Role of MRI-based Tumour Volumetry in Surgical Treatment of Breast Cancer

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**INTRODUCTION**

Breast cancer: the second most common cause of women’s tumour related mortality

Increasing incidence (organized screening) – decreasing mortality

Still high mortality – reason for exploring further prognostic factors

Biologically diverse disease – multidisciplinar therapy

- Surgery
- Oncology
- Radiology
- Nuclear medicine
- Pathology
**BREAST-CONSERVING SURGERY**

**Outdated ‘mechanical perspective’:** intensifying the radicalism = increasing survival  
**Modern ‘biological perspective’:** less radical surgery + oncologic therapy

Stage I and II breast cancers – breast conserving surgery  
Loco-regionally advanced breast cancers – breast conserving (if possible) with adjuvant oncologic therapy  
In some selected cases: preoperative oncologic therapy (Neoadjuvant Chemotherapy NAC)- down-sizing/down-staging possible

The tumour itself – surgical excision/ mastectomy  
The axillary lymphatic nodes – Sentinel lymph node biopsy (SLNB) ± axillary block dissection (ABD)

**Importance:** a less radical operation + good overall survival with better cosmetic results and quality of life
MRI-BASED TUMOUR VOLUMETRY

Prognostic factors

- largest diameter
- diffuse growth pattern
- presence of axillary metastases, distant metastases, largest diameter of the metastases, presence of extracapsular spreading lymph node metastasis, micrometastases
- grade of differentiation
- histologic type
- presence of hormone receptors (ER/PR +), increased HER2 expression
- numbers of mitoses, presence of anuploidity
- vascular invasion, lymphovascular invasion
- age

- primer tumour volume – possible prognostic factor
Aim

Retrospectively creating useful models based on volume measurements—a potential help in surgical treatment of breast cancer

Investigated correspondences

1. tumour volume – positive sentinel nodes
2. tumour volume – axillary metastases (sentinel + non sentinel)
3. $\frac{V_{tumour}}{V_{whole\breast}}$ - tumor excision vs. Masectomy
4. $\frac{V_{tumour}}{V_{whole\breast}}$ - occurrence of tumourous involved resection margins
5. $\frac{V_{tumour\ volume\ after\ NAC}}{V_{tumour\ volume\ before\ NAC}}$ - histologically assessed regression
METHODS - SELECTING PATIENTS

1. **First assessment: 63 patients** were selected and MRI-based tumour volumetry and tumour volume/whole breast volume ratio measurements were carried out retrospectively.
   (From Jan 1st 2013 to July 1st 2014: 445 operations -> 424 primary breast surgery -> preoperative MRI in 69 cases -> 6 excluded (central tumour = contraindication of breast-conserving surgery))

2. **Second assessment: 20 patients** were selected and tumour volumetry ratios were measured and calculated retrospectively based on the previous and the subsequent MRI. Using these ratios MRI-based and histopathologically assessed regression rates were comparable.
   (From June 5th 2012 to April 9th 2015 -> 754 operations -> 53 patients treated with NAC -> MRI before and after the NAC were performed in only 20 cases)
METHODS – MRI SCANS AND VOLUMETRY

- 1.5 T Signa Excite device
- Magnevist contrast agent
- 3D Slicer -version 4.4.0
- editor and label statistics modules
- in difficult cases - opinions of radiologists
METHODS — HISTOPATHOLOGICAL WORKUP

Intraoperative imprint cytological analysis - rapid cytologic diagnosis

• Sentinel lymph nodes

Detailed (final) histological examination

• removed tumour (specimen)
• All of the removed lymph nodes – sentinel and non sentinel ones
METHODS- STATISTICAL ANALYSIS

Measured volumes and volume ratios: a series of continuous variables
• independent sample’s t-tests
• one-way analysis of variance

Predictive value of the models
• ROC analysis

Optimal cut-off points between negative and positive cases
• Youden-indexes

SPSS 20.0
\( \alpha = 0.05 \)
RESULTS- QUESTION NO1.

Is there a correlation demostrable between the measured tumour volumes and the occurrence of positive sentinel lymph nodes?

48 SNBs

- 36 negative (75%)- mean vol= **2368,95 mm³** (SD: 1972,53)
- 12 positive (25%)- mean vol= **4178,46 mm³** (SD: 2767,63)

1. $p = 0,017$ -> significant difference
2. ROC-curve created -> **AUC= 0,731**= sufficient (sufficient above 0,7)
3. Youden-indexes -> optimal cut-off point: **3439 mm³**.
RESULTS- QUESTION NO2.

