Is tumor size on MRI concordant with surgical finding in breast cancer patients treated with neo-adjuvant chemotherapy?


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Introduction

Neoadjuvant chemotherapy (NACT) is a treatment used in those breast cancers initially inoperable due to their size, and also in operable breast cancers where NACT could increase the rate of conservative breast surgery(1,2). To assess tumor response to treatment, clinical examination, mammography, ultrasound, and breast MRI are used. The latter being the modality that yields the best correlation with histologic tumor volume. We evaluated the correlation of tumor sizes as measured by MRI versus surgical pathological specimen in breast cancers treated with NACT. Eighteen patients underwent MRI to monitor NACT; in 15 (83%) of them the final biopsy was obtained. In this group a very good correlation was observed, with a mean difference between MRI and histology of 4 mm, which has allowed an adequate management of patients in our daily practice.

Keywords: Breast MRI, Conservative breast surgery, Neoadjuvant chemotherapy.

¿Es concordante el tamaño tumoral medido en resonancia magnética mamaria y el de la biopsia quirúrgica en pacientes con cáncer de mama, tratadas con quimioterapia neoadyuvante?

Resumen. La quimioterapia neoadyuvante (QTNA) es un tratamiento usado en aquellos cánceres mamarios cuyo tamaño los hace inoperables al momento del diagnóstico y en cánceres mamarios operables, pero cuyo uso podría permitir una cirugía conservadora. Para evaluar la respuesta al tratamiento, se ha utilizado el examen clínico, la mamografía, el ultrasonido y la resonancia magnética mamaria, siendo ésta última la que mejor correlación tiene con el tamaño tumoral histológico. Quisimos evaluar la concordancia del tamaño tumoral medido en resonancia magnética con el de la biopsia quirúrgica, en cánceres mamarios tratados con QTNA. Dieciocho pacientes se realizaron resonancia magnética para monitorización de QTNA, en 15(83%) de ellas se obtuvo la biopsia definitiva. En este grupo observamos una muy buena correlación, con una diferencia promedio de 4 mm, entre el tamaño de la resonancia y el de la histología, lo que permitió en nuestro medio un adecuado manejo de las pacientes.

Palabras clave: Cirugía conservadora de la mama, Quimioterapia neoadyuvante, Resonancia magnética mamaria.


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tissues nor differentiate fibrosis from active tumor. Likewise, mammography does not discriminate between active tumor and fibrosis and when breast density is high, it is likely that tumor margins may not be clearly delineated. As for ultrasound, it does not allow differentiation of viable tumor from fibrosis, besides being an equipment and operator dependent imaging technique, which poses additional disadvantages. MRI in contrast to ultrasound: baseline (mask) and post-contrast sagittal VIBRANT image (Volume Imaging for Breast Assessment); acquisitions of 1 to 7 min; fat saturated sequences; 256x256 matrix; FOV: 20 cm; TR : 4 ms; TE: 1.6/fr ms; thickness of 3 mm/0.826, with a 95% confidence interval 0.51 to 0.94, associated to a p= 0.001. We show the case of a 31-year-old patient, with palpable tumor at diagnosis, whose Core biopsy corresponded to IDC GIII, triple negative hormone receptors. Pre-treatment tumor size was 28 mm. All patients gave informed consent prior to undergoing breast magnetic resonance imaging. MRIs were reported by any of the 7 institutional radiologists; RECIST (Response Evaluation Criteria In Solid Tumors) was applied to our findings. The largest diameter of the lesion was obtained on MRI that was nearest to surgery, generally after the fourth cycle.

The histological analysis was done by a sole pathologist, samples were processed with a standardized method, and the largest histological tumor diameter was selected.

Intra-class correlation coefficient and Bland Altman plot analyses were used for comparative statistical analysis. A correlation coefficient greater than 0.71 was considered indicative of good correlation, whereas p < 0.05 was indicative of meaningful correlation.

Results

Eighteen patients underwent MRI for monitoring NACT; final biopsy was obtained in 15 of them (83%), who formed the analysis group. Mean age was 49.3 years (31 to 67), and most of the patients (88.9%) had no family history of breast cancer.

All tumors corresponded to infiltrating ductal carcinomas (IDC); 40% of them were histologically graded as Grade II (Figure 1) and only 6.7% of cases were triple negative hormone receptors.

All patients received an average of 4.2 NACT cycles (range 1 to 8).

The average tumor size by MRI was 32.33 mm (range 0 to 80 mm), whilst it was 36.93 mm (range 0 to 80 mm) by histology (Table I).

In two patients a MRI complete response was reported, whereas histology confirmed a complete response in one case and found a focus of 1 mm. of ductal carcinoma in situ in the second patient.

