

## **SAMPLE CLINICAL RESEARCH APPLICATION**

### **ABSTRACT:**

**TITLE:** Comparison of the dosimetric planning of partial breast irradiation with and without the aid of 3D virtual reality simulation (VRS) software.

Hypothesis:

1. Using the Focalsim VRS to choose beam angles as part of the planning process for partial breast irradiation will decrease the time it takes to generate an acceptable plan and therefore make the planning process more efficient.
2. Using the VRS will allow for different angles to be chosen as compared to traditional planning techniques.
3. There will be a dosimetric benefit from the use of VRS, as less normal tissue will be irradiated and hotspots will be smaller and more evenly distributed.

Methods:

A complete treatment plan will be generated for each patient using two different methods. For the first method (control group) the full plan will be generated using the XiO software. For the second method, the beam angles will be chosen using the VRS software, and the remaining part of the plan will be completed using XiO. Several different dependent variables will be recorded and compared between the two groups including the time it takes to generate a plan, the angles chosen in each plan, and the dosages delivered to the target volumes and uninvolved organs.

Anticipated results:

It is expected that the use of the 3D VRS will result in an increased efficiency in choosing beam angles, a decreased time to generate a complete treatment plan, significantly different angles than selected by the traditional system, and a dosimetric benefit to the patient with better coverage of the target volume and reduced treatment of normal tissue.

**Research Plan (not to exceed 3-pages):** *This section is very important for the evaluation process and identification of the best proposals for funding.*

### **Background and rationale**

Breast conserving therapy (BCT) techniques provide enhanced cosmetic results and reduced “emotional and psychological trauma” as compared to mastectomy for women undergoing radiation for breast cancer.<sup>1</sup> Until recently the practice of whole breast irradiation (WBI) was standard protocol following a lumpectomy. Standard WBI therapy involves 5 weeks (25 fractions) of external beam therapy followed by a 1-2 week (5-7 fraction) boost to the tumor bed. The goal of this regimen was to eliminate any small local metastasis and to administer a higher dose to the tumor bed. However, more recent research has shown treatment of the breast tissue beyond the quadrantectomy bed to be unnecessary.<sup>2,3,4</sup> Thus, three-dimensional (3D) conformal external beam partial breast irradiation (PBI) techniques have been developed, which require less treatment time (reduced to 1 week) and less irradiation of healthy breast tissue, are more cost-effective, and require no further invasive procedure as is required with brachytherapy.<sup>1</sup> In addition, several recent studies have begun to demonstrate the comparable efficacy of PBI using external beam radiotherapy (EBRT) as compared to other treatment modalities,<sup>5,6</sup> and several patients have already been treated at Loyola using the protocol outlined by the National Surgical Adjuvant Breast And Bowel Project (NSABP)<sup>1</sup>.

One of the difficulties of PBI using EBRT is the relative complexity of the planning process and many dosimetrists’ lack of experience with the specific treatment plan. Treatment of the left breast is particularly difficult in that it requires 5 non-coplanar beams. Virtual reality simulation (VRS) is a new tool that may prove useful in overcoming these difficulties as it allows for 3D visualization of the patient and the machine couch (treatment table) in relationship to the particle accelerator machine. Using VRS, beams can be placed and beam angles chosen with full visualization of where the machine is in space, and how the beams pass through the patient and through the planned treatment volume (PTV). This allows prior simulation of the machines parameters to determine if collisions between the patient or the machine couch and the machine will occur. This was not possible with traditional software and it was left to the dosimetrist’s judgment to determine if collisions would occur followed by a trial run with the patient to check for collisions.

A comprehensive literature search yields very little research into the efficacy of planning treatments using VRS. In order to provide patients with the best treatment plan and to maximize the efficiency of the planning process it is important to determine any potential benefits the use of VRS may have in the planning process. Only patients with left-sided lesions will be included in this study because avoiding irradiation of the heart makes treatment of left-sided lesions inherently more difficult, and it will remove an additional independent variable (right versus left breast) while still looking into the usefulness of VRS.

### **Hypothesis and specific aims**

Using VRS to aid in the first steps of dosimetric planning for PBI will lead to a greater efficiency in planning (reduced time to generate a plan), different angle choices

than compared to traditional planning software, and a dosimetric benefit for the patient.

Specific Aim #1: Determine the average length of time it takes to generate a complete plan for a PBI treatment when the angles are chosen using 3-D VRS versus the average time required when the angles are chosen using standard software.

Specific Aim #2: Compare the beam angles chosen using the 3-D VRS to those chosen using standard software.

Specific Aim #3: Examine the final dose distributions for plans generated with the aid of 3D VRS and compare them to the plans generated with traditional software only, and determine if there is a dosimetric benefit in regards to enhanced PTV coverage and/or decreased irradiation of the heart, healthy breast tissue in the ipsilateral breast, contralateral breast, ipsilateral lung, contralateral lung, and thyroid.

## **Research design and methods**

### **Choosing the Beam Angles:**

Loyola has already treated several patients using the PBI technique while others were randomly assigned to receive WBI. Of these patients, ten who received treatment for left-sided breast cancer will be randomly chosen for inclusion in this study. Although a treatment was already generated in the past for these patients, it will not be used or referenced. The contour lines demarking anatomical structures that were previously drawn for each patient's treatment (from their original CT images) will be used. Two new treatment plans will be generated for each patient-using the PBI with EBRT technique, regardless of whether they received WBI or PBI in the past. The first treatment plan will be generated using the 3D VRS as an aid to choose beam angles with the completion of the planning process using the traditional XiO software. The second plan will be generated entirely using XiO software as is standard practice.

