The Sloane Project

What we have learned

Dr Jeremy Thomas
Western General Hospital
Edinburgh
The Sloane Project – Background and Aims

Background

● Uncertainties about natural history, invasive potential and optimal treatment.

● Clinical trials have produced conflicting results.

Aims

● To improve knowledge about the diagnosis, treatment and clinical outcomes of screen detected carcinoma in situ and atypical hyperplasias.

● To enable patients and health care professionals to make more informed choices regarding treatment in the future.

Named after the late Professor John Sloane
Current Status

- Project now closed for new cases of DCIS
- Continuing audit of ALH & LISN
- 12,000 cases entered 2004-2012
- Approx 50% of all DCIS in Audit
- Form completion ~ 80% across specialties
Learning Points

• Study Design
• Data Collection & Quality
• Variation in Practice
• Follow up & Recurrence
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• Study design:
  – Screen-detected disease only
  – Unit participation 75%
  – Large numbers and uncommon conditions

• Opportunities:
  – Variation in practice
  – Changing practice over time e.g. large vol bx

• Missed opportunities:
  • Core biopsy data
  • Cases that drop out and why
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• Data collection
  – Multidisciplinary and stand-alone
    • Reflected by publications record
  – 50% real-time; 50% retrospective
  – Paper-based
    • Manual
    • Risk of data-entry delays
    • Data quality
    • Long term costs
    • Follow-up
# Operation Types

<table>
<thead>
<tr>
<th>Number of ops</th>
<th>Type of surgery overall</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BCS</td>
<td>Mx</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>3665</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>1233</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>4939</td>
<td>100</td>
</tr>
</tbody>
</table>

% of all cases: 70% BCS, 30% Mx, 100% Total
Sloane BCS Cases
DCIS Size distribution

Histogram

Pathology size (mm)
Frequency

Normal Fit
(Mean=14.651, SD=10.521)
n=2946

95% CI Notched Outlier Boxplot
Median (12.000)
95% CI Mean Diamond
Mean (14.651)
Outliers > 1.5 and < 3 IQR
Outliers > 3 IQR

Pathology size (mm)
Sloane Mx Cases

DCIS Size distribution

Histogram

Normal Fit
(Mean=38.554, SD=26.840)

n=1260

95% CI Notched Outlier Boxplot

Median (32.000)

95% CI Mean Diamond
Mean (38.554)

Outliers > 1.5 and < 3 IQR

Outliers > 3 IQR
Grade/Size/Op type Distribution

Size Distribution of DCIS Grade

Operation type by DCIS Grade
1 Op – Pathology v Radiology Size (mm)

Breast Conservation
1866 Cases

Mastectomy
689 Cases
Pathology/Radiology Agreement

Mastectomies – Hi Grade - X Ray

Mastectomies – Hi Grade – No X Ray
DCIS Size and ER Status

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Mean</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER Pos</td>
<td>1397</td>
<td>21.913</td>
<td>20.882 to 22.944</td>
</tr>
<tr>
<td>ER Neg</td>
<td>376</td>
<td>30.434</td>
<td>28.133 to 32.734</td>
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</tbody>
</table>

2-tailed p=<0.0001
Variation in Practice Across UK

- Radiology
- Surgery
  - Approach to margins – cavity shaves etc
  - A “clear” margin
  - Lymph nodes
- Radiotherapy
- Pathology
  - Specimen handling
  - Receptors and cut points
  - Grading
Lymph Nodes

Histogram

- Normal Fit
  (Mean=4.029, SD=3.381)

- Median (4.000)
- 95% CI Mean Diamond
  Mean (4.029)
- Outliers > 1.5 and < 3 IQR
- Outliers > 3 IQR

Groups - OverallNodes
Grading DCIS
Sloane Data 2012

No of Labs = 209
No of Cases = 7051
Median = 9 Cases
Mean = 34 Cases
Grading DCIS
Sloane Data 2012

n=4245

>80 Cases
Median 62
Mean 62
Range 41-83
CV 16.30%

Histogram
Normal Fit
(Mean=61.736, SD=10.057)

Normal Quantile (Z)
(Skewness=0.09, Kurtosis=-0.30)
(W = 0.98, p = 0.9074)
Grading DCIS
Sloane Data 2012

20-79 Cases

n=2228

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Median</td>
<td>62</td>
</tr>
<tr>
<td>Mean</td>
<td>61</td>
</tr>
<tr>
<td>Range</td>
<td>18-83</td>
</tr>
<tr>
<td>CV</td>
<td>23.60%</td>
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</table>
# Van Nuys Scoring of DCIS

<table>
<thead>
<tr>
<th>VNPI scoring system</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor size (diameter in mm)</td>
<td>less or equal to 15</td>
<td>16-40</td>
<td>greater or equal to 41</td>
</tr>
<tr>
<td>Margin width (in mm)</td>
<td>&gt; or equal to 10</td>
<td>1-9</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Pathologic Classification</td>
<td>non-high grade, (nuclear grades 1 and 2) no necrosis</td>
<td>non-high grade, (nuclear grades 1 and 2) with necrosis</td>
<td>high grade (nuclear grade 3) with or without necrosis</td>
</tr>
<tr>
<td>Overall VNPI score</td>
<td>3 or 4</td>
<td>5-7</td>
<td>8 or 9</td>
</tr>
<tr>
<td>8 year local recurrence-free survival rate (statistics from the original study, not a prediction)</td>
<td>97%</td>
<td>77%</td>
<td>20%</td>
</tr>
<tr>
<td>8 year breast-cancer specific survival rate (statistics from the original study, not a prediction)</td>
<td>100%</td>
<td>97%</td>
<td>100%</td>
</tr>
</tbody>
</table>
VNPI Profile of Sloane BCS DCIS Cases

Histogram

- Normal Fit
  - Mean = 4.9, SD = 1.1

95% CI Notched Outlier Boxplot
- Median = 5.0
- 95% CI Mean Diamond
  - Mean = 4.9

n = 2815
VNPI Profile of Sloane Recurrence Cases

Histogram

Normal Fit
(Mean=5.6, SD=1.3)
n=126

95% CI Notched Outlier Boxplot
Median (6.0)

95% CI Mean Diamond
Mean (5.6)
Comparison of VNPI Profiles

Recurrences

![Boxplot for Recurrences](image)
P = <0.0001

All cases

![Boxplot for All cases](image)
Time to Local Recurrence (months)

Histogram

- Normal Fit
  (Mean=36.3, SD=18.8)

95% CI Notched Outlier Boxplot
- Median (36.5)
- Mean (36.3)
Sloane BCS cases – Final Margin

Final Minimum Radial Margin

- Normal Fit
  (Mean=6.424, SD=4.840)

- 95% CI Notched Outlier Boxplot
  Median (5.000)

- 95% CI Mean Diamond
  Mean (6.424)

- Outliers > 1.5 and < 3 IQR
- Outliers > 3 IQR

n=1827/3080

75th percentile = 9mm
Sloane Rec cases – Final Margin

Histogram

- Normal Fit
  (Mean=4.77, SD=4.27)

n=82/126

95% CI Notched Outlier Boxplot
- Median (3.80)

95% CI Mean Diamond
- Mean (4.77)

Outliers > 1.5 and < 3 IQR
Comparison of Margin Profiles

Recurrences

All cases

P = <0.0024
The Future of Sloane

• Short term – completing all forms

• Medium to long term
  – Follow up/recurrence
  – Tissue collection – outcome predictors
Publications


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