Characterization of lesions associated with microcalcifications BI-RADS 4A over a 11-year period of stereotactic breast biopsies


2. Radiology Department, Hospital Guillermo Grant Benavente, Concepción. Chile.

Abstract: Substantial advances in breast imaging techniques, especially developments in digital mammography, have led to early detection of breast cancer. It is well-known that microcalcifications are present in approximately 55% of nonpalpable breast malignancies and are responsible for the detection of 85-90% of cases of ductal carcinoma in situ (DCIS) through mammographic screening. We evaluated the types of associated lesions and the percentage of malignancy in BI-RADS 4A subcategory (low suspicion of malignancy), by performing a database review of stereotactic biopsies of microcalcifications categorized as BI-RADS 4A, between September 1999 and January 2011, which accounted for 21.4% of biopsied microcalcifications in a total of 159 women. Histological findings corresponded to benign lesions in 43.5%, high-risk lesions in 46.5%, and malignant tumors in 10%. Concerning the latter (16 biopsies), 81.3% were DCIS and 18.7% corresponded to infiltrating ductal carcinoma (IDC). The PPV of BI-RADS 4 A category was 13%, a value consistent with that described in the literature.

Microcalcifications BI-RADS 4A exhibit low suspicion of malignancy, since they mostly correspond to benign lesions (90%). Subcategory 4A constitutes an important ancillary diagnostic tool for a more accurate assessment of lesions suspicious for malignancy; therefore, we strongly recommend its use.

Keywords: BI-RADS 4A, Microcalcifications, Stereotactic biopsy.

Resumen: El continuo avance en las técnicas de imágenes mamarias, especialmente el desarrollo de la mamografía digital, ha permitido detectar cáncer mamario en etapa precoz. Se sabe que las microcalcificaciones están presentes en el 55% de los cánceres no palpables y corresponden al 85-90% de los carcinomas ductales in situ (CDIS) que se detectan con mamografía de screening. Hemos evaluado el tipo de lesiones asociadas y el porcentaje de malignidad de la subcategoría BI-RADS 4A (baja sospecha de malignidad), realizando una revisión de la base de datos de las biopsias estereotáxicas por microcalcificaciones categorizadas BI-RADS 4A entre septiembre 1999 y enero 2011 y que alcanzaron al 21,4% del total de las microcalcificaciones biopsiadas, en un total de 159 mujeres. Los resultados histológicos correspondieron a lesiones benignas en el 43,5%, lesiones de alto riesgo en el 46,5% y malignas en 10%. De las lesiones malignas (16 biopsias), el 81,3% fue CDIS y el 18,7% carcinoma ductal infiltrante (CDI). El VPP de la categoría BI-RADS 4 A fue de 13%, concordante con la literatura.

Las microcalcificaciones BI-RADS 4A son de baja sospecha de malignidad, correspondiendo en su gran mayoría (90%) a lesiones benignas. La subdivisión en 4 A representa una herramienta que facilita un mejor manejo clínico de las pacientes, por lo que recomendamos su utilización.

Palabras clave: Biopsia estereotáctica, BI-RADS 4 A, Microcalcificaciones.


Corresponding Author: Dra. Monserrat Fernández / monsefer@vtr.net

Manuscript received December 25th, 2011; accepted for publication March 19th, 2012

Introduction

Substantial advances in breast imaging techniques have been achieved, especially with the development of full-field digital mammography system, which allows detecting lesions at subclinical stages, thus leading to early diagnosis of breast cancer.

Microcalcifications account for approximately 55% of nonpalpable breast malignancies(1), corresponding...
to 85-90% of cases of ductal carcinoma in situ (DCIS) detected through screening mammography\(^2\).

Therefore, it was necessary to classify and characterize lesions, including microcalcifications, in order to predict their potential risk of malignancy. In 1992 the BI-RADS (Breast Imaging Reporting and Data System) was developed by the American College of Radiology\(^3\), comprising categories from 0 to 6. Biopsy is recommended in patients with lesions BI-RADS 4 and 5, categories exhibiting a probability of malignancy of 23-30%, and 95%, respectively\(^4,5\).

