although most of these cases utilized primary CT for contouring, CT/ T1 weighted MRI fusion post-surgery in treatment position could improve the contouring according to our clinical medical staff. The treatment planning goals were to prescribe 30 Gy in 6 Gy fractions for five consecutive working days to the 95% isotope line of the PTV using five to seven high-energy photon non-coplanar and non-opposed MLC-shaped beams. The PTV included a margin of 3 mm around the CTV utilizing daily stereotactic positioning/targeting of the breast to compensate for set-up variability, interfractional motion, mobility of breast tissue, and respiratory excursion⁷ The dose calculation used tissue inhomogeneity corrections. The dose limitations include those of normal breast, heart, and lung. The stated dose limitations are as follows:

1. Uninvolved normal breast. Less than 50% of the whole breast should receive greater than 50% of the dose and 25% of the whole breast should receive the prescribed dose.
2. Less than 10% of the lung can receive 30% of the prescribed dose.
3. Contra-lateral breast should receive less than 3% of the prescribed dose.
4. Contra-lateral lung: Less than 10% of the lung should receive 5% of the prescribed dose.
5. Heart: less than 5% of the heart should receive 5% of the prescribed dose.

Treatment including image-guided protocol was performed by a Varian 2100EX linear accelerator ser #2090 using 6 MV photons that was calibrated using the Task Group (TG)-51 protocol. A Varian MV portal imager utilizing an imaging review system called Acculoc version MT-NW-425-109 was used to evaluate accuracy of the treatment. Imaging treatment verification was performed daily for each beam daily, initially, an orthogonal pair was checked and adjustments were made, followed by each beam being reviewed and corrected clinically daily by the radiation oncologist prior to treatment.

Dose verification was accomplished by comparing the verification

plan dose profile and the coronal beam profiles (verification plan generated by Eclipse) and comparing those plan results to measurements made in a phantom at a 6cm depth equipped with a diode array system MapCHECK™ Model1175. This N-type diode array has 445 diodes in a 22×22 cm² 2-D array with variable spacing. The entire array of diodes allow measurements of absolute dose in a clinic^[8]. Silicon Diodes, and new detectors such as metal oxide silicon field-effect transistors

Metal-oxide-semiconductor field effect transistor(MOSFETs) are currently available for immediate in-vivo dosimetry and have similar relative dose accuracy compared to TLD and are very easily implemented into a clinical setting^[9,10]. Because there is a need to deliver a significant number of daily machine setting relative to a linear accelerator (MUs) due to the small field sizes, 95% Normalization to PTV, and 6 Gy daily prescription linearity of dose by semiconductor diode (diode) is a challenge for dose/profile analysis due to the linearity of dose in this range. (To address this issue, we measured each beam separately in the linear range) and then used the internal MapCheck program to determine the total dose/profile values). Although there is a small risk that there could be some increased integral dose to the patient due to leakage radiation when increasing MUS (small field sizes vs. standard large field sizes) comparing the out-of field dose to the 3D conformal dose to the patient to be considered^[11], The use of 6 MV beams reduces the risk of neutron production or production of second primaries compared to beams of higher energies^[12].

DISCUSSION/RESULTS

Although the emphasis of this study was on QA Analysis, the accuracy of treatment was based off the planning, rigid positioning of the breast with breath control, and radiation dose/imaging verification prior to every day treatment with MV imaging and Image Guided Radiation Therapy (IGRT).

Planning volumes were greatly assisted by the Radiation Oncologist by fiducial placement; contrast introduced into the cavity at the time of ultrasound –guided placement, and Planning CT/Post surgery T1 MRI fusion supine in treatment position. (Only done in two of the ten cases evaluated) Gross Target Volumes (GTV)'s, CTV's, and PTV's were defined post surgically. Due to fact that 3D-conformal techniques were employed in this case inverse planning dose volume constraints for organs at risk /evaluation of conformality index were not used. The decision on plan approval was based on the isodose distribution, Dose volume histogram, and the compliance to five-point dose limitations of the protocol. All ten approved for treatment cases met the criteria of the protocol. Conformality index (CI) was not available to evaluate in this version of software.

The imaging protocol on based off 3mm accuracy of defined CTV to PTV was very dependent on the stereotactic-like daily set-up reproducibility and careful evaluation of pre-treatment MV imaging. Gold markers placed after surgery was preferred over Titanium due to the fact they were better visualized with MV imaging. (Even though the cost of Gold markers for different vendors may be slightly higher than titanium ones). The department procedure for this protocol requires daily approval by the Radiation Oncologist MV imaging accuracy orthogonally prior to treatment. As quoted by Radiation Oncologist Robert Woodburn III (Medical Director) stated the following “Gold seed fiducials are visualized well than Titanium on Digitally Reconstructed Radiographs of Megavoltage Portal Imaging in contrast to visualizing anatomical structures”

The dose verification protocol show a good agreement between the planned vs. measured central axis doses in the ten patients studied, with the mean dose difference being 2.7%. For the ten cases evaluated. (due the low values of the means values presented in these 10 cases standard deviation was insignificant)

In addition to the planned vs. measured dose comparison at central axis, a profile analysis was performed on all patients using the same standard Gamma guidelines recommended for Intensity Modulated Radiation Therapy (IMRT) profile analysis, for planned vs. Measured i.e., 3% variation per 3 mm, as calculated using the previously used formula^[13]: % Dose Difference=Planned Dose/Delivered Dose×100

A comparison was also performed for the total number of MUs delivered vs dose (lowest to highest) to consider increased leakage radiation to patient due use increased number of small field sizes. and increased patient's daily integral daily dose to 600 cagy (vs. standard 160-300cGy), which may. This leakage issue will increase with the ratio of the number of MUs used vs. dose.

Past research comparison of the Mu ratio vs. the integral dose has indicated that Conformal RT had a lower ratio than IMRT and a significantly lower ratio than the ratio of cyberknife (radiosurgery)^[14].

The Left and Right Breast Statistical Analysis highlighted the structures of the cavity, PTV, Heart, Breasts, Right Lung, Left Lung, and spinal cord met dose/isodose, dose volume histogram criteria, and protocol 5 point dose limitation constraint of the protocol in all ten cases. The results are presented in Tables 1-6

CONCLUSIONS

The results of patient specific QA for this treatment were within expectation (average dose variation of 2.7% mean dose different between measured vs. planned radiation dose. The Mu ratio to radiation dose was f 2.05). It is common in IMRT analysis because of the greater number of dose points sampled to compare the fluency map created vs. the small field size in hypo-fractionated radiotherapy (maximum sampled=223 of possible 445). Conformality seems to be generally achieved for the five to seven beam arrangements, dose prescription/ limitations were met in all ten cases a, although clinical evaluation of this technique is still being investigated.

The Statistical Analysis for Both Right and Left Breasts indicated impressive dose delivery and constraints in the areas of heart, lung, and targeting of the PTV. Each field was filmed every day of the radiation treatment, which required radiation oncologist involvement. The Radiation Oncologist must be present for each daily hypofractionated treatment to evaluate the DRR accuracy prior to treatment.

Currently, there is no feedback mechanism in place to monitor changes of table movement or positional changes for the analysis of intra- and inter-fractional changes except for the film records. Improvements in the delivery of this technique include using real-time correction of the IGRT. This study is pending the outcome of the clinical results. This technique can be implemented with existing equipment and little additional capital equipment investment, along with some clinical training.

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