Study of the nipple-areola complex with MRI and microcoils

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Purpose

To evaluate the use of magnetic resonance imaging (MRI) with microcoils as the main alternative in the study of the nipple-areolar complex by showing the findings in tridimensional reconstructions of lesions and their lobar disposition.

To analyze the attributes and competencies of MRI in the global study of the breast, as in Section 10 of their publication, the European Society of Breast Cancer Specialists (EUSOMA) states that it could be a useful tool in the study of the nipple discharges. [1]

On the basis of the EUSOMA line development recommendations, we have implemented the idea of enhancing indirect ductography techniques using commercially available microcoils, which were destined to be used in osteoarticular areas, fingers, peripheral lesions and small structures, and, more recently, in skin lesions. [2, 3]

As far as our subject matter is concerned, there are previous publications related to the aforementioned microcoils in the high resolution study of different kinds of breast lesions. [4]
Methods and materials

From November 2013 to August 2016, we have studied the areola-nipple complex in 60 patients ranging from 35 to 80 years old, due to serous or serosanguineous and uniporous discharges, palpatory findings and other clinical manifestations, with MRI, using a 1.5-T equipment with microscopic surface coil (diameter: 4.7 cm), focused on the areola, as published. [5]

Due to its design and dimensions, the coil allows ventral and lateral decubitus explorations, according the patient profile, by unfolding the breast in order to avoid lobe collapse (fig 1).

The coil's high performance in its environment penalizes the field coverage, which requires corrections in order to unify the signal.

The solution seems to be the use of an algorithm to recover the depth and uniform signal in the area of interest, which facilitates the study of the areola and the underlying parenchyma up to a minimum distance of 6 cm from the nipple base, including the divisions of the ducts up to the fourth grade.

The parameters and sequences used are shown (table).

As per the FOV, the software adjusts the matrix providing 0.23 × 0.23 mm pixels with 1.5 mm slices in T2 (TSE) and 0.8 mm slices in T1 (FFE3D), building non-isotropic voxels. In spite of this, these dimensions allow the reconstruction in MIP and 3D Volume Rendering in different levels and the recording of demonstrative videos.

The sequences are obtained only in the axial plane:

1. T2 (TSE) (4.19 min)
2. T1 (FFE3D)
   a. Without contrast (4.18 min)
   b. Early contrast sequence T1 EPI (FFE3D) (1.12 min)
   c. Two consecutive sequences (4.18 min)
Total: 17.85 minutes

Both sequences, T2 (TSE) and T1 (FFE3D), without contrast, show the pathological ducts with their signals (hematic, sero-hematic, serous) and their topography in reference to
the sick lobe, and also enable the measurement of its gauge, the filling defects and the distance to the base of the nipple.

The three sequences with contrast show 4 types of enhancement:

1. Unifocal (fig 2, fig 3)
2. Multifocal in scattered nodes (volume reconstructions showed them as crystal balls) (fig 4, fig 5)
3. Non-mass enhancement of clustered rings (volume reconstructions showed them as sponges) (fig 6, fig 7)
4. Mixed pattern (nodes, cysts and rings) (fig 8, fig 9)

Finally, and based on the global assessment of the MRI images, the following relevant findings were described:

1. Duct gauge (dilated > 3 mm)
2. Signal (serous, sero-hematic signal)
3. Types of enhancement with gadolinium
4. Disposition/distribution

It is mainly a morphological study, without dynamic curves due to the fact that the microcoil provides images with a 4-minute average acquisition time. The enhancement hierarchy can be visually estimated.

MIP and Volume Rendering reconstructions and videos are jointly assessed with the surgeon and the pathologist in order to locate the sick lobe and to determine the tridimensional range of the lesions.

A second-look echography was performed to study focal lesions so as to determine the feasibility of the biopsy. With the non-mass lesions, no echography was indicated due to its limited contribution. [6, 7]

Our protocol was applied in:

1. Clinically significant nipple discharge
We grouped the findings in:

1) Globally dilated central ducts with liquid or sero-hematic signal with or without little submillimetric filling defects, without lobar disposition, as signs of chronic inflammatory process (fig 10, fig 11 & fig 12).

