

Pre-operative ultrasound for breast tumour measurements: is there potential for mismanagement?

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SUMMARY: Pre-operative ultrasound for breast tumour measurements: is there potential for mismanagement?

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The pre-operative size of breast tumour is the most important factor in determining feasibility of breast conserving surgery in operable breast cancer. Currently there is no consensus on the most accurate modality to measure tumour size. A prospective study of consecutive and unselected symptomatic patients with invasive breast cancer who had primary surgery between January 2006 and December 2007 was conducted. Patients with multi-focal and multi-centric tumours were excluded. The aim of this study was to find the correlation between histological size of invasive breast cancer and pre-operative tumour size as measured by ultrasound. Over this two year period, data for 192 patients was analysed for this study. The mean tumour diameter on ultrasound and histology was 19.5mm and 29mm respectively. The difference between the means in the two modalities was found to be statistically significant ($P < 0.001$). Ultrasound underestimates the true size of breast tumours as determined histologically. Inaccurate tumour size measurements may result in re-operations to achieve adequate margins.

RIASSUNTO: Valutazione ecografica preoperatoria delle dimensioni del tumore mammario: c'è rischio di inappropriatelyzza?

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Le dimensioni del tumore sono il fattore più importante nel determinare la fattibilità di un intervento chirurgico conservativo della mammella nel carcinoma mammario. Al momento non esiste un consenso sulle modalità più precise per misurare le dimensioni del tumore. È stato condotto uno studio prospettico di pazienti sintomatiche, consecutive e non selezionate, con cancro mammario invasivo sottoposte a chirurgia primaria tra gennaio 2006 e dicembre 2007. Sono state escluse le pazienti con tumori multifocali e multicentrici. Lo scopo era di verificare la correlazione tra le dimensioni del carcinoma asportato e le dimensioni del tumore misurate mediante ultrasuoni. Sono stati analizzati pre-operatoriamente i dati di 192 pazienti. Il diametro medio del tumore agli ultrasuoni e all'istologia era di 19,5 mm e 29 mm rispettivamente. La differenza tra le medie è risultata statisticamente significativa ($p < 0,001$). L'ecografia sottovaluta le dimensioni del tumore. L'incorretta misurazione può esitare in re-interventi per ottenere margini di resezione adeguati.

KEY WORDS: Operable breast tumours - Size - Pre-operative ultrasound - Breast conserving surgery.
Tumore mammario operabile - Dimensioni - Ecografia pre-operatoria - Intervento conservativo.

Introduction

The size of breast tumour plays a critical role in determining both the staging and the treatment of breast cancer. Pathologic tumour size remains the reference standard. Some therapeutic decisions however must be made on the basis of the pre-operative tumour size. This is the

most important factor in determining feasibility of breast conserving surgery in operable breast cancer.

Tumours smaller than 4 cm are considered suitable for breast conserving surgery, while those greater than 4cm in diameter are usually best treated by mastectomy or neo-adjuvant therapy followed by breast conserving surgery if a good response has been obtained.

There is no consensus either on the accuracy of ultrasound or the most suitable modality of measurement. The modalities available for estimating the pre-treatment tumour size include clinical measurement, mammography, Magnetic Resonance Imaging (MRI), Computerised Tomography (CT) scan, and Ultrasound. Some studies have endorsed ultrasound as best form of tumour measurement

(1-3) while others support the use of mammography, and more recently magnetic resonance imaging.

Ultrasound is routinely used in the evaluation of a new breast lump as part of triple assessment. It is non-invasive, rapid and has good patient compliance. Ultrasound permits direct imaging of the tumour, free from magnification and allows multiplanar measurement. In addition, ultrasound assessment may be used as an adjunct to clinical examination in outpatients by breast surgeons. Ultrasound is also of value in performing fine needle aspiration for cytology and in preoperative localization of non-palpable solid lesions.

Underestimation of pre-operative tumour size in a patient who has had breast-conserving surgery may necessitate a second operation that would be a mastectomy or re-excision. Such patients if assessed accurately could have neo-adjuvant therapy, and mastectomy could be avoided (4,5).

Aims and objectives

The aim of this prospective study was to find the correlation between histological size of invasive breast cancer and pre-operative tumour size as measured by ultrasound, and to study its influence on patient management since inaccurate tumour measurements preoperatively result in inadequate surgery.

Patients and methods

Patients

We designed a prospective study of patients with symptomatic, invasive breast carcinoma, who were treated primarily by surgery from 2006 to 2007. All measurements were graded according to AJCC (American Joint Committee on Cancer). Only symptomatic patients were included since a third of screen detected patients have microcalcification which cannot be detected on ultrasound and are mostly T1 tumours. Patients with multi-focal and multi-centric tumours were excluded. Data from 192 patients who met the criteria for this study was analysed.

