Introduction

- Atypical Ductal Hyperplasia (ADH) of the Breast
  - Proliferation of dysplastic monotonous epithelial cell populations in involved ducts
  - High risk lesion classified between usual ductal hyperplasia (UDH) and ductal carcinoma in-situ (DCIS)
  - Relative risk of future breast cancer: 4\(^1-6\)
  - Incidence of breast cancer at 25 years follow-up: 30\%\(^3,7\)

Introduction

- Distinguishing ADH from DCIS
  - Cellular changes of DCIS that occupy less than 2 separate duct spaces
  - <2mm in maximum dimension

Figure 1: Panel A - Atypical ductal hyperplasia with a proliferation of monotonous cells in architecturally complex patterns, including secondary lumens and micropapillary formations. (Reproduced from Hartmann et al)
Introduction

Distinction between ADH and ductal carcinoma in situ (DCIS) equivocal

Sampling error inherent with core needle biopsy (CNB)

Excision biopsy after diagnosis of ADH on CNB is still recommended
Aim of Study

To identify clinico-radiologic factors which predict malignant upstaging of ADH on core needle biopsy (CNB) in an Asian population
Your health matters when your loved ones depend on you.

Breast cancer can strike without you knowing. But the good news is, early detection gives you a better chance of a cure. So go for your mammogram. And regain control of your life.

5 Reasons why a mammogram can save your life:
1. Breast cancer is the most common cancer in women in Singapore and world-wide.
2. Cancer can grow in your breasts without you knowing or feeling any discomfort or lumps.
3. Mammography is the best way to detect breast cancer early.
4. Early breast cancer is curable.
5. Early detection can save your life.

Call our hotline 6536 6000 today for your subsidised* screening mammogram appointment.
*Applicable for women between the ages of 40 to 69 years.

Where can I go for my mammogram?
- Bukit Merah Polyclinic
  Block 163 Bukit Merah Central, Level 4, Singapore 150163
  Tel: 6272 2366
- Queenstown Polyclinic
  590 Sirling Road, Level 3, Singapore 148958
  Tel: 6479 1627
- Geylang Polyclinic
  21 Geylang East Central, Level 1, Singapore 389707
  Tel: 6842 6946
- Pasir Ris Polyclinic
  1 Pasir Ris Drive 4, Level 3, Singapore 519457
  Tel: 6585 5414

想看到儿女们长大成人，首先必须照顾自己的健康。

妇女随时可能患上乳癌。有幸的是，尽早检验能提高疗效甚至达到痊愈。今天就接受乳房X光检验，重新掌控您的人生。

五大原因为何乳房X-光检验能救您一命：
1. 乳癌是新加坡女性最普遍的癌症。
2. 早期乳癌不一定能看或感觉到。
3. 只有定期乳房X-光检验能查出是否有乳癌。
4. 早期乳癌是能够完全治好。
5. 接受定期乳房X-光检验可以挽救您的生命。

想查问乳房X-光检验扑助津贴计划*，今天就拨打6536 6000。
*年龄介乎40至69岁女士们。

哪里可以接受乳房X-光检验？
- 东山综合诊所
  Block 163 Bukit Merah Central, Level 4, Singapore 150163
  Tel: 6272 2366
- 荃湾综合诊所
  21 Geylang East Central, Level 1, Singapore 389707
  Tel: 6842 6946
- 巴西立综合诊所
  1 Pasir Ris Drive 4, Level 3, Singapore 519457
  Tel: 6585 5414
- 女皇镇综合诊所
  590 Sirling Road, Level 3, Singapore 148958
  Tel: 6479 1807
- 龙港综合诊所
  2 Sengkang Square, Sengkang Community Hub
  Level 3, Singapore 549025, Tel: 6462 2236
- 湾瀚湾综合诊所
  1 Tampines Street 41, Level 1, Singapore 529203
  Tel: 6783 6680
Methods

- **Target population:** Consecutive patients who were recalled for imaging abnormalities and had ADH diagnosed on CNB in the National Cancer Centre Singapore between 2010 and 2015.

- **Histologic upstaging:** Lesions diagnosed as ADH on CNB that were subsequently revealed to harbour malignancy (DCIS or invasive carcinoma) on surgical excision biopsy.

47,934 women underwent mammographic screening under BreastScreen Singapore between 2010 and 2015.

5,742 breast CNB performed

2,686 breast CNB performed at National Cancer Centre

89 patients with 91 ADH lesions diagnosed on CNB

Clinico-radiologic features were examined
Methods

• All mammograms are read by at least 3 specialist breast radiologists.
• All core biopsies performed with either 11- or 14-gauge Trucut biopsy or vacuum-assisted breast biopsy needle.
• Associations between clinico-radiological factors were assessed with Fisher’s exact test.
• Independent clinico-radiological factors were identified with multivariate analysis with Cox regression model.
## Results (I) - Demographics

**Table 1. The demographic characteristics of the study patients.**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Not upstaged N=64 n (%)</th>
<th>Upstaged N = 27 n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>63.4 ± 12.6</td>
<td>63.4 ± 19.1</td>
<td>0.268</td>
</tr>
<tr>
<td>&lt;50</td>
<td>26 (41%)</td>
<td>10 (37%)</td>
<td></td>
</tr>
<tr>
<td>≥50</td>
<td>38 (59%)</td>
<td>17 (63%)</td>
<td></td>
</tr>
<tr>
<td><strong>Menopausal status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premenopausal</td>
<td>36 (56%)</td>
<td>15 (56%)</td>
<td>0.889</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>27 (44%)</td>
<td>12 (44%)</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>51 (80%)</td>
<td>20 (74%)</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>6 (9.4%)</td>
<td>4 (15%)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>4 (6.3%)</td>
<td>2 (7.4%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (4.7%)</td>
<td>1 (3.7%)</td>
<td></td>
</tr>
</tbody>
</table>
Results (II) - Radiological Characteristics (a) Breast Densities