The entirety of each treatment plan will follow the guidelines set forth by the NSABP B-39 protocol,<sup>1</sup> including the dose limitations for normal tissues and the dose prescription and delivery. The protocol also gives recommendations for approximate treatment angles. Beginning with these standard angles, beam angles will be chosen for each patient once using the VRS and once using XiO. Half the patients will have their treatment planned first with the aid of the VRS and then with only XiO, while the other half will have their treatment planned first with XiO and then with the aid of VRS. This will be done in an alternating fashion with each subsequent patient. To ensure that familiarity with each system does not affect the results, the student investigator (an inexperienced user of both the VRS and XiO software) will choose angles for three "practice" patients with each system prior to beginning the study to become acclimated with the process and be equally experienced with each program.

### **Completion of the Treatment Plan:**

After angles are chosen for each patient using each system, the experiment will be blinded so that when constructing the plan, the software from which the angles were chosen will remain unknown. At this point, under supervision of a certified dosimetrist in the radiation oncology department, the student investigator will complete the plan

using XiO according to the NSABP protocol. This part of the study involves adjusting the settings of the collimator, weighting each beam, adding wedges, and at times slightly modifying the beam angles in order to achieve a plan that conforms to the requirements and limitations of the protocol.

#### Data Collection and Statistics:

In this study, the main independent variable will be the method used to pick the beam angles. The first dependent variable measured will be the time it takes to complete a plan. This variable will be broken down into several increments including the time it takes to choose the angles, the time it takes to complete the plan with the already chosen angles, and the total time spent on each plan (which will include the previous two measurements as well as any time used in transferring the plan between software programs, etc). The second dependent variable analyzed will be the angles chosen for each treatment. The third dependent variable is the dosimetric benefit to the patient. This will be analyzed using the dose volume histogram of planned treatment. The maximum dose received by the uninvolved normal breast, contralateral breast, ipsilateral lung, contralateral lung, heart, and thyroid will be recorded. Also, the percentages of the PTV receiving more than 90% of the prescribed dose and more than 105% of the prescribed dose will be recorded to assess each plan's coverage of the target area. Furthermore, the percent of each organ receiving more than a certain fraction of the dose as set forth by the NSABP protocol will be recorded to assess each plan's effect on healthy tissue. For example, the protocol allows for 15% of the ipsilateral lung to receive 30% of the prescribed dose, thus the percent of lung receiving less than 30% would be recorded. Other independent variables such as lumpectomy size, patient size, or breast volume and the role they play in the planning process and outcome will be examined. Descriptive statistics comparing the control group (no VRS) and the treatment group (VRS) will be reported. Analysis will be preformed using the appropriate test for significance (T-test or Chi-squared).

#### Anticipated results and interpretation

The data will be analyzed for each of the two groups (with VRS and without VRS) to see if there are any differences between them. Other independent variables such as lumpectomy size, patient size, and breast volume will also be analyzed.

Based on the ability to visualize patient and machine couch position in relationship to the particle accelerator, it is likely that more aggressive treatment angles can be chosen while still avoiding collisions between the accelerator and the patient and/or machine couch. Therefore, it is anticipated that the use of the VRS will allow for significantly different treatment angles to be utilized. This will allow for a dosimetric benefit to the patient, as the PTV will be treated more accurately, and the exposure of healthy tissue will be reduced compared to treatment with angles chosen without VRS. It is anticipated that with VRS, the ability to visualize the patient in the actual treatment position with the actual accelerator will reduce the time it takes to chose beam angles and the time it takes to generate a plan.

References:

- 1 NSABP PROTOCOL B-39 - A Randomized Phase III Study of Conventional Whole Breast Irradiation (WBI) Versus Partial Breast Irradiation (PBI) for Women with Stage 0, I, or II Breast Cancer. March 13, 2007 Available online: <http://www.rtog.org/members/protocols/0413/0413.pdf>
- 2 Morrow M. Rational local therapy for breast cancer. *N Engl J Med* 347:1270-1271, 2002.
- 3 Veronesi U, Cascinelli N, Mariani L, Greco M, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* 347:1227-1232, 2002.
- 4 Smith TE, Lee D, Turner BC, et al. True recurrence vs. new primary ipsilateral breast tumor relapse: an analysis of clinical and pathologic differences and their implications in natural history, prognoses, and therapeutic management. *Int J Radiat Oncol Biol Phys* 48:1281-1289, 2000.
- 5 Formenti SC, Rosenstein B, Skinner KA, et al. T1 stage breast cancer: adjuvant hypofractionated conformal radiation therapy to tumor bed in selected postmenopausal breast cancer patients—pilot feasibility study. *Radiology* 222:171-178, 2002.
- 6 Vicini FA, Remouchamps V, Wallace M, et al. Ongoing clinical experience utilizing 3D conformal external beam radiotherapy to deliver partial-breast irradiation in patients with early stage breast cancer treated with breast conserving therapy. *Int J Radiat Oncol Biol Phys* 57:1247-1253, 2003.