When analyzing the Bland Altman plot a very good correlation between tumor size by MRI and histological size is observed, with an average difference of 4 mm; under the assumption that we might discard the case where the difference between histological size and MRI was 38 mm, the difference will be reduced to only 2 mm.

The intraclass correlation coefficient was rho = 0.826, with a 95% confidence interval 0.51 to 0.94, associated to a p = 0.001.

Objective

To evaluate the correlation of tumor size as measured by MRI versus surgical pathological specimen in breast cancers treated with NACT.

Material and methods

Reports of patients who had undergone magnetic resonance imaging during a 5-year period and who had been given NACT were selected. A Filemaker Pro 8.5 database for assessing demographic data, histology of the lesion, tumor size (largest diameter) and number of chemotherapy cycles was used. All examinations were performed on a 1.5 T MR unit (General Electric Medical Systems, Milwaukee, WI) with a breast coil of 8 channels (Breast Array Coil for General Electric Signa System; MRI Devices, Waukesha, WI). Sequences used were: a series of right and left T2 FAT SAT images, dynamic T1 sequence: baseline (mask) and post-contrast sagittal VIBRANT image (Volume Imaging for Breast Assessment); acquisitions of 1 to 7 min; fat suppressed sequences; 256x256 matrix; FOV: 20 cm; TR : 4 ms; TE: 1.6/fr ms; thickness of 3 mm/1.5 mm (ZIP 2); contrast dose of 0.1 mmol or 0.2 ml/kg of Gd-DTPA, at a flow rate of 2 ml/sec, with automatic infusion pump.

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We show the case of a 31-year-old patient, with palpable tumor at diagnosis, whose Core biopsy corresponded to IDC GIII, triple negative hormone receptors. Pre-treatment tumor size was 28 mm. After four cycles of NACT, a partial response is observed, tumor size reaches12 mm, and in the surgical specimen of this patient a tumor size of 11 mm is seen (Figures 1, 2 and 3).
**Tabla I.**

<table>
<thead>
<tr>
<th>Tumor diameter</th>
<th>Number of patients</th>
<th>Average (mm)</th>
<th>Standard deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>15</td>
<td>32,33</td>
<td>22,96</td>
<td>0</td>
<td>80</td>
</tr>
<tr>
<td>Histology</td>
<td>15</td>
<td>36,93</td>
<td>28,63</td>
<td>0</td>
<td>80</td>
</tr>
</tbody>
</table>

**Figure 1.** MRI of a 31-year-old patient with IDC G3 triple negative hormone receptors. Pretreatment tumor size of 28 mm.

**Table 1.** Tumor diameter.

- MRI: 15 patients, average 32.33 mm, standard deviation 22.96 mm, minimum 0 mm, maximum 80 mm.
- Histology: 15 patients, average 36.93 mm, standard deviation 28.63 mm, minimum 0 mm, maximum 80 mm.

**Graph 1.**

**Blindt-Altman plot** (representing average difference between MRI and histologic size)

**Limits of agreement (Reference Range for difference):**
-33.807 to 24.607.
Mean difference: -4.600 (CI -12.687 to 3.487)
Range: 0.000 to 80.000

**Figure 2.** MRI from the same patient at fourth cycle of NACT, posttreatment tumor size of 12 mm.
Figure 3. Surgical specimen revealing a tumor size of 11 mm.

Discussion
Evaluation of residual disease after NACT helps in determining prognosis and planning of the best surgical option\(^6\).

It has been shown that MRI is a reliable method due to its ability to analyze the morphology and kinetics of tumor contrast uptake, and in various series it has proven to be more accurate than clinical examination, mammography, and ultrasound\(^3,7,8\).

In this work an excellent correlation was observed between the size measured by magnetic resonance imaging and the gold standard, which is the histological size, with an average difference of 4 mm. As stated in Results, if we discard the one case exhibiting an underestimation of 38 mm, the difference will be reduced to 2 mm. A probable explanation for that difference could be given by the fact that MRI was performed at initial stages of applying this imaging technique at our Center, and also due to presence of a motion artifact.

To have a good correlation with the histopathological analysis allows the surgeon to perform a surgical procedure based on adequate margins, thus decreasing reoperation rates. The determination of disease-free margins offered by MRI represents a major contribution in the evaluation of tumor response to NACT, and its role in this entity is supported by our results.

One limitation of our work lies in that it presents a too small number of subjects to generalize results.

Conclusions
In our daily practice we have achieved an adequate estimation of residual tumor size with MRI evaluation, thus improving patient management.

Increasing the number of cases and their follow-up, analysis of morphological and kinetic changes of lesions and evaluation of the usefulness of imaging techniques such as MR spectroscopy and diffusion-weighted imaging, represent a challenge we have already assumed.

Bibliography