2) Globally dilated central ducts, with liquid or sero-hematic signal, without lobar disposition, evidence of chronic inflammatory process, but with some prominent saccule or associated cyst which can host a papilloma (fig 13, fig 14).

3) Dilated central ducts with liquid or hematic signal, with measurable solid filling defect, with or without enhancement, with gadolinium and the most prominent dilation in the proximal segment to the nipple were interpreted as papilloma. Their dimensions and distance to the nipple were assessed (fig 15, fig 16, fig 17, fig 18, fig 19).

4) Central ducts slightly or non-dilated, with clear hematic signal, systematized in lobes, some with lineal or parallel enhancements in their perimeter, in «tram tracks» and associated to non-mass focal or segmentary enhancements localized in a delimited sector of the lobe with clusters of small nodes or rings as a manifestation of intraductal proliferations. [8, 9] The volume reconstructions show them as sponges/coral branches in the stem of the duct. The non-mass enhancements can be better analyzed and characterized in the latest sequences (fig 20, fig 21, fig 22, fig 23, fig 24, fig 25).

5) Central ducts with or without dilation associated to a node or distortion with mass effect (fig 26).

1, 2 and 3 findings were considered benign or probably benign, whilst 4 and 5 findings were considered suspicious of a malignancy.

2. Palpatory findings (fig 27, fig 28, fig 29)

3. Inverted nipple associated to subareolar distortion (fig 30, fig 31)

4. Abscesses (fig 32, fig 33)

5. Paget disease (fig 34, fig 35, fig 36, fig 37, fig 38, fig 39)
The surgeon was asked to share the findings and personally discuss the case, agreeing with the diagnostic impression and the precise localization of the affected lobe.

Finally, we agreed on avoiding surgery or practicing limited resections focalized in lobes harboring papilloma, chronic inflammatory/infectious localized process, suspected cancer, or confirmed cancer.

We excluded 9 out of the 60 patients due to missing data, resulting in a total of 51 patients.

The analysis of the data is presented in tabular and graphical form. To study the association between the variables, the likelihood ratio test was applied, with a statistical significance of 5%.
Images for this section:

![Images showing medical imaging setups](https://example.com/medical-imaging-images)

**Fig. 1:** A) microcoils B) microcoil centered at the nipple C) patient in ventral decubitus in adapted stretcher D) patient in lateral decubitus

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Fig. 2: Sequences MRI with microcoil

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**Fig. 3:** T1 w/gad. Unifocal enhancement (arrow) in a dilated duct with non-bloody (serous) fluid (small arrow)

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Fig. 4: Same patient as fig 3 :T2:Dilated central duct with serous fluid and filling defect (arrow) Histology: Papilloma

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Fig. 5: T1 w/gad. Multifocal in scattered nodes A) MIP, B) volume rendering

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Fig. 6: T1w/gad MIP: Multifocal in scattered nodes, in approximately half of the breast

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Fig. 7: Multifocal in scattered nodes, in approximately half of the breast, volumen rendering showed them as crystal balls (insert)

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**Fig. 8:** A) T2 MIP: Non-dilated duct with sero-hematic fluid in a lobule with cysts of different sizes B) T1 w/gad.: Non-Mass enhancement as conglomerate rings

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Fig. 9: A) Conglomerated rings in triangular-segmental disposition B) Volume rendering representing sponges/corals in branches as a tree

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Fig. 10: Mixed pattern (nodes, cysts and rings) A) T2 with cysts interposed with nodules B) T1 dilated ducts, no blood and nodes

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**Fig. 11:** Mixed pattern (nodes, cyst and rings) A) T1 w/gad.: conglomerated rings B) T1 Volumen rendering with scattered sponges/corals

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Fig. 12: A) MIP and B) Volumen Rendering: Globally dilated central ducts with bright signal, (hematic or sero-hematic), with tiny filing defects without lobar disposition.

