Observer Performance in Detection of Breast Cancer Among Hard-Copy Film and Soft-Copy Readings in 3MP, 5MP-LCD Monitors

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Purpose

• The diagnostic performance of digital mammography (DM) has been recognized, as the DMIST showed that DM using a flat panel detector and computed radiography (CR) system was superior for detecting breast cancer in women aged under 50.
• While the CR mammograms in the DMIST are interpreted mainly for hard-copy films, soft-copy reading of CR mammograms is not in routine use in screening.
• Only a few studies compared the diagnostic performance of CR using hard-copy and soft-copy reading, although with the sampling pitch at 100 μm.
• The sampling pitch of CR for mammography has improved from 100 to 50 μm.
• In this study we compared the diagnostic performances in the detection of breast cancer on hard-copy film, 3-megapixel (3MP) liquid-crystal-display (LCD) monitor and 5MP LCD monitor.
Material

- 200 digital mammograms with 100 subjects
  - 68 normal controls who underwent screening mammography in 2004 and 2005
  - 32 patients with surgically proven breast cancer in Tohoku University Hospital during the same period
- Besides, 33 cases were prepared for training before assessing the 100 cases.

Table 1. The distribution of breast composition of control and breast cancer

<table>
<thead>
<tr>
<th>Breast composition</th>
<th>Control</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extremely dense</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Heterogeneously dense</td>
<td>28</td>
<td>20</td>
</tr>
<tr>
<td>Scattered fibroglandular</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>Entirely fatty</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>32</td>
</tr>
</tbody>
</table>
Digital technology

• Equipment: Mammomat 3000Nova (Siemens Medical Systems, Germany)
• Digitizing reader: Computed Radiography System, FCR 5000MA plus, sampling pitch 50μm (Fujifilm Medical, Japan)
• Printer: Laser film imager, Dry Pix 7000 (Fujifilm Medical, Japan)

Soft-copy display

• 3MP monochrome LCD (20.8inch)×2; EIZO RadiForce FC-2090 (NANAO, Japan)
  • clear base, glare panel
  • brightness 450cd/cm², contrast ratio 600:1,
  • 8-bit grayscale, adjusted to DICOM Part 14 GSDF
• 5MP monochrome LCD (21.3inch)×2; EIZO RadiForce G51G (NANAO, Japan)
  • clear base, glare panel
  • brightness 450cd/cm², contrast ratio 800:1
  • 10-bit grayscale, adjusted to DICOM Part 14 GSDF
Image interpretation

- 12 doctors independently assessed mammograms presented in a random order. (Time: no limitation)
  - Interval between each reading is more than 4 weeks.
- Information before reading
  - 100 subjects including about 30 patients with breast cancer
- Ambient lighting: at around 20 lux
- Soft-copy reading: free to magnify the images and to change the contrast
- Findings: tumor, calcification, others and location
- Probability of malignancy:
  1. 7-point scale
     1. Definitely not malignant
     2. Almost certainly not malignant
     3. Probably not malignant
     4. Possibly malignant
     5. Probably malignant
     6. Almost certainly malignant
     7. Definitely malignant
  2. Continuous probability: 0 ~ 100%
Viewing software

• Prototype software (Fujifilm Medical, Japan)
  – OS: MS Windows2000

Statistical analysis

• Calculation of areas under the ROC curve (AUCs) for 3MP-LCD, 5MP-LCD, and Hard-copy by the software using Jackknife method: LABMRMC ver1.4b

• AUCs with each reading modality were compared on both malignancy scales. Bonferroni correction was used for multiple comparisons, with a P value of 0.017 or less considered to indicate statistical significance.

