

Ultrasound Accuracy in Determining the Tumor Depth for Boost Field Radiotherapy in Breast Cancer in Comparison With CT Scan Plus Clips

Mahdi Aghili¹; Mohammad Reza Barzegar Tahmtan^{1*}; Farhad Samiee¹; Peyman Haddad¹; Farnaz Amouzgar Hashemi¹; Afsane Maddah¹; Farshid Farhan¹; Afsane Alikhasi²; Ramesh Omranipour³; Hasnali Nedae⁴; Ahmad Kaviani⁵

¹Department of Radiation Oncology, Cancer Institute, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

²Department of Radiology, Cancer Institute, Tehran University of Medical Sciences, Tehran, IR Iran

³Department of Surgery, Cancer Institute, Tehran University of Medical Sciences, Tehran, IR Iran

⁴Department of Medical Physics, School of Medicine, Tehran University of Medical Sciences, Tehran, IR Iran

⁵Department of Surgery, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Mohammad Reza Barzegar Tahmtan, Department of Radiation Oncology, Cancer Institute, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, IR Iran. Tel: +98-2161192558, Fax: +98-2166581633, E-mail: mbtahamtan@gmail.com

Received: July 13, 2014; Revised: August 31, 2014; Accepted: September 6, 2014

Abstract

Background: There are miscellaneous methods of boost field determination with different levels of accuracy. One of the important parameters in boost field planning is the tumor bed depth, as it is important for determining electron energy.

Objectives: The purpose of present research was the determination of ultrasound accuracy to estimate the appropriate depth for the tumor bed.

Patients and Methods: Patients who were undergone breast conservative surgery with placing of 5 clips in the tumor bed (lower, upper, medial, lateral, and posterior) were included. The depth and location of the tumor bed were determined using ultrasonography. The optimum field boost was planned with an appropriate 2.5 cm margin. After putting the marker on the field boost, the CT simulation was done and then the obtained depth of the ultrasound report and that of the CT scan-clips were compared.

Results: Twenty five patients were included. The average depth reported by the ultrasound was about 18 mm \pm 3 mm (range 10-26 mm), and the average obtained from the CT scan-clips was about 48 mm \pm 13 mm (range 24-80 mm), (P Value = 0.001). In almost all cases, the depth obtained from the ultrasound was less than that obtained from the CT scan-clips.

Conclusions: Ultrasound is not an accurate method to determine the appropriate depth and field for determination of breast field boost. Thus, it is better not to use ultrasound to estimate the tumor cavity depth; the CT scan images with surgical clips should be used instead.

Keywords: Breast Cancer; Radiotherapy; Tumor

1. Background

Radiotherapy plays an important role in the treatment of breast cancer, and its effects in reducing local recurrence have been proven (1). In breast conserving treatment, the breast radiotherapy is done after the surgery, and chemotherapy is administered in two steps with 50 Gy in 25 fractions firstly, followed by a boost of 10 - 20 Gy in 5 - 10 fractions to the tumor bed (2, 3). In performed trials, this boost dose has decreased local recurrence (1-3). Although most radiation oncologists are in agreement with the boost treatment, especially in patients with higher risks of recurrence, they have different ideas about the method to be used in terms of the type of beam (electron or photon) and the method of radiation delivery (4-7). Delivering the 10 - 20 Gy boost dose necessitates the accurate determina-

tion of the area and depth of the tumor bed. Additionally, the normal tissue of the breast is less exposed to radiation when the tumor bed is determined more accurately, and thus fewer consequent side effects appear. Different methods have been used to determine the tumor bed, including scar surgery, asking the patient to remember the mass, radiography, ultrasound, CT scan, and surgical clips (7-10). The accuracy of the aforementioned methods has been studied. There are different ideas about the accuracy of these methods in different studies. Although using surgical clips is not the best method, most studies have shown that it is the most appropriated one (11). The role of ultrasound in boost radiotherapy treatment has been widely studied, and different results have been obtained.

2. Objectives

The present study has investigated the accuracy of ultrasound in determining the depth of the tumor bed in comparison with using CT-clips.