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Fig. 13: A) T2 central, dilated, bright ducts, no filling defects B) T1 No blood in ducts

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Fig. 14: A) Volumen rendering B) Volumen rendering slice in coronal view showing the extension of pathologic ducts from hour 10 to hour 2 (resection because of repeated episodes of pain and discharges: chronic galactophoritis)

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Fig. 15: Globally dilated central ducts, with liquid signal, with prominent saccules or cysts (galactoceles)

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Fig. 16: Inverted nipple (arrow in C), dilated central ducts, with an associated cyst (arrow in A,B).

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Fig. 17: A) T1, dilated central duct with hematic signal and filling defect by a central papilloma (arrow) B) T1 with gadolinium enhancing the papilloma (arrow)

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Fig. 18: A) 3D Volume Rendering of duct with papilloma (arrow) B) Slice in sagittal plane of Volume Rendering with filling defect by a central papilloma (arrow)

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**Fig. 19:** A) T1 central dilated duct with several filling defects B) MIP T1 proximal dilation (lactiferuos sinus)

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Fig. 20: 3D Volumen rendering Histology: Galactophoroectasia with cronic galactophoritis and papillomas.

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Fig. 21: A) Central ducts slightly dilated, with hematic signal (arrows) B) Non-mass enhancements localized in a circumscribed sector of the lobe with a cluster of rings (arrow)

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Fig. 22: A) axial, B) lateral: Volume reconstructions show sponges/coral branching (arrow) in a stem of the duct as a manifestation of intraductal proliferations in hour 3 of the left breast

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Fig. 23: A) Volumen Reconstruccion of sponges/corals, B&C) Histology : Papillary and cribiform ductal carcinoma

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**Fig. 24:** T1 w/contrast: A) Slice, B) MIP of duct with bright blood in lobules with conglomerated rings

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Fig. 25: Volumen Rendering representing sponges/corals branching in ducts with micropapilar and cribiform patter of ductal carcinoma

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Fig. 26: A) Conglomerated rings: hypointense centers (orange arrows) represent ducts filled by proliferations and the white rings represent new vesels of angiogenesis in the stroma, enhanced by gadolinium (red arrows). Histology: micropapilar and cribriform ductal carcinoma (B & C)

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Fig. 27: A) subareolar distortion B) spiculated mass retracting the nipple (C & D) volume rendering of a classic lobular carcinoma

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Fig. 28: Palpable subareolar lump retracting the nipple A) T1 with gadolinium, slice axial of a spiculated nodule B) Slice sagital

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Fig. 29: Palpable subareolar lump retracting the nipple A) 3D Volume rendering axial view of a spiculated nodule B) 3D Slice of volume rendering

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Fig. 30: 3D Volume Rendering in coronal view, with vessels irrigating the nodule encircling the areola (A front view showing the nipple, B posterior view, showing the nodule)

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**Fig. 31:** A) Volume rendering of retracted nipple B) Slice T1 w/gad. Spiculated subareolar mass

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Fig. 32: A & B Volume rendering of retracting nipple ductal carcinoma

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Fig. 33: Abscess: Retracted and cracked nipple with fistula at medial border of the areola
A) 3D Volume Rendering Coronal B) 3D Sagital with fistulous orifice (arrow)

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**Fig. 34:** Abscess A) T1 with gad.: oval subareolar cavity (arrow), fistula (arrow head), external orifice at medial border of the areola (small arrow) B) 3D Volumen Rendering

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Fig. 35: Biopsy of the nipple: Paget’s disease

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Fig. 36: Paget’s disease A) MIP T1 w/gad: non-mass enhancement (circle) and central dilated duct oriented towards the nipple (arrow) B) MIP T1 w/gad. lateral

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Fig. 37: Paget’s disease: Volume Rendering of lateral segment with sponge/corals

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Fig. 38: Paget’s disease: Volume Rendering rotated showing the central & dilated duct oriented towards the nipple (arrow)

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**Fig. 39:** Paget’s disease: A) Axial volumen rendering of central duct B) Lateral volume rendering showing the compromised segment (arrow)

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Fig. 40: Paget’s disease: Histology: intraepidermic Paget’s disease affecting at least two principal ducts by a solid and cribiform ductal carcinoma

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Results

In Tables 1, 2, 3, 4, and 5 we considered diameter of ducts, type of secretion, enhancement and its association.

