Resection Margins in Breast Conserving Surgery

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Breast Conserving Surgery 1

- Probably one of the most important innovation in cancer surgery
- Main incentive to early diagnosis
- Perceived by women and doctors as first light at the end of the breast cancer tunnel
- Described nearly at the same time in Europe (Veronesi) and in the US (Fisher) with two options: a wider excision (quadrantectomy) vs simple removal of the tumour (tumourectomy or lumpectomy)
Veronesi’s quadrantectomy had since the beginning less local recurrences, but also worse cosmetic results.

Fisher’s lumpectomy was based on the concept that breast cancer is a systemic disease and that the lump is only the tip of the iceberg. Cosmetic results more important than local recurrence rate, since the real treatment is the systemic one.

Local recurrence has a relevant impact on survival.
Breast Conserving Surgery 3

- Now the scenario is quite different:
- Little impact of the TNM classification
- Major impact of the biology of the tumour
- Awareness of the great number of possible different profiles
- Gene profiling
- Oncoplastic surgery
- Patients needs and choices.
Local Recurrence after BCS

- Tumour characteristics
  - Margin status
  - Tumour/breast size
  - Multifocality/centricity
  - Type, EIC, PVI, residual microcalcifications
  - Biological features (HR & HER2 status)

- Patient’s characteristics: age, familial risk
<table>
<thead>
<tr>
<th><strong>0.5 cm</strong></th>
<th><strong>3.5 cm</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TUBULAR</strong></td>
<td><strong>LOBULAR</strong></td>
</tr>
<tr>
<td><strong>G1</strong></td>
<td><strong>G3</strong></td>
</tr>
<tr>
<td><strong>SENTINEL NODE NEG</strong></td>
<td><strong>7/20 METASTATIC LYMPH NODES</strong></td>
</tr>
<tr>
<td><strong>NO VASCULAR INVASION</strong></td>
<td><strong>VASCULAR INVASION</strong></td>
</tr>
<tr>
<td><strong>ER/PGR: 100%</strong></td>
<td><strong>ER/PGR: 0</strong></td>
</tr>
<tr>
<td><strong>KI67: 5%</strong></td>
<td><strong>KI67: 60%</strong></td>
</tr>
<tr>
<td><strong>HER 2 NEG</strong></td>
<td><strong>HER 2 +++</strong></td>
</tr>
</tbody>
</table>
Does age *per se* correlate with positive margins?

- Larger tumours in younger patients
- Biologically “bad” tumours in younger patients
- Less optimal margin resection in younger patients (cosmetic reasons)
- More skin & nipple sparing surgery in younger patients
- When adequate margins are obtained, no difference in local recurrence according to age
Tumour
Are margins important?

- Independent predictors of local recurrence following conservative surgery
- Negative margins do not exclude residual tumor after excision
- Positive margins dictate re-excision or radiotherapy
- What about “close” margins?
Honestly, we do not know. But we need some consensus

- To avoid mastectomies that may not be necessary
- To spare multiple re-excisions
- To avoid performance of unnecessarily wide resections
- To reassure patients and treating physicians on the adequacy of the local treatment
When are they free?

- Not at ink
- >2 mm from ink
- >5 mm from ink
(1) The peritumoral spread of cancer cells is often discontinuous.
(2) The biopsies on the margins of the specimen are “at random”.
Honestly we do not know but..
Breast conservation and negative margins: how much is enough?

M. Morrow*

*Breast Surgery Service, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Table 2
Metaanalysis of the impact of margin width on ipsilateral breast tumor recurrence (IBTR) in ductal carcinoma in situ

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Margin</th>
<th>Crude IBTR</th>
<th>Odds ratio vs 0.5 mm</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>914</td>
<td>No tumor on ink</td>
<td>9.4%</td>
<td>2.56 (1.1–7.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>1239</td>
<td>1mm</td>
<td>10.4%</td>
<td>2.89 (1.3–8.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>207</td>
<td>2mm</td>
<td>5.8%</td>
<td>1.51 (0.51–5.0)</td>
<td>NS</td>
</tr>
<tr>
<td>154</td>
<td>≥5mm</td>
<td>3.9%</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
To margin or not to margin?