3. Patients and Methods

This study has been done in the radiotherapy-oncology department of a cancer institute. The inclusion criteria for cases were as follows: women who had undergone breast conserving surgery, more than 20 days passed from the date of the operation, and at least 5 titanium clips were placed by the surgeon in the upper, lower, medial, lateral, and floor areas of the tumor bed margins. Initially, the patient was requested to specify her tumor bed depth and its area on breast skin. The sonographer mentioned the depth of the tumor bed in all patients. It is noteworthy that all ultrasound tests were performed by a sonographer who was skillful in breast ultrasonography, and the ultrasound was done during the radiotherapy process. After the localization of the tumor bed by the sonologist in the skin, the boost field was defined by a 2.5 cm margin around the bed and a lead wire marker was placed on it. Then, the CT scan simulation (Siemens, SOMATOM Sensation 16) using the breast board (in radiotherapy treatment position) was performed. All scans were done with 5 mm slices from mandible angle to 2 cm under the breast. The planning was done using PCRT3D Activation software (manufacturer: tecnologo radiacion, version 6). In addition to treatment planning, the distance of the placed clips from tumor bed depth and the breast skin was measured (Figures 1 and 2).

Statistical method: the calculated sample size was 25 patients based on former studies and the sample size calculation relation in even data with the confidence interval of 95% (alfa = 0.05, z = 1.96) (12). The obtained results were analyzed using the SPSS software (version 20.0) and the hypothesis was tested using the paired t test.

4. Results

From January 2013 to February 2014, twenty five women were recruited for this study. The mean age of patients was 49 years (from a minimum age of 29 to a maximum age of 70). The most frequent cancer stages were stage I. The average time passed from surgery was 163 days with standard deviation of 64 days (minimum 27 days, maximum 263 days). 23 patients were under the adjuvant chemotherapy, and two of them had no indication for chemotherapy. The PTV (planning target volume) was $95 \text{ mL} \pm 45 \text{ mL}$ (range 41 - 261 mL). The effects of time passed from surgery and chemotherapy on tumor cavity dimensions like depth and PTV, were also studied. The correlation between time passed from the surgery and PTV was not significant (P Value = 0.06). Also, no significant difference was observed between time passed from surgery with depths reported in ultra-

sound (P Value = 0.18) while the difference between the measured depths in CT scan with surgical clips was significant (P Value = 0.04). Since 23 patients out of 25 had undergone chemotherapy, the chemotherapy effect on cavity dimensions, including depth, was not evaluated in this research. The average depth reported from ultrasounds was $18 \text{ mm} \pm 3 \text{ mm}$ (range: 10-26 mm), while the average depth measured from CT scan-surgical clips was $48 \text{ mm} \pm 13 \text{ mm}$ (range: 24 - 80 mm). Almost in all cases, the depth reported from ultrasounds was less than that obtained from CT scan-surgical clips and in paired t test analysis; this difference was strongly significant (P Value = 0.001) (Table 1). Additionally, a positive and direct correlation was observed between depths obtained from ultrasonography and that obtained from CT scan- surgical clips (Pearson coefficient = 0.45), which is statistically significant (P Value = 0.027).

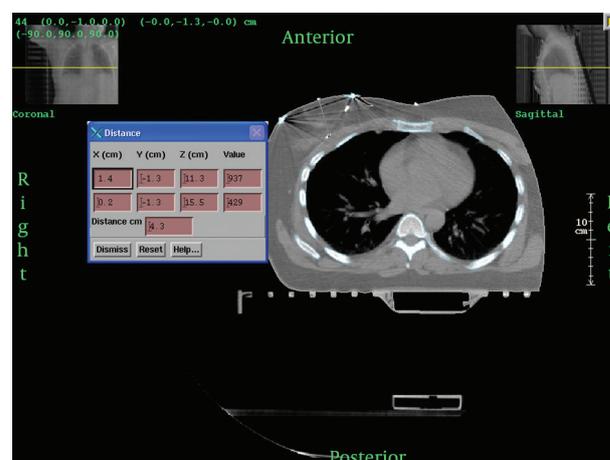


Figure 1. Distance of the Placed Clips From Tumor Bed Depth



Figure 2. Distance of the Placed Clips From the Breast Skin

Table 1. The Measured Depth Observed Between Depths Obtained From Ultrasonography and That Obtained From CT Scan-Surgical Clips

Depth Obtained From CT Scan-Surgical Clips, mm	Depth Obtained From Ultrasound, mm	Patient Number
29	15	1
53	16	2
29	16	3
30	21.1	4
57	18	5
50	20	6
62	21	7
43	21	8
37	10	9
56	20	10
38	18	11
51	25	12
57	20	31
50	14	14
67	20	15
80	19.5	16
61	17	17
54	26	18
62	25	19
34	16	20
24	19	21
43	17	22
53	25	23
38	17.6	24
59	21	25