• Creation of ROC curve: PlotROC (Metz CE, Univ. of Chicago)
Result (1): AUCs of all readers
3MP-LCD vs. 5MP-LCD vs. Hard-copy

<table>
<thead>
<tr>
<th></th>
<th>3MP-LCD</th>
<th>5MP-LCD</th>
<th>Hard-copy</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-point scale</td>
<td>0.954± 0.016 *</td>
<td>0.947± 0.021**</td>
<td>0.956± 0.018***</td>
</tr>
<tr>
<td>Continuous (0 ~ 100%)</td>
<td>0.943± 0.016\textsuperscript{a}</td>
<td>0.923± 0.021\textsuperscript{b}</td>
<td>0.944± 0.018\textsuperscript{c}</td>
</tr>
</tbody>
</table>

Paired-t test with Bonferroni correction: * ∼ ***, a ∼ c: n.s.

ROC curve on a 7-point scale
3MP-LCD vs. 5MP-LCD vs. Hard-copy
ROC curve on a continuous point scale
3MP-LCD vs. 5MP-LCD vs. Hard-copy
**Result (2): AUCs for mass or others**

**3MP-LCD vs. 5MP-LCD vs. Hard-copy**

<table>
<thead>
<tr>
<th></th>
<th>3MP-LCD</th>
<th>5MP-LCD</th>
<th>Hard-copy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>7-point scale</strong></td>
<td>0.936± 0.027*</td>
<td>0.925± 0.033**</td>
<td>0.949± 0.026***</td>
</tr>
<tr>
<td><strong>Continuous (0 ~ 100%)</strong></td>
<td>0.925± 0.027a</td>
<td>0.905± 0.034b</td>
<td>0.932± 0.030c</td>
</tr>
</tbody>
</table>

Paired-t test with Bonferroni correction: * ~ ***, a ~ c: n.s.
Result (3): AUCs for **microcalcifications**
3M-LCD vs. 5M-LCD vs. Hard-copy

<table>
<thead>
<tr>
<th></th>
<th>3MP-LCD</th>
<th>5MP-LCD</th>
<th>Hard-copy</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-point scale</td>
<td>$0.980 \pm 0.011^*$</td>
<td>$0.974 \pm 0.009^{**}$</td>
<td>$0.969 \pm 0.021^{***}$</td>
</tr>
<tr>
<td>Continuous (0 ~ 100%)</td>
<td>$0.975 \pm 0.011^a$</td>
<td>$0.957 \pm 0.019^b$</td>
<td>$0.963 \pm 0.026^c$</td>
</tr>
</tbody>
</table>

Paired-t test with Bonferroni correction: $^* \sim ^{***}$, $^a \sim ^c$: n.s.
Discussion

ACRIN DMIST study by Pisano et al.

Oslo studies by Skaane et al

Double Reading vs Single +CAD
8) Gromet M: Comparison of CAD to double reading of screening mammograms: Review of 231,221 mammograms. AJR 2008;190: 354-359
As these studies focused on the ability of DM to detect BC, a full evaluation of soft-copy reading may not have been achieved. For instance, the Oslo I and II studies both compared screen-film MG and FFDM, although soft-copy reading was not specifically evaluated.

We took full advantage of the benefits of the existing CR system and soft-copy-reading, i.e., the 50μm spatial resolution, and free adjustment of the windows and contrast.

Furthermore, we took care in selecting the subjects to fit for breast cancer screening. Indeed, 53% of cancers were detected in screening with small size of mass.

Skaane has discussed the importance of the reading environment for soft-copy reading. Our study provided an appropriate environment with quiet reading places and the ambient light set at 20 lux, as the glare panel used in our study reflected the objects.
Conclusion

- Soft-copy readings in 3MP- and 5MP-LCD monitors were comparable to the reading on hard-copy film in detection of breast cancer.