Methods

Ultrasound was performed by breast radiologists prior to breast biopsy. The results of breast imaging and histology were discussed in the local breast multidisciplinary meeting. A comparison was made between the pre-treatment ultrasound size and the histological size of the invasive carcinoma. An independent statistician analysed the data. All graphs and analysis were produced using the statistical software package Stata (version 9.2) (StataCorp LP, 4905 Lakeway Drive, College Station, TX 77845, USA).

Results

Between 2006 and 2007, 192 symptomatic patients with invasive carcinoma on histology were included in

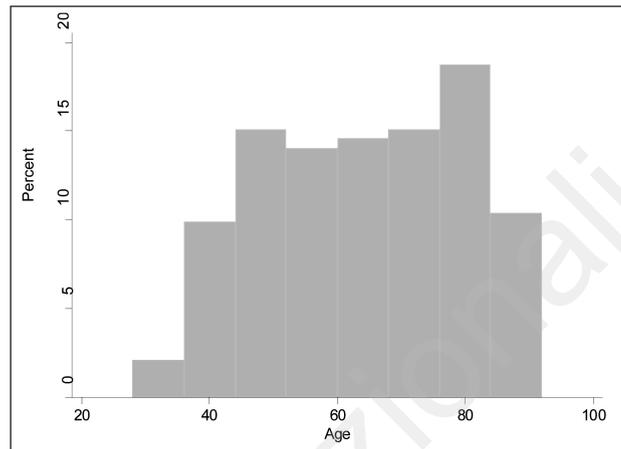


Fig. 1 - Distribution of age of patients with breast carcinoma.

the study. The age range was 28 to 92 years. The mean age was 63 with a standard deviation of 15 years. The distribution of the age of the patients is shown in Figure 1. Of the 192 patients, 86 patients has primary mastectomy and 106 had breast conserving surgery. 164 patients (85%) had invasive ductal carcinoma, 19 patients had invasive lobular carcinoma, 5 had mucinous carcinoma, and 4 had mixed tumours. In 36 patients the tumour was grade 1, in 97 it was grade 2, and in 59 it was grade 3. Lymph node involvement was seen in 84 patients, and lymphovascular invasion was seen in 68 patients. The range of tumour diameter on ultrasound was 4 mm to 70 mm, and on histology it was 2.6 to 165 mm. Distributions of the ultrasound and histology values are positively skewed as shown in Figure 2 and Figure 3 respectively. Figure 4 shows a normal distribution of the difference in measurements on ultrasound and histology. Therefore, the paired t-test was also used to compare the mean of the two sets of values. The mean tumour diameter on ultrasound was 19.5 mm and on histology was

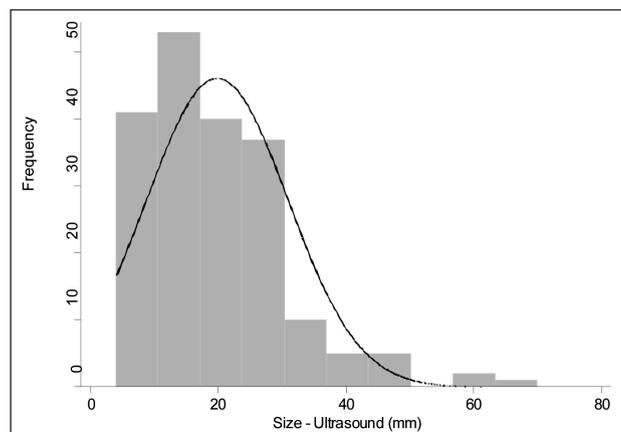


Fig. 2 - Distribution of ultrasound size.

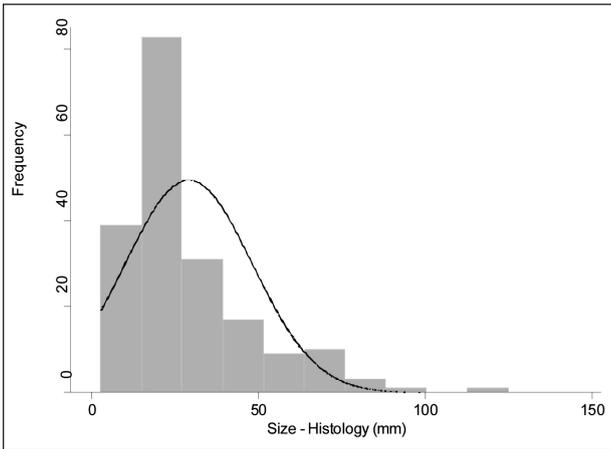


Fig. 3 - Distribution of histological size.

