

Tissue Expanders and Proton Beam Radiotherapy: What You Need to Know

Ashley L. Howarth, MD*
 Joshua R. Niska, MD†
 Kenneth Brooks, BSc‡
 Aman Anand, PhD†
 Martin Bues, PhD†
 Carlos E. Vargas, MD†
 Raman C. Mahabir, MD*

Summary: Proton beam radiotherapy (PBR) has gained acceptance for the treatment of breast cancer because of unique beam characteristics that allow superior dose distributions with optimal dose to the target and limited collateral damage to adjacent normal tissue, especially to the heart and lungs. To determine the compatibility of breast tissue expanders (TEs) with PBR, we evaluated the structural and dosimetric properties of 2 ex vivo models: 1 model with internal struts and another model without an internal structure. Although the struts appeared to have minimal impact, we found that the metal TE port alters PBR dynamics, which may increase proton beam range uncertainty. Therefore, submuscular TE placement may be preferable to subcutaneous TE placement to reduce the interaction of the TE and proton beam. This will reduce range uncertainty and allow for more ideal radiation dose distribution. (*Plast Reconstr Surg Glob Open* 2017;5:e1390; doi: 10.1097/GOX.0000000000001390; Published online 23 June 2017.)

BACKGROUND

External Beam Radiotherapy

Photon

Conventional external beam photon radiotherapy, the most commonly used radiation technique for breast cancer,¹ deposits radiation with a characteristic build-up region, maximum dose, and exit dose. For example, 6-megavolt photon beams deposit their maximum dose 1.5 cm below the tissue surface, followed by an exponential dose fall-off as the beam continues. Thus, tissues superficial and deep to the primary target receive unwanted radiation.² When radiation is delivered to the chest, minimizing its effect on the heart and lungs is essential. Characteristics of the photon beam make this challenging; and in certain patients with breast cancer, the cancer-specific survival benefit of adjuvant radiotherapy may be offset by increased risk of cardiac death related to radiation dose to the heart.³

Proton

Proton beam radiotherapy (PBR), another form of external beam radiation, delivers radiation using accelerated

protons within a cyclic particle accelerator.⁴ PBR targets cancerous tissue by depositing energy with specificity and abundance a few millimeters from the proton beam end of range. When plotting a curve of radiation dose as a function of depth in tissue for protons, the result is an entrance dose leading to a sharp peak and maximum dose near the distal end of range of the protons. This peak is abruptly followed by a dramatic dose fall-off with no exit dose. These are the typical characteristics of the dose-deposition curve for charged particle therapy, known as the Bragg peak curve.⁵ The Bragg peak is the physical characteristic of proton dose deposition that provides the main advantage of integral dose sparing of healthy tissues in PBR over photon radiotherapy. The ability to control the kinetic energy of protons during treatment increases dose precision and accuracy of the PBR. There is limited damage to healthy peripheral tissue, particularly beyond the Bragg peak. The safe delivery of therapeutic doses of ionizing radiation requires precise estimation of tissue-equivalent path lengths through which the protons travel. The addition of a prosthesis that contains high atomic number (Z) elements, such as a metal port or internal struts, may introduce uncertainties in the tissue-equivalent path length. Consequently, a targeted tumor could receive less than the required treatment dose, and peripheral healthy tissue could receive unwanted radiation damage.

Tissue Expanders

Numerous studies have evaluated the use of tissue expanders (TEs) for breast reconstruction in the setting of an-

From the *Division of Plastic and Reconstructive Surgery, Mayo Clinic Hospital, Phoenix, Ariz.; †Department of Radiation Oncology, Mayo Clinic Hospital, Phoenix, Ariz.; and ‡University of Arizona, College of Medicine, Tucson, Ariz.

Received for publication January 3, 2017; accepted May 5, 2017.

