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Ultrasound-guided boost irradiation of tumor cavity after lumpectomy in breast cancer

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► ***Original article***

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ABSTRACT

Background: After breast conserving surgery, most recurrences occur around the primary tumor site. This justifies the use of boost radiotherapy to the primary site of tumor. Surgical scar is not always a good surrogate for the location of the lumpectomy cavity. The aim of this study was to evaluate ultrasonic guidance for detection of the lumpectomy cavity after breast conserving surgery for electron beam boost field planning. ***Materials and Methods***: 35 breast cancer patients who treated with whole breast irradiation after breast conserving surgery underwent ultrasonic evaluation for measurement of depth and size of lumpectomy cavity. Results of ultrasonic imaging were used to define electron boost field size and depth of treatment. These results were compared with clinical measurements that made by two expert radiation oncologists. ***Results:*** The operative bed was well visualized in all of the patients. In only 21 patients (60%) cavity was located on the scar. Depth determined by ultrasonography was not significantly correlated with depth determined by clinical impression (r=0.304, P<0.01). This means that the results of the two methods are quite different (these results are also true for other variables). In 88% of patients, the depth of treatment and electron beam energy that were selected by clinical measurements were changed. ***Conclusion:*** Ultrasound is found useful tool for measurement of depth and size of lumpectomy cavity and could be used for boost planning. It is easily available, non-invasive and inexpensive.

Keywords: *Breast cancer, radiotherapy, boost, ultrasonography.*

INTRODUCTION

After breast cancer surgery with lumpectomy or mastectomy, breast cancer patients may need to have radiotherapy. After mastectomy, indications of radiotherapy for breast cancer include lymph node involvement or tumor size equal to or greater than 5cm. In these circumstances, radiotherapy reduces the risk of local recurrence and may also affect survival [(1)]. In selected patients with early stage breast cancer, conservative surgery followed by radiation therapy has become a widely accepted mode of therapy. Data concerning the need for a radiotherapy boost to the lumpectomy cavity are contradictory. Most authors have reported that 65% to 80% of breast recurrences after conservative surgery and irradiation occur around the primary tumor site [(2)]. These data justify the use of boost of radiotherapy to the primary site of tumor. Other authors have restricted it to cases with positive margins. The results of the EORTC trial also support the use of boost dose to the lumpectomy cavity [(3)].

Boost dose planning based on clinical assessment is guided by information obtained from surgical report, to determine tumor position and quadrant, preoperative

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mammogram, and a pathological report which determine the tumor size and its depth within the specimen. Surgical scar is not always representative for the location of the lumpectomy cavity. The lumpectomy cavity changes in size, shape, and location with time after surgery. It has been hypothesized that there are differences between clinical and ultrasound measurements of lumpectomy cavity. The goal of this study is to evaluate ultrasonic guidance to detect the lumpectomy cavity after breast conserving surgery. This can be helpful for planning of radiation therapy boost field and to choose optimal electron beam energy.

MATERIALS AND METHODS

35 patients with breast cancer, who were referred to the Radiation Oncology department after surgical Lumpectomy and chemotherapy, were enrolled. All patients were treated with external beam radiotherapy to the whole breast with a total dose of 50Gy and daily dose of 2Gy, 5 fractions per week with Linac machine, and then they all received a boost dose of 10Gy to the lumpectomy cavity with a mean duration of 8 months after conservative surgery (minimum 3 months and maximum 12 months). All patients had pathologically negative surgical margins. None of the patients had oncoplastic surgery and surgical clips were not used for any of them.

At sixth week of whole breast radiation treatment, all patients underwent sonographic localization of the biopsy site for boost planning with General Electric Voluson 730 Expert machine (made in General Electric Company of USA) with small port 7.5 MHz probe. An expert radiologist, reported sonographic visibility, appearance, diameter, and depth of the lumpectomy cavity in supine position. The lumpectomy cavity was marked on the skin by radiologist.

The results of sonographic measurements were compared with results of clinical evaluation (tumor size, preoperative mammography, and scar) with two expert radiation oncologists.

Accurate localization of the lumpectomy cavity is essential for optimal delivery of radiation in breast cancer electron boost treatment. The depth of the cavity is required to determine appropriate electron beam energy in order to deliver the prescribed dose. The goal was to include side walls and floor of cavity within the 90% isodose line.

