

# Estimation of tumor size in breast cancer comparing clinical examination, mammography, ultrasound and MRI – correlation with the pathological analysis of the surgical specimen

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**Background:** To evaluate the best method in our center to measure preoperative tumor size in breast tumors, using as reference the tumor size in the postoperative surgical specimen. We compared physical examination *vs.* mammography *vs.* resonance *vs.* ultrasound. There are different studies in the literature with disparate results.

**Methods:** This is a retrospective study. All the included patients have been studied by clinical examination performed by gynecologist or surgeon specialists in senology, and radiological tests (mammography, ultrasound and magnetic resonance imaging). The correlation of mammary examination, ultrasound, mammography and resonance with pathological anatomy was studied using the Pearson index. Subsequently, the results of such imaging tests were compared with the tumor size of the infiltrating component measured by anatomopathological study using a student's *t* test for related variables. The level of significance was set at 95%. Statistical package R. was used.

**Results:** A total of 73 cases were collected from October 2015 to July 2016 with diagnosis of infiltrating breast carcinoma. Twelve cases of carcinoma in situ and seven cases of neoadjuvant carcinoma are excluded. Finally, a total of 56 cases were included in the analysis. The mean age of the patients is 57 years. The histology is of infiltrating ductal carcinoma in 46 patients (80.7%), lobular in 8 (14%) and other carcinomas in 3 cases (5.2%). We verified the relationship between preoperative tumor size by physical examination, mammography, ultrasound (US) and magnetic resonance imaging (MRI), and the final size of the surgical specimen by applying a Pearson correlation test. A strong correlation was found between the physical examination results 0.62 (0.43–0.76 at 95% CI), ultrasound 0.68 (0.51–0.8 at 95% CI), mammography 0.57 (0.36–0.72 at 95% CI) and RM 0.51 (0.29–0.68 at 95% CI) with respect to pathological anatomy. The mean tumor size of the surgical specimen was 16.1 mm. Mean of tumor size by physical examination was 12.1 mm ( $P < 0.05$ ), by 14 mm US ( $P < 0.05$ ), by mammography of 14.3 ( $P < 0.05$ ) and by MRI of 22.53 mm ( $P > 0.05$ ).

**Conclusions:** Ultrasonography is the best predictor of tumor size in breast cancer, compared with clinical examination, mammography, and resonance. Our work could help the decision-making process such as the type of conservative surgery, the possible need for oncoplastic surgery or the decision to start treatment with neoadjuvant therapy, in patients with unifocal tumors.

**Keywords:** Breast cancer; tumor size; ultrasound (US); magnetic resonance imaging (MRI); mammography

Submitted Jan 10, 2017. Accepted for publication Feb 20, 2017.

doi: 10.21037/gs.2017.03.09

View this article at: <http://dx.doi.org/10.21037/gs.2017.03.09>

## Introduction

Estimation of tumor size is basic in order to decide the type of treatment in breast cancer: mastectomy or lumpectomy, or if it is necessary to start with neoadjuvant chemotherapy (NAC). For decision making in clinical practice we rely on clinical examination and imaging tests, which are mammography, magnetic resonance imaging (MRI) and ultrasound (US). Mammography has always been considered the gold standard for diagnosis and to know the tumor size, but in recent years high resolution US and MRI have been strongly incorporated. These imaging techniques inform about the size of the lesion in order to choose the best treatment for the patient, always taking into account that the size of the lesion is given in the final pathologic examination (surgical specimen in millimeters).

Mammography has the disadvantage of being less accurate in high density breast (young age), but it is very useful in patients with microcalcifications (1). The use of digital mammography and 3D tomosynthesis mammogram has greatly improved the sensitivity of these techniques (2). MRI has a high sensitivity but low specificity, as it tends to overestimate lesion size, but it is very useful to discover multicentricity (3,4).

High definition US is a not expensive and it is also a simple technique, but it is operator dependent. It has the advantage of detecting non-palpable lesions in the operating room avoiding the use of wires or radioguided occult lesion localization (ROLL).

There are numerous studies comparing mammography, US and MRI between them and separately, with disparate results. Some studies report that US is better than MG (4,5). Other studies report that MRI is superior to that of the MG and the US (6,7).