Copyright © 2017 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/GOX.0000000000001390

Disclosure: At the time of the writing of this article, there were no disclosures. Dr. Mahabir is now part of the Mentor Advisory Board. No funding was received for this manuscript and Mentor was not involved in the production of this article. The other authors have no financial interests to disclose. The Article Processing Charge was paid for by the authors.

anticipated radiation. Whether the expander should be placed and, if placed, whether it should be inflated or deflated during radiotherapy has been debated.⁶ Likewise, reconstruction failure in patients who had postmastectomy radiation with concurrent TE has been a topic of interest.⁷ Further complicating this debate, the metal TE port produces artifacts on computed tomography (CT) that may introduce errors within PBR planning, can change location of the Bragg peak, and manipulate energy deposition—potentially causing dose errors within target and peripheral tissue. Photon radiotherapy is less affected by high-Z materials than PBR,⁸ so metal TE ports have not been a cause for concern in the past. However, as PBR becomes more common in the adjuvant treatment of breast cancer, careful study of how the metal TE port interacts with the proton beam is necessary.

METHODS

We performed a series of experiments to evaluate potential dynamic changes of PBR due to metal injection ports and internal struts. An *ex vivo* Eclipse treatment plan (Varian Medical Systems, Palo Alto, Calif.) was developed to identify changes in proton beam range caused by TE-beam interaction. TEs of similar dimensions, with and without internal struts, were acquired from Mentor (Artoura and CPX4, Mentor Worldwide, Irvine, Calif.). Photoelectric and Compton scatter-based evaluations of the TEs were performed using CT scans. Eclipse Treatment Planning System (ETPS; Mentor Worldwide) software was used to calculate PBR treatment plans and the effect of TE-beam interaction on proton beam range. TEs were filled with saline to their maximum fill volume and placed on the chest wall of an anthropomorphic phantom to simulate subcutaneous TE placement. A single dose of PBR was passed through each TE toward a virtual tumor, and proton beam range was evaluated.

RESULTS

The presence of the metal port altered the proton beam range and the radiologic path length relative to when the beam passed through the saline section of the TE (Table 1). As expected, the radiologic path length and beam range were different as the proton beam passed through the saline section of the TE and through the port. The port yielded abundant CT artifacts, potentially obscuring visualization (Fig. 1). ETPS findings demonstrated heterogeneities, hot beam streaks, and overreaching of the PBR into critical structures (Fig. 2). The TE internal

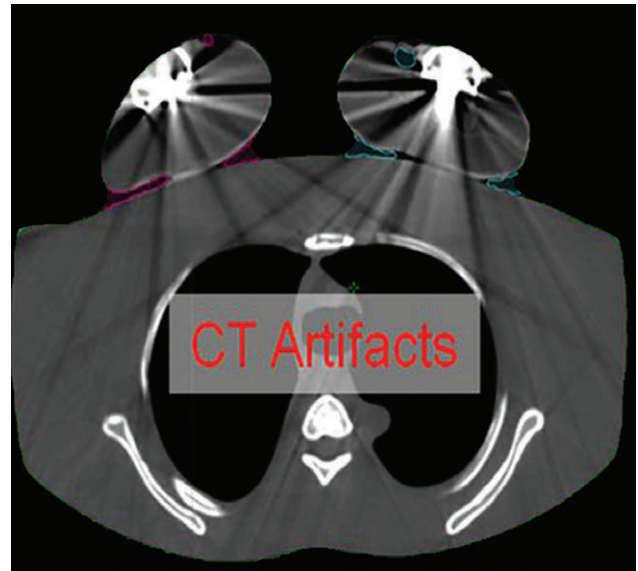


Fig. 1. Abundant CT artifact caused by proton beam interaction with the high-Z metal ports of the TE.

struts did not seem to substantially impact planning or delivery of PBR.

DISCUSSION

Treating breast cancer with PBR is an important topic within the medical community. Bradley et al.⁹ identified improvements in regional nodal irradiation for breast cancer patients who underwent PBR compared with patients receiving conventional radiotherapy. In a study comparing PBR with photon beam radiation, Lin et al.¹⁰ reported that PBR was associated with reduced radiation doses to the whole heart, the left anterior descending artery, and the lung in patients with left-sided breast cancer. These findings indicate that PBR may be very useful for treating breast cancer. Therefore, identifying variables that limit or alter PBR efficacy is important.