Modified by Beppe Viale from W. Shakespeare
Review Article

Locoregional Treatment of Primary Breast Cancer

Consensus Recommendations From an International Expert Panel

Manfred Kaufmann, MD¹; Monica Morrow, MD²; Gunter von Minckwitz, MD¹; Jay R. Harris, MD³; and The Biedenkopf Expert Panel Members
studies show higher rates of IBTR with positive margins, but we lack consistent evidence that margins wider than tumor not touching ink decrease IBTR.

In general, invasive or intraductal cancer at an inked surface necessitates a re-excision.

The Panel endorses the adoption of ‘tumor not touching ink’ as the standard definition of an adequate negative margin in patients with invasive cancer.
Since **DCIS**, particularly low and intermediate grade lesions, may grow discontinuously within the ducts, adequate negative margins for DCIS should be larger than those for invasive carcinoma.

A **2 mm margin** was endorsed by the Panel as an appropriate standard. Margins less than 2 mm are not an absolute indication for mastectomy, but should be considered along with other factors influencing local recurrence rates.
Anterior and posterior margins of less than 2 mm are not of concern if there is no residual breast tissue. All suspicious micro-calcifications associated with the DCIS should be removed surgically.

Lobular carcinoma in situ at the margin is not considered an indication for further surgery.
Still, a free margin does not eliminate the risk of local rec

- Tumour type
  - Ductal vs lobular
- Tumour focality
- Extensive intraductal component
  - High-grade vs low-grade
- Peritumoral vascular invasion
- Biological features
# Tumor Biology and Local Recurrence

<table>
<thead>
<tr>
<th>Subtype</th>
<th>% 5-year LR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER/PR Pos, HER2 Neg</td>
<td>0.8</td>
<td>0.3-2.2</td>
</tr>
<tr>
<td>ER/PR Pos, HER2 Pos</td>
<td>1.5</td>
<td>0.2-10</td>
</tr>
<tr>
<td>ER/PR Neg, HER2 Pos*</td>
<td>8.4</td>
<td>2.2-30</td>
</tr>
<tr>
<td>ER/PR Neg, HER2 Neg</td>
<td>7.1</td>
<td>3.0-16.0</td>
</tr>
</tbody>
</table>

*no adjuvant trastuzumab

Nguyen PL. JCO 2008;26;2373.
# Sites of First Events

<table>
<thead>
<tr>
<th>Patients</th>
<th>Trial B-31</th>
<th></th>
<th>Trial N9831</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control Group</td>
<td>Trastuz Group</td>
<td>Control Group</td>
<td>Trastuz Group</td>
</tr>
<tr>
<td>All patients with follow-up</td>
<td>872</td>
<td>864</td>
<td>807</td>
<td>808</td>
</tr>
<tr>
<td>Patients alive and event-free</td>
<td>701</td>
<td>781</td>
<td>717</td>
<td>758</td>
</tr>
<tr>
<td>Patients with any first event</td>
<td>171</td>
<td>83</td>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td>Local or regional recurrence</td>
<td>35</td>
<td>15</td>
<td>22</td>
<td>12</td>
</tr>
<tr>
<td>Distant recurrence</td>
<td>111</td>
<td>60</td>
<td>63</td>
<td>30</td>
</tr>
<tr>
<td>Contralateral breast cancer</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Other second primary cancer</td>
<td>15</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Death with NED</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Take home messages

Margins should be considered in the context of multiple factors that influence local control

- Obsessing about differences of 1-2mm does not take into account the uncertainties in the pathologic processing and the differences in tumour biology

- Margins management has biological, prognostic, cosmetic and financial implications.
The end

Note the inked margin