We do not want to check which the best diagnostic method is. The aim of this study is to compare tumor size estimated by clinical examination and new imaging techniques (3D tomosynthesis mammography, US high resolution, MRI) with the tumor size (in millimeters) in surgical specimen, in order to assess which is the most accurate method to know the “true” tumor size.

## Methods

We retrospectively collected cases of breast cancer from November 2015 to July 2016 in our center. All patients were diagnosed using Core-biopsy. The mean age and histological type of tumor in all patients is recorded. Ductal carcinoma in situ (DCIS) and patients who underwent NAC were excluded.

All patients were studied by: clinical examination performed by senology expert gynecologist or surgeon, with measure ruler, mammography 3D tomosynthesis, high resolution US (General Electric Logiq9), and MRI. Surgical specimens were studied by the same pathologist.

Correlation with tumor size was studied calculating Pearson correlation index. A Wilcoxon signed-rank test was applied to measure differences between values obtained with each of the techniques versus real tumor size. The concordance correlation (Lin, 1989) coefficient is a useful index to evaluate precision and accuracy of different diagnosis techniques. It adds a bias correction to the Pearson coefficient that measures how far the best-fit line deviates from the 45° line through the origin. Lin's index was calculated for each of the techniques. Level of significance was set at 95% ( $P=0.05$ ). R studio software was used for statistical calculations (RStudio v.0.99.879: integrated development environment for R. R studio, Inc., Boston, MA, USA 2015).

## Results

A total of 73 cases were collected from October 2015 to July 2016 with diagnosis of invasive breast carcinoma. Twelve cases of DCIS and seven patients who underwent NAC were excluded. We also excluded three cases with positive margins. Finally, a total of 56 cases were included in the analysis. Excision of the lesions was guided either by US (even if palpable), wire or ROLL. The mean age of the patients was 57 years.

Histological types were invasive ductal carcinoma (IDC) in 46 patients (80.7%), invasive lobular carcinoma (ILC) in 8 (14%), and other carcinomas in 3 cases (5.2%).

When comparing mean values in each of the diagnostic techniques *vs.* tumor size (16 and 10 mm), a significant higher value was observed with MRI (22 and 53 mm). No significant differences were observed with clinical exploration, US and mammography, 12,17; 14,5 and 14,32 respectively (*Table 1*).

All diagnostic techniques showed a significant association with tumor size when Pearson coefficient was calculated.

Pearson correlation results were the following: for the physical exam 0.62 (0.43–0.76; 95% CI), for US examination 0.68 (0.51–0.8; 95% CI), for mammography 0.57 (0.36–0.72; 95% CI), and for MRI 0.51 (0.29–0.68; 95% CI), compared to surgical specimen examination by pathologist (*Figure 1*).

Lin's index was 0.65 for US and 0,55; 0,57 and 0,41 for mammography, physical exam and MRI respectively, indicating that sonography was more precise than the other techniques (*Table 2*).

**Table 1** Mean values (mm) in each of the diagnostic techniques versus tumor size

Diagnostic tool	Mean	P
Clinical exam.	12.17	>0.05
Ultrasound	14.5	>0.05
Mammography	14.32	>0.05
MRI	22.53	<0.05

MRI, magnetic resonance imaging.

Bland-Altman plots shows distribution of differences observed with each diagnostic technique compared with infiltrative component of biopsies (*Figure 2*).

## Discussion

There are several studies that compare the accuracy of MM, US and MRI to predict tumor size (3–11). These studies are summarized in *Table 3*.