Statistical analysis

The statistical SPSS package version 17 for windows (Chicago, Illinois, USA), was used for analysis. Variables which distributed normally are presented as mean and standard error of mean (SEM). Pearson's correlation test was employed to assess the correlation of variables. The analysis was repeated using partial correlation to assess the correlation between variables after few months of surgery.

RESULTS

35 patients with early breast cancer (stage I and II) were included in this study with mean age of 47.7 years (SD=12.31; range, 31–70 years). In all patients, the surgical cavity was visible on ultrasonography; in 21 patients cavity was located on the scar, in 8 patients was abutted to the scar and in 6 patients was away of the scar. In one patient surgical scar was around the nipple and cavity was far away in lateral upper quadrant. The operative bed was well visualized in all of the patients.

Clinical and sonographic characteristics of the surgical cavity are presented in table 1. As shown in this table, the mean depth measured by ultrasound (12.40mm) is lower than mean depth measured by clinical evaluation (29.14mm) and mean length measured by ultrasound (43.03 mm) is lower than mean length measured by clinical impression (65.43 mm) and finally, mean width measured by ultrasound (41 mm) is also lower than mean width measured by clinical evaluation (64.86 mm). Table 2 shows the correlation between variables. The value $r = 1$ means a perfect positive correlation and the value $r = -1$ means a perfect negative correlation.

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As shown in this table, there is no positive correlation between dimensions measured by ultrasound and dimensions measured by clinical method which is statistically significant for all dimensions ($p<0.01$). This means that the results of the two methods are quite different.

Sonographic findings were used to define the electron boost field size and depth of radiation treatment, which determines the electron beam energy.

Ultrasound measurement of boost depth ranged from 4 mm to 20 mm. The mean depth of surgical cavity, as was determined by ultrasonography, was 12.40 mm. Clinical measurement of surgical cavity depth ranged from 10 mm to 50mm with mean depth of 29.14 mm.

In 88 % of patients, the depth of boost dose and electron beam energy that were selected by clinical measurements, were changed based on sonographic evaluation.

Table 1. clinical and sonographic characteristics of the surgical cavity.

Lumpectomy cavity dimensions	Statistics	Size (mm)
Depth determined by USG (mm)	Mean	12.40
	Lower Bound	10.62
	Upper Bound	14.18
Depth determined by clinical impression (mm)	Mean	29.14
	Lower Bound	25.60
	Upper Bound	32.69
Length determined by USG (mm)	Mean	43.03
	Lower Bound	39.36
	Upper Bound	46.70
Length determined by clinical impression (mm)	Mean	65.43
	Lower Bound	60.20
	Upper Bound	70.65
Width determined by USG (mm)	Mean	41.00
	Lower Bound	35.89
	Upper Bound	46.11
Width determined by clinical impression (mm)	Mean	64.86
	Lower Bound	59.43
	Upper Bound	70.28

USG: ultrasonography

Table 2. Pearson Correlation between ultrasound and clinical impression

	Correlation (r)	P-value
Width	0.274	P<0.01
Depth	0.304	P<0.01
Length	0.169	P<0.01

USG: ultrasonography
The value $r = 1$ means a perfect positive correlation and the value $r = -1$ means a perfect negative correlation. As can be seen, there is no positive correlation between dimensions measured by ultrasound and clinical method which is statistically significant for all dimensions ($p<0.01$).

DISCUSSION

In case of breast carcinoma, improvement in local control is caused to a large extent by dose escalation and the use of more advanced radiotherapy techniques. Radiation therapy boost field is required to fully encompass the lumpectomy cavity.

Two randomized trials have shown the benefit of boost radiation to the tumor bed after lumpectomy. Results of a randomized trial that was done by the Lyon Breast Cancer Trial showed that delivery of a boost of 10Gy to the tumor bed significantly reduces the risk of early local recurrence. At 5 years, 10 out of 521 patients (3.6%) who received a boost had a local relapse compared to 20 out of 503 (4.5%) who did not received a boost (p value = .044). After adjustment for the main prognostic variables, the relative risk was still significantly lower for the boost group (HR=0.3; 95% CI; range, 0.12 to 0.95) [4]. The results of the EORTC trial support the use of boost dose [3]. According to this study, 109 out of 2661 patients in boost dose arm and 182 out of 2657 patients in no boost arm developed local recurrence (p value < 0.001). Results of this trial indicated that a boost dose of 16Gy should be delivered to the lumpectomy cavity after 50Gy for whole breast irradiation (at least for patients younger than 50 years).

