Sonographic tomography for the preoperative staging of breast cancer prior to surgery

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KEYWORDS

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Abstract *Introduction:* This study is a preliminary retrospective analysis of a new imaging technique, sonographic tomography, for the determination of the exact extent of disease prior to definitive surgery for breast cancer.

Materials and methods: Forty-one women were diagnosed with breast cancer had preoperative staging using sonographic tomography, between August 2007 and June 2008. All these women subsequently underwent bilateral contrast-enhanced MRI prior to surgery to determine if there were areas of tumor extension, multifocality, axillary adenopathy, or contralateral disease that would affect their planned surgery. Both imaging techniques were then compared retrospectively for accuracy to pathologic truth.

Results: Sonographic tomography accurately staged breast cancer preoperatively in 68% of cases, while MRI did so in 54% of cases. The resulting improvement in overall accuracy is 14% (2–28%). Sonographic tomography appears non-inferior to contrast enhanced, bilateral breast MRI.

Conclusions: Further, prospective, study is needed to further evaluate this new imaging technique in preoperative staging prior to definitive surgery.

Sommario *Introduzione:* Scopo del presente lavoro è effettuare un'analisi preliminare retrospettiva di una nuova tecnica ad immagini, la TC ad ultrasuoni, utilizzata per determinare l'estensione della massa neoplastica mammaria, prima di decidere un'eventuale asportazione chirurgica.

Materiali e metodi: Nel periodo compreso tra agosto 2007 e giugno 2008, 41 donne con diagnosi di tumore mammario hanno avuto una stadiazione della neoplasia usando la TC a ultrasuoni. In seguito le pazienti sono state sottoposte a risonanza magnetica con mezzo di contrasto del seno per evidenziare ulteriori aree di estensione tumorale, la presenza di linfadenopatie del cavo ascellare, di multifocalità e di bilateralità, che avrebbero potuto compromettere l'intervento chirurgico. Entrambe le tecniche sono state poi comparate per confrontarne l'accuratezza.

Risultati: L'accuratezza della nuova tecnica, la TC ad ultrasuoni è stata del 68%, mentre quella della risonanza magnetica del 54%. L'incremento dell'accuratezza della diagnosi che ne è

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derivato è stato del 14% (2–28%). La TC ad ultrasuoni non appare, pertanto, inferiore alla risonanza magnetica.

Conclusioni: È necessario un ulteriore studio per meglio valutare la capacità e le prospettive di questa nuova tecnica nella fase pre-operatoria.

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Introduction

Conservative surgery is currently the treatment-of-choice for early-stage breast cancer. The survival rate is equivalent to radical surgery [1] and the psychological outcome is better [2,3]. However, there are challenges with conservative surgery. Up to 60% of patients require repeat surgical procedures [4–6] and attempts at conservative therapy can fail when unappreciated, extensive disease necessitates eventual mastectomy, because clear margins cannot be obtained despite multiple re-excisions [4]. This can result in an overall higher cost and longer time-to-remission.

Preoperative staging using contrast-enhanced magnetic resonance imaging (MRI) prior to definitive surgery has been shown to decrease the number of surgical procedures to obtain clear margins [7]. It can also detect additional foci of cancer that may result in a change in surgical management [7–9], accurately identify patients who are not candidates for conservative surgical management [10] and possibly reduce the rate of recurrence following conservative surgery [11].

While MRI has many advantages, it also has several disadvantages including a relatively low specificity, which requires that positive MRI findings be evaluated by an additional biopsy prior to a change in surgical plan [7,12]. This results in a relatively high cost, due to the necessity of both imaging and the subsequent confirmatory biopsy. The requirement for a biopsy to confirm the MRI finding also introduces a time delay between the imaging session and definitive surgery. Additionally, imaging using MRI requires that the patient be placed in the prone position, which makes localization of the tumor during surgery more difficult, as surgery is done in the supine position. MRI can also be contraindicated in patients who are pregnant or who have metallic implants and requires use of a contrast agent which can have side effects.

