Computer-aided detection applied to full-field digital mammography. Performance in detection of very small invasive breast cancers

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Purpose

1- To assess the performance of CAD with full-field digital mammography (FFDM) in very small (equal to or less than 1 cm) invasive breast cancers.

2- To assess the influence of CAD on the following variables: mammographic features of the lesion (following BI-RADS descriptors), BI-RADS classification, breast density, size, and histology.
Methods and Materials

-Patient selection:

Institutional review board approval was obtained. We have retrospectively studied 68 invasive breast cancers with a size equal to or lesser than 1 cm diagnosed in women aged 49 to 69 from our population-based breast cancer screening program.

Our population-based breast cancer screening program involves three districts in the city of Barcelona (Sants-Montjuic, Eixample esquerre and Les Corts). Between June 2007 to May 2010, 40139 women were screened. A four views FFDM was performed. 235 breast neoplasms were diagnosed (detection rate of 5.85 per thousand). Fifty seven (24.2%) were ductal carcinoma in situ which were excluded because we had planned to assess the sensitivity of CAD in invasive breast cancer. Sixty-eight out of 178 (38.2%) were invasive breast cancers that fulfilled the inclusion criteria.

CAD (SecondLook, version 7.2, iCAD, Inc) with FFDM (Senographe 2000 D, General Electric Healthcare) were used. Only screening mammograms were included. Each case had a craniocaudal (CC) and mediolateral oblique (MLO) views of the breast with cancer at the time of cancer diagnosis.

-Mammographic and histologic variables:

Mammographic appearance of all visible cancers was recorded. Mammographic lesion types were classified as follows: masses, calcifications, masses with calcifications, architectural distortions, and asymmetries. To describe and classify radiologic findings, we adhered to the Bi-RADS lexicon.

Masses were classified according their morphology (round, oval, lobular and irregular), margins (well-defined, microlobular, ill defined, obscured and spiculated) and density (hyper, iso and hypodensity compared to surrounding fibroglandular tissue).

Classification of calcifications was performed according their morphology, the number of flecks per cluster and the size of the cluster. Regarding the morphology: punctate, amorphous, pleomorphic, linear, branching or casting. When at least one fine linear or branching calcification was clearly present, the cluster was classified in the last subgroup. Regarding the number of flecks per cluster: less than 10, 10-30, more than 30. Regarding the size of the cluster: less than 1 cm, 10-30 mm, more than 30 mm.
An architectural distortion was defined as the presence of distortion without an associated mass. We measured the total size of the lesion in mammograms and the thickness of the spicules. We considered the spicules were thin (1 < mm), medium (1-2 mm) or thick (>2 mm) in order to compare with the role of the CAD.

A focal asymmetry was considered when an asymmetry could not be accurately identified as a true mass (lack of any border).

Mammographic breast density was determined following ACR criteria.

We also collected the histologic type of the neoplasm. The invasive cancers were histopathologically categorized as follows: invasive ductal carcinoma, lobular carcinoma and a miscellaneous group including colloid, medullary and tubular types.

-CAD mark evaluation:

CAD operating point was set at "H", which means maximum sensitivity with poor specificity. CAD used two types of marks: ovals for masses (including true masses, asymmetries and architectural distortions) and rectangles for calcifications. Each CAD mark was classified as either a true-positive or a false-negative mark. True-positive marks indicated correctly a malignant lesion. False positive marks were all other CAD marks. For cancers appearing as masses, true positive was considered if the center of the lesion fell within the mark. The same marking principle was used for architectural distortions and asymmetries. For calcifications, true positive was considered when the CAD mark involved the majority of the elements of the cluster.

CAD marking according to view was also recorded.

-Statistical analysis:

The sensitivity of the CAD system was calculated as the number of cancers correctly marked divided by the total number of cancers.

The influence of several variables such as mammographic features (following BI-RADS descriptors), BI-RADS classification, breast density, and histology was compared using the Chi square test.

The influence of size was compared using "t" test.
**Results**

Sixty eight cancers were detected in women with a median age of 62. We found 37 (54.4%) masses, 17 (25%) calcifications, 6 (8.8%) masses with calcifications, 7 (10.3%) architectural distortions and 1 asymmetry (1.5%). The average tumor diameter of invasive cancers detected on the basis of masses was 7.35 mm, calcifications 5.24 mm, masses with calcifications 7 mm, architectural distortions 6.6 mm.

CAD showed an overall sensitivity of 86.7 % (masses: 86.5%; calcifications: 100%; masses with calcifications: 100%; architectural distortion: 57.14%) Table 1 on page 7.

CAD detected 59 out of 68 cases: 35 out of 59 were marked in both views, 13 out of 59 were marked in craniocaudal view and 11 out of 59 were marked in mediolateral oblique view. CAD failed to detect 9 out of 68 cases: 5 out of 37 masses, 3 out of 7 architectural distortions and 1 out of 1 asymmetry Table 2 on page 7.

Fifteen out of 37 masses were hyperdense and all of them were detected by CAD. In 9 out of 15 hyperdense masses CAD marked both views. One out of 37 was hypodense and CAD failed to detect. No association was seen among mass morphology or margins and ability of the CAD to mark.

Sixteen out of 37 masses were marked in both views, 8 were marked in CC view (only one showed spiculae) and 8 were marked in MLOBL view.

Fourteen out of 17 groups of calcifications showed a cluster larger than 1 cm and all of them contained more than 10 flecks. Fourteen of 17 were marked in both projections, 2 out of 17 were marked in CC view and 1 out of 17 was marked in MLOBL view. Morphology of the flecks was amorphous in 3 cases, pleomorphic in 9, and linear or branching in 5.