There are various methods of boost delivery including interstitial brachytherapy, cone-done photon boost and electron beam boost. The choice of the boost technique is dependent on the treating radiation oncologist preference. At our institution we prefer electron beam boost because of its ease of use and lower cost.

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Organ targeting is one of the critical steps in radiation treatment planning and a noninvasive, easy and rapid imaging technique for this purpose is ultrasound imaging. This imaging technique specifically has been used to a greater extent in prostate cancer brachytherapy than in other sites. For breast cancer radiotherapy, ultrasound can accurately locate the tumor bed and particularly can demonstrate the depth and size of the lumpectomy cavity.

Numerous studies have reported volume changes in the lumpectomy cavity. There is radial shrinkage and displacement of the lumpectomy cavity over time. Without adjusting for the changes in the cavity shape and location, a portion of the volume will be undertreated unless the margins of radiation treatment are increased. Empiric drawing of boost field according to surgical scar may result in under-dosage of tumor bed and normal tissue may receive unnecessary irradiation. In almost all of these studies, serial computed tomography scans have shown significant reduction in the size of the cavity with time; thus, a repeat simulation is necessary in order to exactly localize the lumpectomy cavity. These anatomic uncertainties decrease the accuracy of dose delivery to the target. On the other hand, smaller treatment volumes will result in reduced radiation toxicity. As can be seen in table 2, here we showed that there is no correlation between dimensions of lumpectomy cavity that determined by ultrasound and clinical measurements ($P<0.01$). This lack of correlation can represents a change in the location and dimensions of the lumpectomy cavity after surgery.

In a series of 53 early-stage postoperative breast cancer patients, Helyer and coworkers found that in 60% of patients, electron beam energy that was chosen by the clinically assessed measurements, was changed based on sonographic evaluation [5]. In another series, when electron beam energies that were selected on the basis of clinical evaluation were compared with an ultrasound measurement, the target volume was under-dosed in 21 of 30 patients [6]. In our study also in 88 % of patients, the depth of treatment and electron beam energy that were selected by clinical measurements were changed based on sonographic assessment. These findings are consistent with findings of studies that cited above.

On the contrary, other authors have shown that compared with radiographic evaluation of surgical clips, ultrasound significantly underestimates all 3 dimensions of the lumpectomy cavity and, therefore, underestimates volume at risk [7]. These authors concluded that ultrasound should not be used to guide the design of boost fields. In general, CT-based planning has superseded ultrasound assessment of chest wall thickness and localization of the internal mammary structures and the excision site. In a study conducted by Charles Leonard, they concluded that ultrasound can successfully be used to localize the biopsy site and facilitate boost field planning in patients treated with lumpectomy and radiation [8].

Our study shows that measurements of size, depth and dimensions of lumpectomy cavity that taken by clinical assessment are different with that can be obtained from ultrasound. This result is in agreement with results of other studies. As is shown in table1 and table 2, depth of lumpectomy cavity that was measured by ultrasound was significantly shorter than that clinically assessed ($P<0.01$). This finding may indicate an overestimation of the tumor depth as determined by clinical assessment, or vice versa, it may represent an underestimation of sonographic assessment of tumor depth. Only in 21 patients (60%) the lumpectomy cavity was located on the scar. Thus, the position of the scar cannot always be used to locate the primary tumor site. Ultrasonic guidance may offer an easily implemented solution to localizing the lumpectomy cavity [9].

Previous studies have indicated a relationship between CT and 3D-Ultrasound (3D-US) in the visualization and localization of the lumpectomy cavity [10].

CONCLUSION

In conclusion ultrasonic guidance was found more precise than simply use of surgical scar for visual placement of boost field. Ultrasound is

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useful tool for measurement of size of lumpectomy cavity and to determine its location and can be used for boost planning. It is easily available, non-invasive and inexpensive.

Conflicts of interest: *none to declare.*

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