Table 1: Patients and ductal diameter

<table>
<thead>
<tr>
<th>Ductal diameter</th>
<th># of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated</td>
<td>34</td>
<td>66.7</td>
</tr>
<tr>
<td>Non-dilated</td>
<td>17</td>
<td>33.3</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 2: Patients and nipple discharge

<table>
<thead>
<tr>
<th>Discharge</th>
<th># of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematic</td>
<td>19</td>
<td>37.3</td>
</tr>
<tr>
<td>Sero-hematic</td>
<td>32</td>
<td>62.7</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 3: Nipple discharge and ductal diameter

<table>
<thead>
<tr>
<th>Discharge</th>
<th>Ductal diameter</th>
<th># of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-dilated</td>
<td>Dilated</td>
</tr>
<tr>
<td>Hematic</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Sero-hematic</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>34</td>
</tr>
</tbody>
</table>

p < 0.0001

In 17 patients with non-dilated ducts, 13 (76.5%) presented bloody discharge, while in 34 patients with dilated ducts, 28 (82.4%) presented sero-hematic discharge. This relationship was statistically significant (p <0.0001) (Table 3)

Table 4: Patients and enhancement pattern
<table>
<thead>
<tr>
<th>Enhancement pattern</th>
<th># of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal balls</td>
<td>6</td>
<td>12.5</td>
</tr>
<tr>
<td>Sponge/corals</td>
<td>11</td>
<td>22.9</td>
</tr>
<tr>
<td>Mass</td>
<td>18</td>
<td>37.5</td>
</tr>
<tr>
<td>Mixed</td>
<td>12</td>
<td>25.0</td>
</tr>
<tr>
<td>No enhancement</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>48</td>
<td>100</td>
</tr>
</tbody>
</table>

**missing data of 3 patients**

Table 5: Patients, enhancement pattern and ductal diameter

<table>
<thead>
<tr>
<th>Enhancement pattern</th>
<th>Ductal diameter</th>
<th>Total patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-dilated</td>
<td>Dilated</td>
</tr>
<tr>
<td>Sponge/corals</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>No enhancement</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total patients</strong></td>
<td>16</td>
<td>32</td>
</tr>
</tbody>
</table>

**missing data of 3 patients**

p < 0.0001

Among the 16 patients with non-dilated ducts, the enhancement presented as "crystal balls" in 1 patient, as "sponges/corals" in 10 patients and as "mass" in 5 patients. There were no cases with mixed pattern. With dilated ducts, the enhancement was mass or mixed pattern in the great majority of the patients. This relationship was statistically significant (p <0.0001) (Table 5). Thirty-five (68.6%) patients where referred to surgery, and pathology reported papilloma in 10 patients (27.8), cancer in 13 patients (36%) and no-cancer in 13 patients (36%) (Table 6)

Table 6: Patients referred to surgery and results of histology

<table>
<thead>
<tr>
<th>Histology</th>
<th># of patients</th>
<th>% of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilloma</td>
<td>10</td>
<td>28.6</td>
</tr>
</tbody>
</table>
Table 7: Patients referred to surgery, type of nipple discharge, ductal diameter, enhancement pattern and histology

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Yes</th>
<th>No</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of nipple discharge</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematic</td>
<td>17</td>
<td>2</td>
<td>p = 0.013 *</td>
</tr>
<tr>
<td>Sero-hematic</td>
<td>18</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Ductal diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated</td>
<td>20</td>
<td>14</td>
<td>p = 0.033 *</td>
</tr>
<tr>
<td>Non-dilated</td>
<td>15</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Enhancement pattern</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sponge/corals</td>
<td>11</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>22</td>
<td>14</td>
<td>p = 0.007 *</td>
</tr>
<tr>
<td>No enhancement</td>
<td>1</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papilloma</td>
<td>10</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>12</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Not specific</td>
<td>13</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

** Significant at 5%

Among the cases of non-dilated duct, in 12 patients (80%) it resulted to be cancer.