5. Discussion

The present research has been performed to determine the accuracy of ultrasonography in the determination of the depth and area of the tumor bed in planning the radiotherapy boost for breast cancer, as the tumor depth is important for selecting the proper energy of electron beams. The efficacy of adjuvant radiotherapy in breast conservative therapy and boost to the tumor bed has been proven in least at 4 valid trials (EORTC BOOST TRIAL, LYON BOOST TRIAL, EBCTCG TRIAL, and NSABP TRIAL). The accurate determination of boost field is of much importance, since delivering the perfect boost to the tumor bed results in reduction of the risk of local recurrence; and also reduces the delivered dose to normal breast tissue and diminishes the side effects (1-3, 7, 13). The effect of variables like time passed from surgery and having chemotherapy or radiotherapy on the dimension and volume of the tumor cavity has been widely studied, indicating that these variables can affect the dimensions and also the cavity position (14-17).

In this study, the correlation coefficient of time passed from surgery and tumor cavity dimensions (including depth and PTV) was demonstrated a relation between the measured depth based on CT scans with surgical clips and time passed from surgery. Although no significant relationship was observed between PTV and time passed from surgery, it was close to being statistically significant, which can be important medically. The reason for insignificance may be the limited number of samples and also high variety and distribution compared to other studies. In two separate studies, Sharma et al. (16) and Tersteeg et al. (14) have suggested that the CT scan treatment planning should be conducted again after the radiotherapy treatment of breast to treat the boost. The use of ultrasounds to determine the boost field of radiotherapy has been widely studied. Rabinovitch et al. (8) have compared the ultrasound and surgical clips for 29 patients, indicating that the ultrasound estimates less treatment volume and consequently less electron beam energy. Therefore, it should not be applied in determining the boost field, especially in patients receiving adjuvant chemotherapy treatment. Rabinovitch et al. (8) have measured the length, width, and depths of tumor using ultrasound in patients having surgical clips, showing that the tumor bed depth has been significantly underestimated by ultrasound in 23 out of 29 patients (8). Chitapanarux et al. (18) have considered 41 patients in 2009 using ultrasound with radiography to determine the tumor bed depth, indicating that the ultrasound underestimated the depth in 85% of patients (P Value = 0.27). In this work, the findings show that the determined depth by ultrasound is less than that estimated by surgical clips in almost all 25 patients. Thus, it can be concluded that ultrasonography is not an appropriate method to estimate the depth of boost field since it will result in using lower energy electron beams and insufficient coverage for planning target volume (PTV). The main reasons for the difference between depth measured with ultrasound and that of surgical clips include: having different criteria to determine the floor of tumor cavity by sonographers and surgeons, changes of dimension and tumor cavity position during the time elapsing since surgery, and the effects of chemotherapy on dimension and tumor cavity position (14-17). In fact, surgeons remove the normal breast tissue under the tumoral zone in addition to the tumor mass, then clean the zone to the pectoralis major muscle and place the posterior clips on the edge of the anterior fascia of the pectoralis muscle. The sonographers often observe the seroma in the cavity and measure its distance from the breast skin. Underestimating the depth potentially increases the chance for local recurrence because of insufficient boost dose. Additionally, it may cause cosmetic side effects by delivering higher doses to normal tissues.

Ultrasound is not an accurate method for planning the boost dose to breast and its use is discouraged. Treatment

planning based on surgical clips and CT scan seems to be a better choice. We suggest that more comprehensive studies to be done on the cavity size and position changes as well as its dependence on radiotherapy, chemotherapy, and amount of time passed from surgery.

Acknowledgements

It reminded that this article is a part of thesis entitled “a comparison of ultrasound and CT scan- surgical clips in boost field radiotherapy planning of breast cancer” and we are thankful all helpful supports especially Mr Mohammedi, Ms Mostaghis, Ms Aslani, and Ms Hosumi.