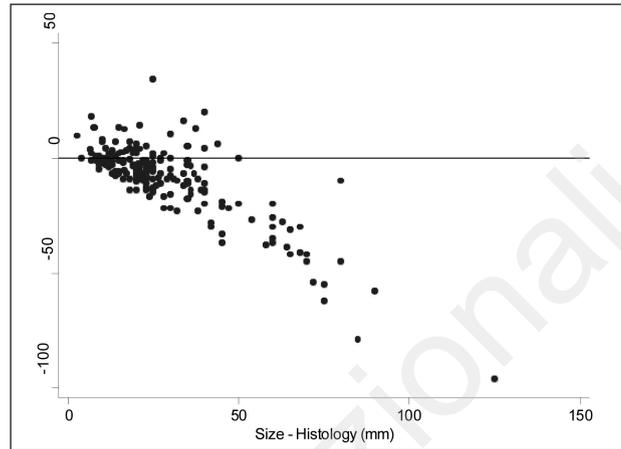


Fig. 5 - Box-plot of the ultrasound and histological size of breast tumours.

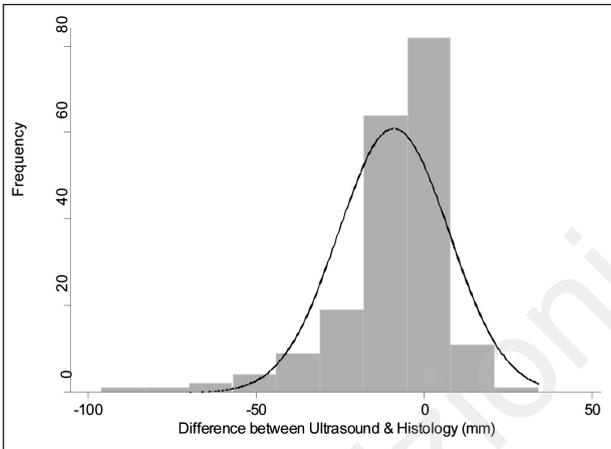


Fig. 4 - Distribution of the difference in size of the ultrasound and histological size of breast tumours.

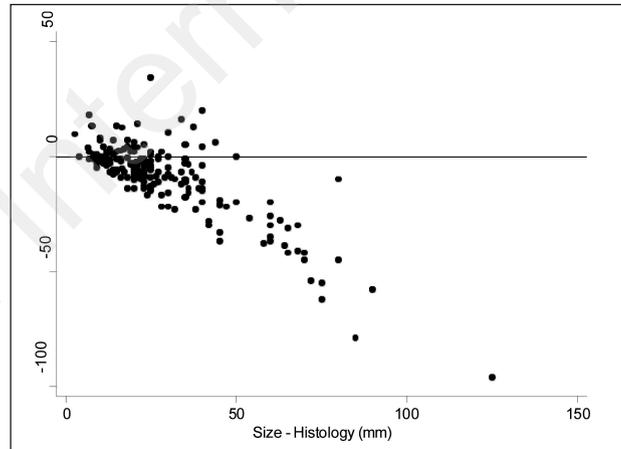


Fig. 6 - Scatter plot showing the relationship between the histology size and the difference in sizes between ultrasound and histology for all tumours.

29 mm (Fig. 5). The difference between the means of the ultrasound and histology was -9 (95% CI; p-value of <0.001). The difference between histology and ultrasound increases with increased tumour size for all tumours (Fig. 6) and for invasive ductal carcinoma. The Pearson correlation test gave a correlation of -0.76 for the relationship between histology size and the difference between histology and ultrasound size (p-value <0.001) implying a strong negative association between the two variables.

The mean tumour size for invasive lobular cancers was 17mm on ultrasound and 31 mm on histology. The mean tumour size was 19.4 mm on ultrasound and 26.4 mm on histology for invasive ductal carcinomas. Of the 164 patients with invasive ductal carcinoma, 155 patients had tumour size less 40mm on ultrasound. Of these patients, 32(20%) patients had a histological size more than 40mm. The mean tumour diameter on mammogram was

20mm (range 5 to 130 mm), indicating that the accuracy of this modality is not better than ultrasound in determining tumour size.

A total of 113 patients had tumour size less than 20 mm on ultrasound; however 43 of these were pT2 on histological staging (38%); 71 tumours were between 20-40 mm on ultrasound and of these 22 (30%) were greater than 40 mm on histology i.e., pT3 and pT4 (Table 1).

Based on final histology and multi-disciplinary team decision, a total of 15 patients underwent re-operation (7.8%). All these patients had invasive tumour in the margins. In this group 10 patients required mastectomy and 5 had re-excision as a second operative procedure. In patients who had re-operation, the mean ultrasound size was 18.6 mm whereas the mean histologic size was 37 mm and ultrasound underestimated the size in 12 out of 15 patients (80%).