As of 2003, BI-RADS (fourth edition) divided category. BI-RADS 4 in three subgroups 4A (low suspicion of malignancy), 4B (intermediate suspicion of malignancy) and 4C (moderate suspicion, but not classic for malignancy), which according to some studies has led to increase the positive predictive value (PPV) of BI-RADS 4 category\(^6,7\) and to stratify risk of malignancy in the broad spectrum of microcalcifications BI-RADS 4\(^8\).

**Objective**

To evaluate both the type of associated lesions and the percentage of malignancy in subcategory BI-RADS 4A in stereotactic biopsies (SB) for microcalcifications.

**Material and methods**

We conducted a retrospective review, using Filemaker Pro 8.5 database, selecting those SB for microcalcifications classified as BI-RADS 4. The search was conducted between September 1999 and January 2011.

Images were analyzed on conventional film until March 2007 and then in two workstations (AGFA 3000 MA) with 5-megapixel monitors, connected to the RIS-PACS system. All patients had medio-lateral oblique (MLO) and craniocaudal (CC) breast mammograms along with craniocaudal and true lateral magnification views. Mammogram readings and biopsies were performed by seven radiologists specialized in Breast Imaging, with more than five years' experience in these diagnostic procedures and techniques.

We used a stereotactic table (Hologic Lorad Com., Multicare Platinum Asy-00072) with mammotome system (control module with SmartVac, Ethicon Endo-Surgery. Inc.J & J Com.) 8G needle and Suros 9G needle (Hologic ATEC Breast biopsy and excision system, Model TM Saphire Unit, Handpiece). A marking metallic clip was placed at the site of microcalcification extraction and post-procedural mammographic control was performed. The histological analysis was performed by a sole institutional pathologist. Histologies of SB as well as of surgical biopsy (in cases where the patient was operated) were assessed.

Lesions were divided into benign, malignant and high-risk abnormalities, including in this latter category atypical ductal hyperplasia (ADH), flat epithelial atypia (FEA), lobular intraepithelial neoplasia (LIN) grades I, II and III, and mucocele-like lesion.

All patients signed informed consent forms prior undergoing the SB.

Demographic data, lesion characteristics, procedure and histological results were assessed.

**Results**

Over the analyzed period, 751 SB for microcalcifications were performed.

Biopsied microcalcifications were classified as BI-RADS 2 (1), BI-RADS 3 (15), BI-RADS 4 (493), BI-RADS 4A (161), BI-RADS 4B (52), BI-RADS 4C (17) and as BI-RADS 5 (12) (Table I).

**Table I. BI-RADS classification of SB microcalcifications.**

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>Nº biopsied</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>0,1</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>2,0</td>
</tr>
<tr>
<td>4</td>
<td>493</td>
<td>65,6</td>
</tr>
<tr>
<td>4A</td>
<td>161</td>
<td>21,4</td>
</tr>
<tr>
<td>4B</td>
<td>52</td>
<td>6,9</td>
</tr>
<tr>
<td>4C</td>
<td>17</td>
<td>2,3</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>1,7</td>
</tr>
<tr>
<td>Total</td>
<td>751</td>
<td>100</td>
</tr>
</tbody>
</table>

Microcalcifications BI-RADS 4A (161) accounted for 21.4% of biopsied microcalcifications in a total of 159 women.

Average age of patients was 51.9 years, ranging from 34 to 76 years. The average size of biopsied foci of microcalcifications was 9.3 mm, ranging from 2 to 50 mm.

In each biopsy 6 to 40 specimens were extracted, with an average of 16.7; in all cases a digital mammogram of breast excision specimens was performed (Figure 1a and 1b) and complete removal was achieved in 52% of cases (Figure 2).

There were minor complications in three patients (1.9%), corresponding to bleeding at the puncture site, which was controlled at the end of the proceeding with no further repercussions.

Histological results (Graph 1) corresponded to benign lesions in 70 cases (43.5%) (Figure 3a and 3b), high-risk lesions in 75 cases (46.5%) (Figure 4a and 4b) and malignant tumors in 16 biopsies (10%) (Figure 5).
**Figure 1a.** Digital Mammography of SB specimens extracted, showing microcalcifications.