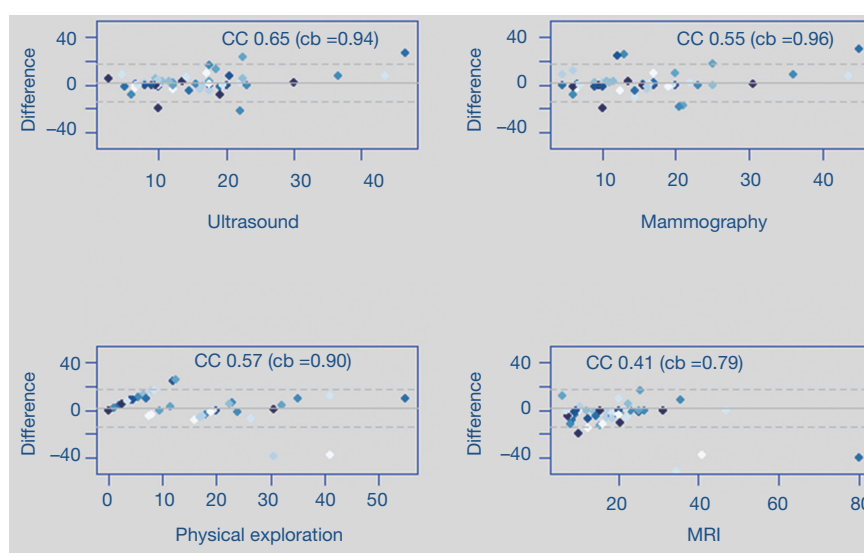
In one of the most recent study, Leddy *et al.* (9) consider that the MRI overestimates tumor size and measurements obtained with US and MM are more accurate independently of breast density, and the US was superior to MM to predict the tumor size.

In our study US was considered the best predictor of tumor size in breast cancer, comparing with clinical examination, mammography, and MRI. We also observed that MRI significantly overestimated the lesion size. These

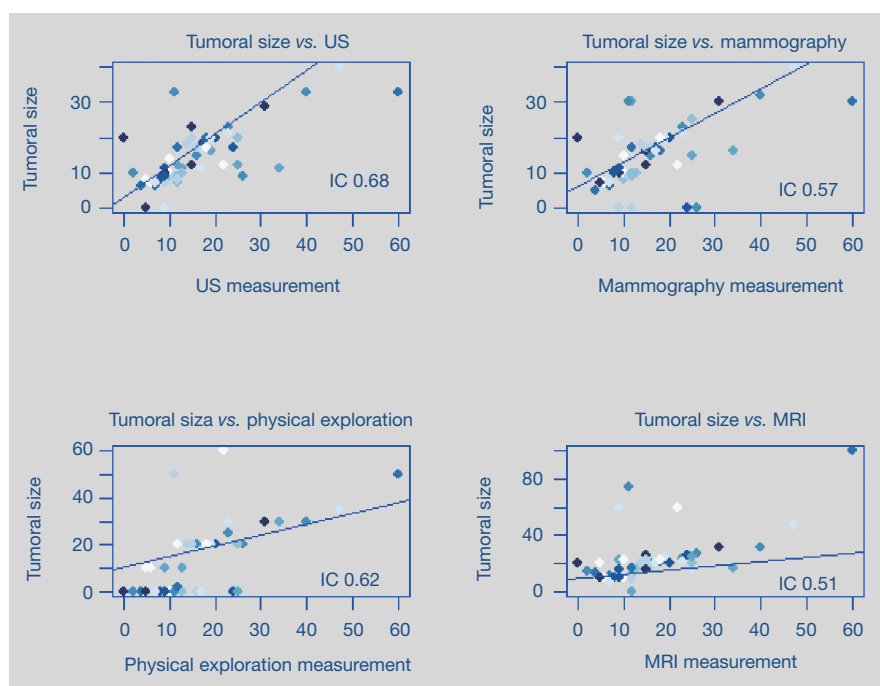
**Table 2** Lin's coefficient of every diagnostic tool

Diagnostic tool	Lin's coefficient	95% CI
Ultrasound	0.65	0.48–0.77
Mammography	0.55	0.35–0.71
Clinical exam	0.57	0.39–0.71
MRI	0.41	0.23–0.57

MRI, magnetic resonance imaging.



**Figure 1** Pearson correlation results compared to surgical specimen. MRI, magnetic resonance imaging.



**Figure 2** Bland-Altman plots observed with each diagnostic technique compared with infiltrative component of biopsies. MRI, magnetic resonance imaging; US, ultrasound.