PBR is increasingly being employed as adjuvant radiotherapy for the treatment of certain breast cancers. The appeal of PBR is based on the potential for high dose conformity and limited damage to normal tissues, principally the heart and lungs. These advantages hinge upon clinicians' being able to design robust treatment plans. The metal port of TEs used in reconstruction impacts PBR dynamics and must be factored into treatment planning. This is similar to conventional photon radiotherapy but with greater sensitivity. Placement of TEs subcutaneously during PBR may increase the probability of erroneous beam planning, reduce radiation effectiveness, and lead to damage to healthy peripheral tissue. Placement of TEs submuscularly could lessen concerns for aberrant PBR activity, given reduced TE-beam interaction, while adequately treating any residual disease and still allowing for breast reconstruction. Although placing the TE subcutaneously rather than submuscularly may be better for managing breast shape during reconstruction,¹¹ the benefits of submuscular placement for PBR may outweigh potential

Table 1. Radiologic Path Length in Saline and Metal Port Regions

Breast TE	Saline Region (cm)	Metal Port (cm)
Beam range in the tank without TE device	19.757	19.757
Beam range in the tank with device	14.973	14.433
Radiologic path length	4.041	4.581
Silicone thickness in port	0.89	0.89
Magnet thickness in port	0.482	0.482
Metal shield thickness of port	1.5	1.5
Effective thickness = metal + shell	1.945	1.945
Radiologic physical thickness	2.096	2.636