References

1. Darby S, McGale P, Correa C, Taylor C, Arriagada R, Clarke M, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. *Lancet*. 2011;**378**(9804):1707-16.
2. Romestaing P, Lehingue Y, Carrie C, Coquard R, Montbarbon X, Ardiet JM, et al. Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France. *J Clin Oncol*. 1997;**15**(3):963-8.
3. Bartelink H, Horiot JC, Poortmans PM, Struikmans H, Van den Boogaert W, Fourquet A, et al. Impact of a higher radiation dose on local control and survival in breast-conserving therapy of early breast cancer: 10-year results of the randomized boost versus no boost EORTC 22881-10882 trial. *J Clin Oncol*. 2007;**25**(22):3259-65.
4. Kovner F, Agay R, Merimsky O, Stadler J, Klausner J, Inbar M. Clips and scar as the guidelines for breast radiation boost after lumpectomy. *Eur J Surg Oncol*. 1999;**25**(5):483-6.
5. Machtay M, Lanciano R, Hoffman J, Hanks GE. Inaccuracies in using the lumpectomy scar for planning electron boosts in primary breast carcinoma. *Int J Radiat Oncol Biol Phys*. 1994;**30**(1):43-8.
6. Graham P, Fourquet A. Placing the boost in breast-conservation radiotherapy: A review of the role, indications and techniques for breast-boost radiotherapy. *Clin Oncol (R Coll Radiol)*. 2006;**18**(3):210-9.
7. Van Parijs H, Reynders T, Heuninckx K, Verellen D, Storme G, De Ridder M. Breast conserving treatment for breast cancer: dosimetric comparison of different non-invasive techniques for additional boost delivery. *Radiat Oncol*. 2014;**9**:36.
8. Rabinovitch R, Finlayson C, Pan Z, Lewin J, Humphries S, Biffi W, et al. Radiographic evaluation of surgical clips is better than ultrasound for defining the lumpectomy cavity in breast boost treatment planning: a prospective clinical study. *Int J Radiat Oncol Biol Phys*. 2000;**47**(2):313-7.
9. Benda RK, Yasuda G, Sethi A, Gabram SGA, Hinerman RW, Mendenhall NP. Breast boost: are we missing the target? *Cancer*. 2003;**97**(4):905-9.
10. Pezner RD, Tan MC, Clancy SL, Chen YJ, Joseph T, Vora NL. Radiation therapy for breast cancer patients who undergo oncoplastic surgery: localization of the tumor bed for the local boost. *Am J Clin Oncol*. 2013;**36**(6):535-9.
11. Harrington KJ, Harrison M, Bayle P, Evans K, Dunn PA, Lambert HE, et al. Surgical clips in planning the electron boost in breast cancer: a qualitative and quantitative evaluation. *Int J Radiat Oncol Biol Phys*. 1996;**34**(3):579-84.
12. Sadat Hashemi S, Ghorbani R, Kavhie B. Sample size determination for matched studies. *koomesh*. 2006;**8**(1):55-62.
13. Kirwan CC, Al Sarakbi W, Loncaster J, Chan HY, Thompson AM, Wishart GC. Tumour bed clip localisation for targeted breast radiotherapy: compliance is proportional to trial-related research activity: tumour bed clip localisation in breast radiotherapy. *Eur J Surg Oncol*. 2014;**40**(2):158-62.
14. Tersteeg RJHA, Roesink JM, Albregts M, Warlam-Rodenhuis CC, van Asselen B. Changes in excision cavity volume: prediction of the reduction in absolute volume during breast irradiation. *Int J Radiat Oncol Biol Phys*. 2009;**74**(4):1181-5.
15. Oh KS, Kong FM, Griffith KA, Yanke B, Pierce LJ. Planning the breast tumor bed boost: changes in the excision cavity volume and surgical scar location after breast-conserving surgery and whole-breast irradiation. *Int J Radiat Oncol Biol Phys*. 2006;**66**(3):680-6.
16. Sharma R, Spierer M, Mutyala S, Thawani N, Cohen HW, Hong L, et al. Change in seroma volume during whole-breast radiation therapy. *Int J Radiat Oncol Biol Phys*. 2009;**75**(1):89-93.
17. Prendergast B, Indelicato DJ, Grobmyer SR, Saito AI, Lightsey JL, Snead FE, et al. The dynamic tumor bed: volumetric changes in the lumpectomy cavity during breast-conserving therapy. *Int J Radiat Oncol Biol Phys*. 2009;**74**(3):695-701.
18. Chitapanarux I, Muttarak M, Na-Chiangmai W, Trakultivakorn H, Somwangprasert A, Kamnerdsupaphon P, et al. Can radiographic plain film be used to determine the depth of the tumour bed in the absence of surgical clips for breast boost planning. *Biomed Imaging Interv J*. 2009;**5**(3): e11.