Regarding the architectural distortions, spicules were thin (very thin lines) in 3 cases which were all false negative. Conversely, four cases in which CAD was able to detect, spicules were medium (1 mm) or thick (2 mm).

Regarding the relationships between BI-RADS classification and CAD, CAD failed predominantly in lesions that were labelled as BI-RADS 4a. Likewise, CAD did not fail any case classified as BI-RADS 4c and 5 Table 3 on page 8.
There were no significant differences when comparing size and breast density with role of the CAD Table 4 on page 7.

Analysis of histopathologic diagnosis: invasive ductal carcinoma was the predominant type accounting for 58 cases. There were 4 infiltrating lobular carcinoma, 5 infiltrating tubular carcinoma and 1 coloid carcinoma. CAD detected all of these 10 carcinomas.

The CAD false positive rate was 2.36 marks per mammography.
### Table 1: Sensitivity according to mammographic appearance of cancer

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<table>
<thead>
<tr>
<th>Mammographic appearance</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcifications</td>
<td>100 %</td>
</tr>
<tr>
<td>Masses with calcifications</td>
<td>100 %</td>
</tr>
<tr>
<td>Masses</td>
<td>86.5 %</td>
</tr>
<tr>
<td>Architectural distortions</td>
<td>57.14 %</td>
</tr>
</tbody>
</table>

### Table 2: Characteristics of cancers that were missed by CAD

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<table>
<thead>
<tr>
<th>Mammographic appearance</th>
<th>Breast density</th>
<th>BI-RADS*</th>
<th>Size</th>
<th>Histology</th>
<th>Morphology</th>
<th>Margins</th>
<th>Density</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass</td>
<td>Dense</td>
<td>4a</td>
<td>6</td>
<td>IDC</td>
<td>Lobular</td>
<td>Ill-defined</td>
<td>Iso</td>
</tr>
<tr>
<td>Mass</td>
<td>Fatty</td>
<td>4b</td>
<td>9</td>
<td>IDC</td>
<td>Irregular</td>
<td>Spiculated</td>
<td>Low</td>
</tr>
<tr>
<td>Mass</td>
<td>Fatty</td>
<td>4a</td>
<td>9</td>
<td>IDC</td>
<td>Irregular</td>
<td>Microlobulated</td>
<td>Iso</td>
</tr>
<tr>
<td>Mass</td>
<td>Fatty</td>
<td>4a</td>
<td>6</td>
<td>IDC</td>
<td>Irregular</td>
<td>Ill-defined</td>
<td>Iso</td>
</tr>
<tr>
<td>Mass</td>
<td>Fatty</td>
<td>4a</td>
<td>8</td>
<td>IDC</td>
<td>Irregular</td>
<td>Spiculated</td>
<td>Iso</td>
</tr>
<tr>
<td>Architectural distortion</td>
<td>Dense</td>
<td>4b</td>
<td>1</td>
<td>IDC</td>
<td>Thin spicules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Architectural distortion</td>
<td>Dense</td>
<td>4b</td>
<td>5</td>
<td>IDC</td>
<td>Thin spicules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Architectural distortion</td>
<td>Fatty</td>
<td>4b</td>
<td>7</td>
<td>IDC</td>
<td>Thin spicules</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymmetry</td>
<td>Fatty</td>
<td>4a</td>
<td>7</td>
<td>IDC</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 4: Table 4: Breast density and CAD

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<table>
<thead>
<tr>
<th>Breast density ACR</th>
<th>CAD sensitivity</th>
<th>CAD failed</th>
<th>CAD marked both views</th>
<th>CAD marked CC view</th>
<th>CAD marked MLOBL view</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=17)</td>
<td>88.2 %</td>
<td>2</td>
<td>11</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>2 (n=21)</td>
<td>81 %</td>
<td>4</td>
<td>9</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>3 (n=25)</td>
<td>88 %</td>
<td>3</td>
<td>13</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>4 (n=5)</td>
<td>100 %</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Sensitivity ACR 1-2: 84.2 %

Sensitivity ACR 3-4: 90 %

Table 3: Table 3: Relationships among BI-RADS classification, role of CAD and mammographic appearance

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<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>CAD sensitivity</th>
<th>CAD mistakes</th>
<th>Masses</th>
<th>Calcifications</th>
<th>Masses with calcifications</th>
<th>Architectural Distortions</th>
<th>Asymmetries</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a (n=26)</td>
<td>80.8%</td>
<td>5 *</td>
<td>22</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4b (n=23)</td>
<td>83.0%</td>
<td>4 **</td>
<td>7</td>
<td>7</td>
<td>3</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>4c (n=7)</td>
<td>100%</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>5 (n=12)</td>
<td>100%</td>
<td>0</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*: two were related to lesions only seen on one view. **: three corresponding to architectural distortions

Table 3: Table 3: Relationships among BI-RADS classification, role of CAD and mammographic appearance

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Conclusion

1- CAD has shown a high sensitivity (86.7%) in this group of very small invasive breast cancers.

2- Lesion size, histology and breast density do not influence sensitivity.

3- Radiologic pattern influences sensitivity Table 1 on page 10.

4- Mass density influences sensitivity.

5- Thickness of the spicules in architectural distortion influences sensitivity.
**Images for this section:**

<table>
<thead>
<tr>
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<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcifications</td>
<td>100 %</td>
</tr>
<tr>
<td>Masses with calcifications</td>
<td>100 %</td>
</tr>
<tr>
<td>Masses</td>
<td>86.5 %</td>
</tr>
<tr>
<td>Architectural distortions</td>
<td>57.14 %</td>
</tr>
</tbody>
</table>

**Table 1**: Table 1: Sensitivity according to mammographic appearance of cancer

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Acknowledgements:

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References:

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