Among the cases of dilated duct, in 10 patients (50%) it resulted to be papilloma and in 1 (5%) it resulted to be cancer. This relationship was statistically significant (p <0.0001).
There were 10 cases of papilloma: 9 of these had a dilated duct and a mass enhancement. That is to say, 9 out of 10 cases presented these three categories: papilloma, mass enhancement and dilated duct.

There were 19 cases of hematic secretion, 11 of which were cancer and 8 of which presented "sponge/corals" enhancement and non-dilated ducts. In other words, 4 out of 10 cases presented these four categories: hematic secretion, cancer, "sponge/corals" enhancement and non-dilated diameter.
Conclusion

Through the MRI application of sequences in microcoils, very high resolution images are obtained which allow the precise localization of the lobe/lobes in a sufficient extension in order to cover the "major ducts", as per Ohuchi. [10]

In this series, 63 % of the patients showed benign lesions, mainly with dilated ducts, harboring measurable central papillomas, with their major expansion in the proximal segment, some of which enhanced with the gadolinium and a mixed pattern of random nodes and cysts.

In 35 patients referred to surgery, 16 presented blood discharge. In 11 of these, the ducts where non-dilated, 9 of which showed "sponges/corals" enhancement pattern and in 7 of which the final diagnosis was cancer.

That means that only 7 out of 35 patients referred to surgery corresponded with cancer, bloody discharge, non-dilated ducts and enhancement as conglomerates rings (sponge/corals at volume rendering).

Those cancers presented intraductal carcinomas of low or intermediate grade, with micropapilar and cribiform patterns, silent as per Tot [11], developed in the surroundings, at subsegmentary level, where the ductal-lobular terminal units are installed and where multiple papillomatosis and proliferations coexist with different grades of atypia. [12]

These types of cancer deserve special attention since they appear in discontinuous patches, towards the nipple.

Three dimensional reconstructions showed them as groups of "sponges" or "coral formations" branching on a main duct, not so dilated, with evidence of hematic content, some with lineal enhancements in their walls, representing the macroscopic extension and topography in the sick lobe, and, frequently, pyramid shaped, triangular in two plans with MIP. This supports the data published by Tokuda [8], which confirms the high positive predictive value of the association between the ring enhancement pattern and the "segmentary" disposition (fig 4.1, fig 4.2).

The highest intensity reconstruction (MIP), which is routinely used in conventional CTs and MRIs, is a bi-dimensional presentation. Therefore, we have implemented Volume Rendering reconstructions. There is a large number of publications with the most diverse attempts to reproduce the ductal disposition in the context of the lobe anatomy, with the
most varied conclusions regarding the number of pores, drainage ducts (some of which are canalized), their segmentation and divisions. They all conclude in the lack of a unique systematized model, as there is in other sectors (bronchial tree, hepatic segmentation). [13, 14]

Three dimensional anatomy is a contribution to the sick lobe hypothesis and the concept of breast carcinoma as lobe disease, having found lobes that host small cysts and compromised segments with spots of micropapilar and cribiform carcinomas. [15, 16]

A 37% of the malign lesions found could be due to the selective removal guided by the 3D images of the lobes that host type 4 findings, as described above.

For the exploratory resection, at least the topography and the extension of the compromised segment should be previously defined, and the pathologist requires that information in order to identify the lesions, especially when they present as papillary proliferations and still pose difficulties with the small biopsy. [17]

The results of this series are promising and should be supported by other studies including a larger number of cases and experience in order to prove our hypothesis that, in the aforementioned clinical situations (nipple discharge, subareolar distortion, inverted nipple, Paget’s disease, doubtful palpatory finding), the MRI with microcoil could be the main resource repositioning the diagnostic algorithm in relation to traditional tests.
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