**Figure 1b.** Close-up of microcalcifications in Stereotactic Biopsy specimens.

**Figure 2.** Digital Spot Mammography where no residual microcalcifications are observed and metallic clip at the biopsy site may be seen.

**Figure 3a and 3b.** Magnifications of CC and LT projections of microcalcifications classified as BI-RADS 4A, histologically benign on stereotactic biopsy.
Out of the 16 malignant lesions, 81.3% corresponded to DCIS, whilst a 18.7% were cases of invasive ductal carcinomas (IDC) (Graph 2); all patients underwent surgery. Definitive biopsy results of one patient operated at another center were not available. Final histological findings in the 15 remaining patients showed concordance rates of 100% as compared with those of the SB. It must be noted that even in 31.3% of cases (5/16) there was no residual tumor on the surgical biopsy specimen (Table II).

Among the 75 high-risk type lesions, ADH accounted for 52% (39) and FEA corresponded to 30.7% (23); ADH associated with FEA was present in 12% of cases (9). Other high-risk type tumors found in lower percentage were LIN II in 4% (3) and mucocele-like lesion observed in 1.3% of patients (1) (Graph 3)).
Concerning the group of patients with high-risk histological results, we have data on either surgical biopsy or follow-up of 60 patients (80%). Fifty patients underwent enlarged surgery; in 88% of them (44/50) the final histology was consistent with the SB (Table 3). In the 6 remaining patients, surgical biopsy specimen revealed malignancy: two cases of IDC, three DCIS and one infiltrating lobular carcinoma. Thus, our histological underestimation rate in high-risk type lesions reached 12%.

In a group of 11 patients whose SB specimens revealed high-risk lesions, clinical and radiological follow-ups instead of surgery were carried out. To date they have an average follow-up of 24 months (range 6-47 months), without further changes evidenced on exams. No data is available concerning the 14 remaining patients.

### Table III. Histological concordance of high-risk lesions.

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histological concordance</td>
<td>44/50</td>
</tr>
<tr>
<td>Underestimation</td>
<td>6</td>
</tr>
<tr>
<td>Clinical and radiological follow-up</td>
<td>11</td>
</tr>
<tr>
<td>Patients with no histology available</td>
<td>14</td>
</tr>
<tr>
<td>High-risk lesions total</td>
<td>75</td>
</tr>
</tbody>
</table>

Regarding stereotactic biopsies of histologically benign lesions (70 cases), we have follow-up data in an 80%, i.e. 56 patients, with an average 24.7 months (range 4 to 66).

Concerning the 70 benign lesions (Graph 4), the vast majority of them corresponded to either fibrocystic changes associated or not with epithelial hyperplasia or with columnar cell changes (CCC) in 74%.

### Discussion

Subcategorization BI-RADS 4A allows early detection of suspicious lesions and improves understanding between clinicians and radiologists. Sanders et al. (6), Lazarus et al. (7) and Bent et al. (8) obtained a PPV of BI-RADS 4A microcalcifications between 6% and 13%, which is consistent with our series, which exhibited a PPV of 13%.

The low percentage of microcalcifications categorized as BI-RADS 4A in our series, about 21.4%, may be explained by the fact that we started to perform Stereotactic Biopsies in 1999 whilst subcategorization of BI-RADS 4 was developed by 2003. In our daily practice we consider subcategorizations 4A, B, and C as indispensable tools both for internal audit and research purposes.

It should be noted that there was an excellent correlation between SB and definitive biopsy in malignant lesions as well as in high-risk tumors, along with the low rate of histologic underestimation which reaches only about 12% as for high-risk lesions versus cancer. There was no underestimation rate when evaluating cancer in situ versus infiltrating ductal carcinoma, which may be attributed to the extensive experience of radiologists and a multidisciplinary team working that promotes appropriate monitoring of patients.

We conclude, therefore, that BI-RADS 4A microcalcifications exhibit low suspicion for malignancy, mostly corresponding to benign lesions (90%).

Subdivision 4-A represents a useful tool to facilitate better clinical management of patients. Therefore, we strongly recommend its use.
References