TABLE 1 - ULTRASOUND AND HISTOLOGICAL SIZE OF INVASIVE BREAST CANCERS.

Ultrasound Size	Histological Size		
	<20 mm	20-40 mm	>40 mm
<20 mm (n=113)	63	43	7
20-40 mm (n=71)	9	40	22
>40 mm (n=8)	0	5	3

Discussion

There does not appear to be concordance between ultrasonographic dimensions and histological tumour size in both T₁ and T₂ tumours. This may not matter so much with T₁ tumours as these would still have been treated by breast conserving surgery. However, T₂ tumours may be inappropriately treated in the first instance by breast conserving surgery due to the underestimation of tumour size. These patients subsequently may require a second operative procedure, which may be mastectomy. This small cohort of patients may have been better treated by neo-adjuvant chemotherapy or hormonal therapy, if the correct tumour size was known pre-operatively. The main aims of neo-adjuvant chemotherapy are to achieve operability in locally advanced breast cancer and to improve the breast conservation rate in operable breast disease. The Royal Marsden trial clearly demonstrated the downstaging role of neo-adjuvant chemotherapy with a reduction in the mastectomy rate from 22% to 10 % (6). Downsizing of the tumour with neo-adjuvant therapy would then avoid a mastectomy.

A second operative procedure is not without its disadvantages. Additional procedures for residual cancer can increase the risk of wound infection; delay the initiation of adjuvant chemotherapy and radiation therapy, increase post operative anxiety and result in worse aesthetic outcomes (7,8). Local recurrence is generally lowest in patients who have clear margins after their first procedure and higher in patients with initially nonnegative margins who are converted to clear margins by re-excision (9).

Although diagnosis of breast cancer had a negative impact on the psychology of all patients, those undergoing breast-conserving surgery or mastectomy with delayed reconstruction were more satisfied and reported a lower impact on their self-esteem and sexual life versus those who only had mastectomy (10).

While one study has shown that ultrasound underestimated tumours greater than 30 mm², another has shown the ultrasound underestimated all tumours⁵. Accuracy rates have ranged from 58% to 95%³. One study has shown that 83% of invasive ductal tumours and 100% of tumours fell within a 1 cm and

2cm extension respectively of the ultrasound measured tumour size (1).

With larger tumours, ultrasound and clinical measurement have equivalent accuracy in measuring tumour size. This could be due to the limitations of ultrasound. Tumours larger than the diameter of the ultrasound probe (which is mostly 40mm) are not measured accurately. Also presence of extensive DCIS or invasive lobular carcinoma makes ultrasound measurement inaccurate. The accuracy also depends on the operator experience and the equipment used. Accuracy has ranged from 58-95% (7,8).

Presence of blurred margins or 'halo' on the monitor can cause difficulties in accurately determining tumour size. Higher frequency transducers have improved resolution but allow a smaller field of vision and reduced tissue penetration (3). Other limitations include artefacts, shadowing, reverberation, refraction and restriction of the width of image field to 4 cm at 1.5 cm depth.

Advances such as high frequency transducers, microbubble contrast agents, harmonic and compound three-dimensional imaging all carry promise of further increases in ultrasound utility in the accurate diagnosis and detection of breast disease. To improve correlation between pre-treatment tumour size and histological size a combination of modalities have been suggested. One such is the formula put forth by Pain et al (5): Pathological size = 0.5* mammographic size + 0.5* size by physical examination. Another one is by Bosch et al¹¹: Pathological tumour size (mm) = sonographic tumour size (mm) + 3 mm.

MRI has shown to be accurate and reliable size measurement and assessing focality (11,12). The National Institute of Clinical Excellence (NICE) recommends offering MRI of the breast to patients with invasive lobular cancer if breast conserving surgery is being considered. But NICE does not recommend the routine use of pre-operative MRI in invasive breast cancer.

In our study though the discrepancy between the ultrasound and histology was greater in invasive lobular carcinomas, MRI can be used to improve the accuracy of the pre-operative size in keeping with NICE guidelines. But for invasive ductal cancers which represents 85% of all tumours in our study the underestimation of size on ultrasound continues to be a serious problem.

Conclusion

Ultrasound underestimates the size in both T1 and T2 tumours. Underestimation of pre-operative tumour size in a patient who had breast-conserving surgery may necessitate a second operation and that could be a mastectomy. If such patients were assessed accurately for tu-

mour size, they could have neo-adjuvant therapy and avoided a second operation. Using MRI or a combination of modalities has shown promise in improving the accuracy of tumour size measurement.

Conflict of interest: the authors declare there is no conflict of interest.

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