This paper describes the use of a new technique, sonographic tomography (ST), for preoperative staging in women with breast cancer. Sonographic tomography images the breast using an automated ultrasound probe which obtains a $14 \times 17 \times 5$ cm three-dimensional image dataset (termed a volume). During ST, 4–6 volumes are obtained to image the entire breast and axilla, and these volumes are reformatted into coronal tomographic slices for interpretation. Findings observed on coronal view are further evaluated using spot views in transverse, sagittal, radial or anti-radial orientations. ST is currently indicated for diagnostic purposes as an adjunct to mammography, however, if ST were to perform equivalently to MRI for preoperative staging it would have several other advantages. ST is less expensive, uses no contrast agents, and is performed with the patient in the supine position so the lesions may be more readily found during surgery. This study aims to

evaluate ST as a tool for preoperative staging compared to MRI.

Materials and methods

This study is a retrospective review of 41 women diagnosed with breast cancer by vacuum-assisted percutaneous biopsy between 8/1/2007 and 6/10/2008 in an outpatient clinic setting.

Women included in this review were initially referred for radiographic or clinical abnormalities that required further evaluation. All underwent a diagnostic work-up for these abnormalities that included bilateral mammography and, for those that required further ultrasound evaluation; bilateral sonographic tomography was used beginning in July 2007 when our clinic acquired a Somo.VTM automated breast ultrasound system (U-Systems, San Jose, CA). Women with suspicious (BI-RADS 4-5) [13] lesions then proceeded to vacuum-assisted biopsy. Forty-one women, on biopsy, were found to have malignant lesions and prior to definitive surgery, underwent bilateral, contrast-enhanced MRI, which is the standard preoperative staging method at our facility.

After 10 months of experience, the ST and MRI imaging findings of the 41 women with breast malignancies who had undergone both imaging techniques were reviewed retrospectively and compared to pathologic truth.

Tomographic technique

Sonographic tomography was performed using the Somo.VTM automated breast ultrasound system (U-Systems, San Jose, CA), in the supine position with the back of the hand on the forehead. A $14 \times 17 \times 5$ cm automated scanning probe was used to obtain three-dimensional ap, lateral, medial, and axillary volumes. Women with large breasts were additionally imaged using superior and inferior volumes. Each volume was then reformatted into coronal tomographic slices 2 mm thick with 50% overlap and viewed from the skin to the chest wall using a separate workstation. Findings seen on the coronal slices were confirmed on two orthogonal spot views (i.e., transverse and sagittal view or radial and anti-radial views).

MRI technique

MRI imaging was performed using a GE Signa 1.5 Tesla short-bore MRI (GE Healthcare, Piscataway, NJ) in the prone position using an Invivo 1.5T Biopsy Breast Array Coil — Model BBC (8 channel) (Invivo, Orlando, FL). Images were analyzed using the GE VIBRANT imaging technique for simultaneous bilateral study.

Physiologic (enhancement curve) imaging

Images were obtained before and at 0, 1, 2, 3, 4, 5, and 6 min post-injection of 20 cc gadolinium (Magnevist – Bayer HealthCare Pharmaceuticals, Berkeley, California). T1 weighted, sagittal images were then obtained with thin sections through areas of interest (2–3 mm), if needed. Subtraction images were used to generate enhancement curves using an independent workstation with CADstream software (GE Healthcare).

Anatomic imaging

Axial and coronal Short T1 Inversion-Recovery (STIR) images were obtained using the Invivo Biopsy Breast Array Coil, after completion of CADstream processing to obtain anatomic information for the breast and axilla.

Evaluation of staging accuracy

For the purposes of this study, not every suspicious (BI-RADS 4-5) imaging finding was considered positive. Only those findings that, if confirmed pathologically prior to surgery, would have resulted in a significant change in surgical management, were considered positive. A significant change in surgical management would include conversion of a unilateral procedure to a bilateral procedure, conversion of a conservative procedure to a mastectomy or vice versa, or extending a lumpectomy more than 2 cm beyond the original planned diameter of resection.