Is there a correspondence between the measured tumour volumes and the occurrence of metastatic axillary lymph nodes demonstrable (sentinel and non-sentinel also)?

60 tumours

- 39 cases: no metastasis (65%)- mean vol= 2278,61 mm$^3$ (SD: 1946,15)
- 21 cases: metastasis (35%)- mean vol= 4556,75 mm$^3$ (SD: 3109,18)

1. $p= 0,001$ -> significant difference
2. ROC-curve created -> AUC= 0,759= sufficient
3. Youden-indexes -> optimal cut-off point: 1175,4 mm$^3$. 
**RESULTS- QUESTION NO3.**

Is there a demostrable connection between the measured tumour volume/ breast volume ratios and the occurrence of mastectomy?

\[
\frac{V_{tumour}}{V_{whole\ breast}}
\]

65 tumours

- 38 excisions (58,46%)- **mean vol ratio= 0,36% (SD: 0,43)**
- 27 mastectomies (41,54%)- **mean vol ratio= 1,21% (SD: 2,23)**

1. \( p = 0,061 \) -> non significant
2. ROC-curve created -> **AUC= 0,776= sufficient**
3. Youden-indexes -> optimal cut-off point was **11,86%**
RESULTS- QUESTION NO4.

Is there a correspondence between the measured volume ratios and the occurrence of incomplete tumour excision (positive resection margin)?

\[
\frac{V_{tumour}}{V_{whole\ breast}}
\]

38 excisions

- 27 cases: negative margins (71,05%)- mean vol ratio= 0,3% (SD: 0,27)
- 7 cases: the tumour close to the margin (only 1-2 mm wide tumour-free zone) 18,42% - mean vol ratio= 0,34% (SD: 0,63)
- 4 cases: tumourous involved resection margin (10,53%)- mean vol ratio= 0,83% (SD: 0,74)

\[p = 0.07\rightarrow \text{non significant.}\]
RESULTS- QUESTION NO5.

Is there a correlation between the measured and calculated regression rates based on MRI and the histopathologically assessed regression grades?

\[
\frac{V_{tumour \ volume \ after \ NAC}}{V_{tumour \ volume \ before \ NAC}}
\]

20 tumours

- TRG1 (n=11) - mean vol ratio= 20,25% (SD: 31,1)
- TRG2 (n=3) - mean vol ratio= 6,96% (SD: 8,27)
- TRG4 (n=6) - mean vol ratio= 5,37% (SD: 8,54)

\[p=0,442\]: non significant
SUMMARY AND CONCLUSION

1. A significant correlation (0.017) found between tumour volumes and occurrence of positive sentinel nodes. Cut-off point: 3439mm$^3$, AUC= 0.731.

2. A significant correspondence (0.001) found between tumour volumes and occurrence of any metastatic axillary lymph nodes. Cut-off point: 1175.4mm$^3$, AUC= 0.759.

3. A close to significant connection (0.061) between the estimated tumour volume/breast volume ratios and the occurrence of mastectomy. Cut-off point: 11.86%, AUC= 0.776.

4. A close to significant correspondence (0.07) between the measured volume ratios and the occurrence of incomplete tumour excision.

5. No significant correlation (0.442) demonstrable between the measured and calculated regression rates based on MRI and the histopathologically assessed regression grades.
FUTURE PERSPECTIVES

1. Improving the models: more MRI scans -> more data; excluding extreme values
2. Investigating the accuracy of MRI-based volumetry via histopathological volumetry
3. Designing tumour excisions: creating 3D tumour models in advance to help the work of surgeons
THANK YOU FOR YOUR ATTENTION.
Six following 21-day-long cycles:

- *Taxotere (docetaxel):* 75 mg/m² i.v. bolus on the first day,
- *Epirubicin:* 75 mg/m² i.v. bolus on the first day,
- *Xeloda (capecitabine):* 2x1000 mg/m² per os on 1-14. days of each cycles.
# Tumor Regression Grade (Sinn et al)

<table>
<thead>
<tr>
<th>TRG0</th>
<th>No signs of regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRG1</td>
<td>Tumour sclerosis with focal inflammation and/or min. cytopathic effect (tumour &gt; 5mm)</td>
</tr>
<tr>
<td>TRG2</td>
<td>Extensive tumor sclerosis ± multifocal minimally invasive residual tumour (max. 5mm ± intraductal spread)</td>
</tr>
<tr>
<td>TRG3</td>
<td>No invasive residual tumour</td>
</tr>
<tr>
<td>TRG4</td>
<td>No invasive or in situ residual tumour demonstrable</td>
</tr>
</tbody>
</table>
RESULTS- QUESTION NO1.