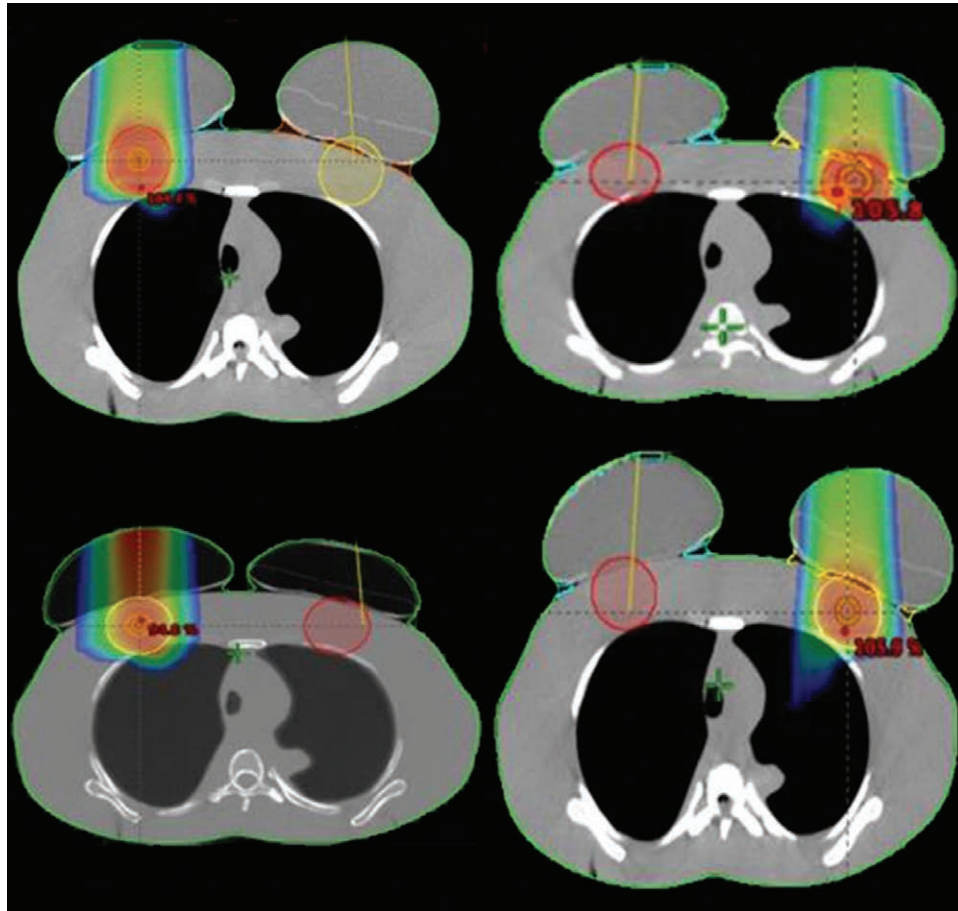


Fig. 2. Eclipse treatment planning. Changes in beam depth are demonstrated as the proton beam passes through the TE with internal struts (600 cc) vs. the TE without (right) internal struts (650 cc). TEs were placed on the chest wall of an anthropomorphic phantom to simulate subcutaneous TE placement. A single dose of PBR was then passed through the TE to target a virtual chest wall tumor. The pathway of the radiation extended beyond the targeted virtual tumor (red circle), affecting tissue not originally intended for radiation treatment (overreaching of PBR into critical structures, as noted, with the green and blue effects in the lungs).

cosmetic benefits. The presence of internal struts did not substantially impact PBR dynamics and has the theoretical advantages of increased lower pole expansion and better pocket match if shaped implants are used in reconstruction.

Although we recognize that partial or full submuscular TE placement may be considered standard for many surgeons, increasing numbers of surgeons are opting for subcutaneous TE placement.¹¹ To demonstrate the potential pitfalls of subcutaneous TE placement in the context of adjuvant PBR, we opted to design our model to simulate subcutaneous TE placement. However, more detailed, subsequent study of PBR in the context of submuscular TE placement would be helpful.

In conclusion, the presence of metal TE ports may lead to substantial dose errors in patients undergoing concurrent PBR. Likewise, ETFS findings suggest that subcutaneous TE placement leads to greater contact between the TE and proton beam, affecting the depth that protons penetrate tissue and potentially harming critical thoracic

structures during breast cancer treatment. Therefore, if PBR is planned in the context of TEs, submuscular TE placement may limit proton beam range errors within the patient and result in greater PBR safety and efficacy.

Raman C. Mahabir, MD

Division of Plastic and Reconstructive Surgery
Mayo Clinic Hospital
5777 E Mayo Blvd
Phoenix, AZ 85054
E-mail: mahabir.raman@mayo.edu

REFERENCES

1. Miralbell R, Lomax A, Cella L, et al. Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumors. *Int J Radiat Oncol Biol Phys.* 2002;54:824–829.
2. Nguyen PL, Trofimov A, Zietman AL. Proton-beam vs intensity-modulated radiation therapy. Which is best for treating prostate cancer? *Oncology (Williston Park).* 2008;22:748–754; discussion 754, 757.
3. Clarke M, Collins R, Darby S, et al.; Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of radiotherapy and of

- differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;366:2087–2106.
4. Wilson R. *A Brief History of the Harvard University Cyclotrons*. Cambridge, Mass.: Harvard University Press, Department of Physics; 2004.
 5. Paganetti H, Bortfeld T. Proton beam radiotherapy: the state of the art. Available at <http://www.aapm.org/meetings/05AM/pdf/18-4016-65735-22.pdf>. Accessed October 3, 2016.
 6. Celet Ozden B, Guven E, Aslay I, et al. Does partial expander deflation exacerbate the adverse effects of radiotherapy in two-stage breast reconstruction? *World J Surg Oncol*. 2012;10:44.
 7. Fowble B, Park C, Wang F, et al. Rates of reconstruction failure in patients undergoing immediate reconstruction with tissue expanders and/or implants and postmastectomy radiation therapy. *Int J Radiat Oncol Biol Phys*. 2015;92:634–641.
 8. Wei J, Sandison GA, Hsi WC, et al. Dosimetric impact of a CT metal artefact suppression algorithm for proton, electron and photon therapies. *Phys Med Biol*. 2006;51:5183–5197.
 9. Bradley JA, Dagan R, Ho MW, et al. Initial report of a prospective dosimetric and clinical feasibility trial demonstrates the potential of protons to increase the therapeutic ratio in breast cancer compared with photons. *Int J Radiat Oncol Biol Phys*. 2016;95:411–421.
 10. Lin LL, Vennarini S, Dimofte A, et al. Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer. *Acta Oncol*. 2015;54:1032–1039.
 11. Tomita K, Yano K, Nishibayashi A, et al. Effects of subcutaneous versus submuscular tissue expander placement on breast capsule formation. *Plast Reconstr Surg Glob Open*. 2015;3:e432.