Tomographic findings considered suspicious (BI-RADS 4-5) [13]

In the breast, tomographic findings that were considered suspicious were hypoechoic lesions or areas of architectural distortion on coronal projection seen on at least 2 volumes which were found to be a solid or complex mass on transverse view and found to be suspicious by Stavros' criteria on two orthogonal views (i.e., transverse and sagittal view or radial and anti-radial view [14]).

In the axilla, tomographic findings that were considered suspicious were hypoechoic lesions within a space bounded by the clavipectoral fascia, latissimus dorsi muscle, chest wall and axillary vein seen on coronal view, or lesions found to be suspicious by Stavros' criteria on transverse and sagittal view [15].

Tomographic findings considered positive

Tomographic findings that were considered positive were as follows.

- Extension – suspicious breast findings >2 cm beyond mammographic extent of disease.
- Multifocality – suspicious breast findings >2 cm away from identified primary tumor.
- Lymph node involvement – suspicious findings within 1 or more lymph nodes.
- Contralateral disease – suspicious breast or nodal findings present on the contralateral side.

MRI findings considered suspicious (BI-RADS 4-5) [13]

In the breast, MRI findings that were considered suspicious were >100% enhancement, Peak or Plateau-type enhancement with rapid wash-in and wash-out, lesions that were

Table 1 Cancer histology.

Cancer type	Number of cases
Ductal carcinoma in situ (DCIS)	6
Invasive ductal carcinoma (IDS)	29
Invasive lobular carcinoma (ILC)	6

>5 mm in diameter or with malignant type anatomic characteristics [16].

In the axilla, suspicious MRI findings included generalized lymph node enlargement, cortical asymmetry and loss of hilum visible on axial and coronal STIR images.

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Accuracy index

Each patient was assessed for staging accuracy of all findings using both imaging techniques. Each imaging technique was then compared to pathologic truth. The preoperative staging imaging study was then determined to be accurate if the following criteria were met.

- (1) Imaging extension = pathologic extension AND
- (2) Imaging multifocality = pathologic multifocality AND
- (3) Imaging LN involvement = pathologic LN involvement AND
- (4) Imaging contralateral disease = pathologic contralateral disease (if pathology is available).

Any disagreement between an imaging finding and pathologic truth is considered indicative that the imaging technique is inaccurate.

For each imaging study, an accuracy index was computed as the number of cases that were accurately staged using that imaging modality divided by the total number of cases.

Table 2 Pathologic stage^a.

Stage	Number of cases
0	6
1	12
2	15
3	4

^a AJCC version 6 (18).

Table 3 Accuracy by Finding.

Site	Histologic finding		Total N	Accuracy		Accuracy improvement	Statistically significant?
	Positive	Negative		Tomography	MRI		
Lymph node	14	23	37 ^a	27/37	21/37	16% (1–31%)	Y
Extension	3	25	28 ^b	26/28	28/28	–7% (–17 to 3%)	N
Multi-focality	11	30	41	38/41	37/41	3% (–6 to 10%)	N
Contralateral	4	3	7 ^c	4/7	4/7	0%	N

^a Four patients – did not have an axillary staging procedure.

^b Thirteen patients – tumor diameter could not be assessed by mammography.

^c Thirty-four patients – did not have contralateral surgery.

In a number of cases there were missing pathologic data which could not be used in the assessment of staging accuracy (e.g., contralateral surgery was not performed or extension could not be assessed). In these cases, the imaging findings corresponding to those missing pathologic findings were not included in the determination of accuracy for that individual. As an example, if a subject in the study did not have contralateral surgery, then the accuracy of her imaging studies would be based on the imaging findings and pathologic truth for extension, multifocality, and lymph node involvement alone. Contralateral imaging findings would not be used, as pathologic truth is not available.