**Table 3** Studies that compare the accuracy of MM, US and MRI to predict tumor size

Study	Compares	Result
Hieken <i>et al.</i> , 2001	MM vs. US	MM > US
Madjar <i>et al.</i> , 1993	MM vs. US	MM > US
Lehman <i>et al.</i> , 2007	MM vs. US	US > MM
Fasching <i>et al.</i> , 2006	MM vs. US	US > MM
Boetes <i>et al.</i> , 1995	MM vs. US vs. MRI	MRI
Wasif <i>et al.</i> , 2009	MM vs. US vs. MRI	MRI
Ramirez <i>et al.</i> , 2012	MM vs. US vs. MRI	MM
Gruber <i>et al.</i> , 2013	MM vs. US vs. MRI	MM
Yang <i>et al.</i> , 1997	MM vs. US vs. MRI	US
Berg <i>et al.</i> , 2016	MM vs. US vs. MRI	US
Leddy <i>et al.</i> , 2016	MM vs. US vs. MRI	US

MM, mammography; US, ultrasound; MRI, magnetic resonance imaging.

results are congruent with other studies published in the literature (6-9,12,13).

Breast density had a negative influence on the sensitivity

of mammography, with sensitivity of 30–48% in very dense breast (10,14-16). Our study compares the three techniques in all patients, we do not use analogic or digital MM, we use Mammography3D tomosynthesis, maybe can explain why we visualized the tumor by MM in all of our patients independently of mammary density, since in other studies MM does not always visualize the tumor when using analogic or digital MM (5,6,12,15-17). However, mammography continues to be a gold standard test, since it allows visualization of lesions such as microcalcifications or in situ carcinoma, in which US has a low utility.

The use of MRI has been implemented in all breast units, and in many centers it is practiced on a regular basis. MRI has a very high sensitivity (90–99%) but low specificity. Houssami *et al.* (14) report that Resonance overestimates size, performing more mastectomies than necessary, making the process more expensive, since its low specificity makes it necessary to perform “2nd US look” and more biopsies. Behjatnia *et al.* (18) reported that MRI overestimated the size in 70% of their patients. Leddy *et al.* (9) also report that MRI overestimates the size of the lesion compared to the surgical specimen.

Ultrasonography, in our study, is the most accurate method when compared to the tumor size of the surgical

specimen. It is a simple, noninvasive and fast technique, but it is operator dependant. Our study has been performed in a single institution, tests have been performed by the same radiologists and surgeons, and surgical pieces have been studied by the same pathologist.

In our series only 14% were ILC. It is known that ILC, due to its diffuse histological growth through collagen, is more difficult to evaluate by US and mammography (19,20), but in our study we did not see a worse correlation. In these histological subtypes the MRI could play a more important role. Leddy *et al.*, report that MRI underestimates the tumor size of the ILC in 78% of the cases.

In breast cancer, it is necessary to individualize each case, since depending on the biology of the tumor and other factors the estimation of tumor size by US can vary, and we must take into account all methods of pre-surgical study, using clinical examination, mammography, US and MRI as complementary tests, knowing the strengths and weaknesses of each test, in order to plan the best treatment for the patient.

Our study was retrospective and with a small number of patients, but we observed that in patients with a unifocal tumor, MM and US provided a more accurate estimation of tumor size than the MRI, which overestimated it. These results have to be taken judiciously, as we need more prospective studies with larger series. Our work could help in the decision-making process such as the type of conservative surgery, the possible need for oncoplastic surgery or the decision to start treatment with neoadjuvant therapy.

## Acknowledgements

None.

## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* Due to the retrospective nature of this study, the Institutional Review Board has exempted the ethics approval.

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**Cite this article as:** Cortadellas T, Argacha P, Acosta J, Rabasa J, Peiró R, Gomez M, Rodellar L, Gomez S, Navarro-Golobart A, Sanchez-Mendez S, Martinez-Medina M, Botey M, Muñoz-Ramos C, Xiberta M. Estimation of tumor size in breast cancer comparing clinical examination, mammography, ultrasound and MRI—correlation with the pathological analysis of the surgical specimen. *Gland Surg* 2017;6(4):330-335. doi: 10.21037/gs.2017.03.09