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- Naoko Shimada, M.D.
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### Summary of RCTs of Breast Cancer Screening

<table>
<thead>
<tr>
<th>Study (duration)</th>
<th>Screening Protocol</th>
<th>Frequency</th>
<th>Age</th>
<th>Invited</th>
<th>Control</th>
<th>Years of follow-up</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIP (1963-69)</td>
<td>2V MM CBE</td>
<td>12M</td>
<td>40-49</td>
<td>14,432</td>
<td>14,701</td>
<td>18</td>
<td>0.77 (0.53-1.11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 rounds</td>
<td>50-64</td>
<td>16,568</td>
<td>16,299</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Edinburgh (1979-88)</td>
<td>1 or 2V MM CBE (initial)</td>
<td>24M</td>
<td>45-49</td>
<td>11,755</td>
<td>10,641</td>
<td>12.6</td>
<td>0.81 (0.54-1.20)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 rounds</td>
<td>50-64</td>
<td>11,245</td>
<td>12,359</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Kopparberg (1977-85)</td>
<td>1V MM</td>
<td>24M</td>
<td>40-49</td>
<td>9,650</td>
<td>5,009</td>
<td>15.2</td>
<td>0.67 (0.37-1.22)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 rounds</td>
<td>50-74</td>
<td>28,939</td>
<td>13,551</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Ostergotland (1977-85)</td>
<td>1V MM</td>
<td>24M</td>
<td>40-49</td>
<td>10,240</td>
<td>10,411</td>
<td>14.2</td>
<td>1.02 (0.59-1.77)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 rounds</td>
<td>50-74</td>
<td>28,229</td>
<td>26,830</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Malmo (1976-90)</td>
<td>1 or 2V MM</td>
<td>18-24M</td>
<td>45-49</td>
<td>13,528</td>
<td>12,242</td>
<td>12.7</td>
<td>0.64 (0.45-0.89)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 rounds</td>
<td>50-69</td>
<td>17,134</td>
<td>17,165</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Stockholm (1981-85)</td>
<td>1V MM</td>
<td>28M</td>
<td>40-49</td>
<td>14,185</td>
<td>7,985</td>
<td>11.4</td>
<td>1.01 (0.51-2.02)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 rounds</td>
<td>50-64</td>
<td>25,815</td>
<td>12,015</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Gothenburg (1982-88)</td>
<td>2V MM</td>
<td>18M</td>
<td>39-49</td>
<td>11,724</td>
<td>14,217</td>
<td>12</td>
<td>0.56 (0.32-0.98)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 rounds</td>
<td>50-59</td>
<td>9,276</td>
<td>16,394</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>CNBSS-1, 2 (1980-87)</td>
<td>2V MM CBE</td>
<td>12M</td>
<td>40-49</td>
<td>25,214</td>
<td>25,216</td>
<td>10.5</td>
<td>1.14 (0.83-1.56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4-5 rounds</td>
<td>50-59</td>
<td>19,711</td>
<td>19,694</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Mammography is the only modality proven to reduce mortality from breast cancer

- Limitation in women aged \(<\) 49
- These RCTs were designed more than 30 years ago.
Breast cancer incidence according to age

Rate of mammograms based on breast density (High and heterogeneously dense)
- 40-49: 69%
- 50-59: 26%
- 60-69: 12%

Sensitivity of mammography screening based on Miyagi cancer registry
- 40-49: 71%
- 50-59: 85%
- 60-69: 87%

Is mammography effective enough for women aged 40-49?
Japan Strategic Anti-cancer Randomized Trial (J-START)

RCT on effectiveness of ultrasonography (US) for breast cancer screening

Background
1. Breast cancer mortality is increasing in Japan
2. Highest incidence in 40s, with higher breast density
3. US is clinically available, but not for screening use
4. No evidence of mortality reduction by US screening

Targets: 100,000 women aged 40-49, 50,000 of each

Method: R C T
- Mammography + US versus Mammography

Outcomes until 2011
- Primary Endpoint: Sensitivity, Specificity, Detection rate
- Secondary Endpoint: Incidence rate of advanced BC

Final outcome: Mortality reduction

Standardization of US technique and interpretation in screening

Promotion of large-scaled RCT according to the National Cancer Act (effective from 2007)

- 2007〜2011
- Budget: $10 Milion