<table>
<thead>
<tr>
<th>(mm³)</th>
<th>negative SNB (n=36)</th>
<th>positive SNB (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>2368.95</td>
<td>4178.46</td>
</tr>
<tr>
<td>CI: 95%</td>
<td>1701.54; 3036.36</td>
<td>2414.99; 5931.93</td>
</tr>
<tr>
<td>SD</td>
<td>1972.53</td>
<td>2767.63</td>
</tr>
<tr>
<td>minimum</td>
<td>418.93</td>
<td>1196.47</td>
</tr>
<tr>
<td>maximum</td>
<td>7681.20</td>
<td>11410.26</td>
</tr>
<tr>
<td>range</td>
<td>7262.27</td>
<td>10213.79</td>
</tr>
</tbody>
</table>
RESULTS - QUESTION NO2.

<table>
<thead>
<tr>
<th>(mm³)</th>
<th>Non metastatic axilla (n=39)</th>
<th>metastatic axilla (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>2278,61</td>
<td>4556,75</td>
</tr>
<tr>
<td>CI: 95%</td>
<td>1647,74; 2909,48</td>
<td>3141,47; 5972,03</td>
</tr>
<tr>
<td>SD</td>
<td>1946,15</td>
<td>3109,18</td>
</tr>
<tr>
<td>minimum</td>
<td>418,93</td>
<td>1196,47</td>
</tr>
<tr>
<td>maximum</td>
<td>7681,20</td>
<td>11456,37</td>
</tr>
<tr>
<td>range</td>
<td>7261,27</td>
<td>10259,90</td>
</tr>
</tbody>
</table>
### Results - Question No3.

<table>
<thead>
<tr>
<th>(%)</th>
<th>Excision (n=38)</th>
<th>Mastectomy (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>0.36%</td>
<td>1.21%</td>
</tr>
<tr>
<td><strong>CI: 95%</strong></td>
<td>0.22%; 0.51%</td>
<td>0.33%; 2.09%</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>0.43%</td>
<td>2.23%</td>
</tr>
<tr>
<td><strong>Minimum</strong></td>
<td>0.01%</td>
<td>1.13%</td>
</tr>
<tr>
<td><strong>Maximum</strong></td>
<td>1.92%</td>
<td>11.86%</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>1.91%</td>
<td>11.73%</td>
</tr>
</tbody>
</table>
**RESULTS - QUESTION NO4.**

<table>
<thead>
<tr>
<th>(%)</th>
<th>negative (n=27)</th>
<th>1-2 mm close (n=7)</th>
<th>pozitive(n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>0.3%</td>
<td>0.34%</td>
<td>0.83%</td>
</tr>
<tr>
<td>CI: 95%</td>
<td>0.19%; 0.41%</td>
<td>-0.24%; 0.93%</td>
<td>-0.34%; 2%</td>
</tr>
<tr>
<td>SD</td>
<td>0.27%</td>
<td>0.63%</td>
<td>0.74%</td>
</tr>
<tr>
<td>minimum</td>
<td>0.01%</td>
<td>0.03%</td>
<td>0.29%</td>
</tr>
<tr>
<td>maximum</td>
<td>1.04%</td>
<td>1.77%</td>
<td>1.92%</td>
</tr>
<tr>
<td>range</td>
<td>1.03%</td>
<td>1.74%</td>
<td>1.62%</td>
</tr>
</tbody>
</table>
## Results - Question No5.

<table>
<thead>
<tr>
<th>(%)</th>
<th>TRG1 (n=11)</th>
<th>TRG2 (n=3)</th>
<th>TRG4 (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean</td>
<td>20.25%</td>
<td>6.96%</td>
<td>5.37%</td>
</tr>
<tr>
<td>CI: 95%</td>
<td>-0.64%; 41.15%</td>
<td>-13.58%; 27.49%</td>
<td>-3.59; 14.34%</td>
</tr>
<tr>
<td>SD</td>
<td>31.1%</td>
<td>8.27%</td>
<td>8.54%</td>
</tr>
<tr>
<td>minimum</td>
<td>0.007%</td>
<td>0.21%</td>
<td>0.002%</td>
</tr>
<tr>
<td>maximum</td>
<td>104.48%</td>
<td>16.18%</td>
<td>19.21%</td>
</tr>
<tr>
<td>range</td>
<td>104.48%</td>
<td>15.97%</td>
<td>19.2%</td>
</tr>
</tbody>
</table>