Statistical analysis

The accuracy index was determined for both imaging techniques and the difference in index rates was computed. The 95% confidence interval for the difference of these paired proportions was then calculated using the Scores method [17].

A statistically significant result ($p < 0.05$) using the Scores method occurs when the lower bound on the 95% confidence interval is greater than the accuracy index of the least accurate imaging technique.

Results

This study retrospectively evaluates the accuracy of sonographic tomography (ST) compared to MRI in 41 women, ranging in age from 33 to 91 years, who were diagnosed with breast cancer by needle biopsy between 8/1/2007 and 6/10/2008. Twenty-nine women had invasive ductal carcinomas, six had ductal carcinoma *in situ* (DCIS) and six had invasive lobular carcinoma (Table 1). Although most women had stage 1 and 2 cancers, six patients had DCIS and four were stage 3 at diagnosis (Table 2).

The accuracy of the two imaging methods was compared to pathologic truth, as shown in Table 3. Of the 41 women evaluated in the study, lymph node histology was available in 37, with 14 being found to have metastatic nodal involvement. Preoperative lymph node staging was found to be accurate in 27 of 37 women evaluated by ST and in 21 of 37 women and evaluated by MRI. This represents an improvement in accuracy of 16% (1–31%) for ST over MRI.

In 28 women, extension of the cancer more than 2 cm beyond the mammographically visible diameter of disease was present in three out of 28 patients. MRI was superior in the evaluation of extension, with all 28 women being accurately assessed. ST was inaccurate in two out of 28

cases, for an overall accuracy of 7% below that of MRI. This result is not significant, however, due to the small sample size. In the evaluation of multifocal disease ST and MRI were essentially equivalent with 38 of 41 and 37 of 41 women being accurately assessed. Similarly, for contralateral disease, ST and MRI were equivalent with the accurate staging of 4 of 7 women in each group.

The overall accuracy for ST was 68% with 28 of 41 cases being accurately assessed compared to 54% for MRI with accurate staging in 22 of 41 cases (Table 4). This yields an overall improvement in accuracy with ST of 14%, with 95% confidence intervals ranging from 2 to 28%.

Discussion

Preoperative staging has the potential to improve breast cancer outcomes by decreasing the number of operative procedures necessary to achieve remission, thereby decreasing operative complications and cost. An accurate staging method may also decrease the likelihood of eventual recurrence. Moreover, it provides women with cancer better information with which to make decisions regarding their surgical therapy. The decrease in the number of operative procedures would occur as a result of decreasing the probability of obtaining positive margins at the initial resection. Also, a good preoperative staging methodology would decrease poor outcomes such as failed conservative therapy, where multiple attempts at resection fail to achieve clear margins, leading to eventual mastectomy.

In order to accomplish these goals, any preoperative staging method must have high sensitivity thereby allowing reliable detection of abnormalities that would change the surgical plan, and have high specificity, thereby allowing the surgeon to change the surgical plan without the need for confirmatory needle biopsy of imaged abnormalities prior to surgery.

Currently MRI is the established method for preoperative staging and it is highly sensitive, especially for DCIS. However, it has relatively low specificity, high expense and the requirement for intravenous contrast agents.

Table 4 Overall accuracy.

MRI	Sonographic tomography	Improvement using tomography
22/41 cases (54%)	28/41 cases (68%)	15% (95% CI = 2–28%)

Our data show that ST is non-inferior to MRI for the preoperative staging of women with breast cancer diagnosed by needle biopsy. Most of this improvement in accuracy comes from a better appreciation of whether or not women with breast cancer have positive nodes. Additionally, our data suggest that extension of disease may be better evaluated by MRI (although this data is not statistically significant). If in the future, extension is shown to be better evaluated by MRI, then the combination of the two techniques would maintain the sensitivity of MRI, while improving specificity. We recognize that there are several limitations of this study, first of which is that the number of cases is small. Further prospective data will be required to fully assess the utility of this new imaging technique.

Conflict of interest statement

The authors have no conflict of interest.

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