<table>
<thead>
<tr>
<th>Mammographic Parenchymal Density</th>
<th>Almost entirely fat</th>
<th>Scattered fibroglandular tissue</th>
<th>Heterogeneously dense</th>
<th>Extremely dense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion amongst n=89 patients</td>
<td>0% (n=0)</td>
<td>10% (n=9)</td>
<td>65% (n=58)</td>
<td>25% (n=22)</td>
</tr>
</tbody>
</table>

Figure 2: Distribution of mammographic parenchymal density among patients with CNB-diagnosed ADH (n=89)
Results (II)- Radiological Characteristics
(b) Radiological Abnormalities

- Microcalcification was the most common finding for ADH
- Microcalcification distribution
  - Diffuse distribution more likely to be upstaged

Figure 3: Abnormalities noted on screening mammogram in n=89 patients.
### Results (II) - Radiological Characteristics (c) Univariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Upgrade to DCIS or IBC (total n=91 lesions)</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (n=64)</td>
<td>Yes (n=27)</td>
<td></td>
</tr>
<tr>
<td>Mass present on US, N (%)</td>
<td>3 (4.7)</td>
<td>6 (22.2)</td>
<td>5.81 (1.33 - 25.32)</td>
</tr>
<tr>
<td>Mass lesion on MMG, N (%)</td>
<td>1 (1.6)</td>
<td>4 (14.8)</td>
<td>10.96 (2.63 - 45.6)</td>
</tr>
<tr>
<td>Microcalcification distribution, N(%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>3 (4.7)</td>
<td>6 (22.2)</td>
<td>0.17 (0.04 - 0.75)</td>
</tr>
<tr>
<td>Diffuse</td>
<td>2 (3.1)</td>
<td>3 (11.1)</td>
<td></td>
</tr>
<tr>
<td>Regional</td>
<td>9 (14.1)</td>
<td>1 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Grouped</td>
<td>34 (53.1)</td>
<td>11 (40.7)</td>
<td></td>
</tr>
<tr>
<td>Segmental</td>
<td>16 (25.0)</td>
<td>6 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Mammographic parenchymal density N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scattered areas of fibroglandular density</td>
<td>4 (6.3)</td>
<td>6 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Heterogenously dense</td>
<td>40 (62.5)</td>
<td>19 (70.4)</td>
<td>0.32 (0.08 - 1.26)</td>
</tr>
<tr>
<td>Extremely dense</td>
<td>20 (31.3)</td>
<td>2 (7.4)</td>
<td>0.07 (0.01 - 0.46)</td>
</tr>
</tbody>
</table>

Table 2: Univariate analysis of factors predicting for upgrade to DCIS or invasive carcinoma on excision biopsy.
## Results (II) - Radiological Characteristics

### (d) Multivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate analysis</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value</td>
<td>Hazard ratio</td>
<td>95% CI</td>
</tr>
<tr>
<td>Mammographic parenchymal density (compared to scattered areas of fibroglandular density)</td>
<td>0.014</td>
<td>0.30</td>
<td>0.07 - 1.24</td>
</tr>
<tr>
<td>- Heterogeneously dense</td>
<td>0.095</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Extremely dense</td>
<td>0.004</td>
<td>0.04</td>
<td>0.005 - 0.35</td>
</tr>
<tr>
<td>Presence of mass on ultrasound</td>
<td>0.010</td>
<td>10.51</td>
<td>1.74 - 63.36</td>
</tr>
</tbody>
</table>

Table 3: Multivariate analysis of factors predicting for upgrade to DCIS or invasive carcinoma on excision biopsy.
Discussion (I) - Radiological Features

- Presence of mass on imaging
  - More aggressive lesion with higher potential of local invasiveness
  - Consistent with previous studies ¹,²
- Breast parenchymal density
  - Scattered areas of fibroglandular density more likely to be upstaged
- 20% upstaging rate in the absence of residual calcification after biopsy

Results (III) – Biopsy Needle Size

Univariate analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needle gauge size (compared to size 11) Size 14</td>
<td>3.53 (1.23 - 10.11)</td>
<td>0.019</td>
</tr>
<tr>
<td>No. of tissue cores obtained</td>
<td>0.89 (0.80 - 0.99)</td>
<td>0.026</td>
</tr>
<tr>
<td>Core biopsy method (compared to Trucut biopsy) Vacuum assisted biopsy</td>
<td>0.21 (0.05 - 0.83)</td>
<td>0.031</td>
</tr>
</tbody>
</table>

No significant variables were identified on multivariate analysis. Factors investigated include:
- Core biopsy method
- Needle gauge size
- Number of tissue cores obtained
- ADH foci to core ratio
- Residual calcifications post biopsy
Conclusion

- First known study in Southeast Asia in this decade reviewing upstaging rate of CNB-diagnosed ADH and the predictive factors

- Upstaging rate: 29.7%
  - 27.5% DCIS, 2.2% invasive ductal carcinoma
  - Lower end of spectrum of upstaging of 18-69% ¹-⁴

Conclusion

• Upstaging of CNB-diagnosed ADH independently associated with presence of mass on ultrasound and breast parenchymal density of scattered fibroglandular density
• Increased needle gauge size, increased number of cores obtained and use of vacuum assisted device associated with lower risk of upstaging
• In the absence of residual calcification after biopsy, significant upstaging rate of 20%
• Future work
  • Include histologic factors
  • Nomogram to risk-stratify CNB-diagnosed lesions to reduce unnecessary surgical intervention in low-risk patients
Thank You