Minimally invasive, Maximal outcomes in Breast surgery

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Comprehensive molecular profiling of breast cancers

- Significantly mutated genes and correlations with genomic and clinical features

Longstanding controversies

- Halsted’s classic operation
  - en bloc removal of the entire breast, regional lymphatics, and pectoralis muscles
  - first performed in 1882, and published his classic work in 1894 in the Johns Hopkins Hospital reports (50 cases)

- Fisher alternative thesis (1968)
  - the product of laboratory investigation
  - supported by results obtained from a series of randomized clinical trials

- The spectrum theory (1994)
  - heterogeneous disease that can be thought of as a spectrum of proclivities tendencies extending from a disease that remains local throughout its course to one that is systemic when first detectable
Major turning points in breast surgery

- The Pre-Halsted Era
- Halsted Radical Mastectomy
- Seeking a Less-Extensive Operation
- Breast-Conserving Surgery
- Axillary Lymph Nodes/Sentinel Node Biopsy
- Oncoplastic Surgery
- Axillary node skipping in node positive cases
- Preemptive surgery
- Image guided therapy, non surgical method
Major types of surgery through the years, Korea

Dose the local recurrence impact on distant metastasis or overall survival?

Is the local recurrence a marker of risk or a cause of distant disease?
Twenty-Year Follow-up of a Randomized Trial NSABP-06

Cumulative incidence of ipsilateral breast tumor recurrence (NEJM, 2002)
Twenty-Year Follow-up of a Randomized Trial NSABP-06:
Cumulative incidence of death (NEJM, 2002)
Overall survival from Nottingham data set
(World J surg, 2012)

Survival Function – BCS 1990-99

RRR from avoidance of LR = 69%
Dose the local recurrence impact on distant metastasis or overall survival? : YES

Is the local recurrence a marker of risk or a cause of distant disease?
Local recurrence and breast cancer mortality
(EBCTCG review of PMRT, Lancet 366:2087)
Local recurrence and breast cancer mortality
(DBCG 82 b&c PMRT, Radiother oncol, 2007)
Local recurrence and breast cancer mortality
(DBCG 82 b&c PMRT, Radiother oncol, 90:74)
Dose the local recurrence impact on distant metastasis or overall survival?  
: YES

Is the local recurrence a marker of risk or a cause of distant disease?  
: YES, May be
When a surgeon makes the decision that a lumpectomy is appropriate, he or she must appreciate that a patient’s outcome is apt to depend on the surgeon’s skills as well as those that the other members of the ‘team’ possess (Fisher B, 1989).

Surgeon should not be a ‘reductionist’
61/F
16.4.2 Lt. BCS with SLNBx
IDC pT1N0M0(T 1.1cm, LN 0/2, TNBC)
Lt Breast, UOQ ~ Subareolar & Mid Inner
: Suspected multicentric lesion with EIC.
53/F diffuse DCIS (8cm sized) 
s/p Lt. NAC sparing mastectomy with implant reconstruction
Decision making factors for surgical method

- **Tumor factors**
  - extent: size and DCIS component
  - multi-focal or multi-centric
  - biology: luminal vs Her2 (+) vs triple negative

- **Patients factors**
  - desire: oncologic safety vs cosmetic result
  - economics
  - genetic background: BRCA 1, 2 related
  - concerns of radiation therapy
Current challenges

- Primary surgery for patient with disseminated disease
- Surgical treatment after neo-adjuvant chemotherapy
- Axillary saving for positive sentinel node
- Conservation after breast conserving surgery
- Mastectomy vs Conservation in genetically high risk patient
The more challenges

- Nipple areolar complex (NAC) saving mastectomy vs Conservation + RT
- Surgical method by molecular subtype or genetic profiling
- Preemptive surgery
- Non surgical method, image guided therapy
- No treatment for indolent LCIS, DCIS, and some invasive cancer of fragile patient
Post Neoadjuvant Chemotherapy
## PCR rates after Neoadjuvant chemotherapy

<table>
<thead>
<tr>
<th>Subtype</th>
<th>GEPAR Quattro</th>
<th>CALGB 40603</th>
<th>NCC, Korea</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>445</td>
<td>404</td>
<td>322</td>
</tr>
<tr>
<td>pCR</td>
<td>32%</td>
<td>58%</td>
<td>Entire 9.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>HR+/HER2- 6.6%</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>HR+/HER2+ 13.8%</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>HR-/HER2+ 26%</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>TN 5.5%</td>
</tr>
</tbody>
</table>
Literature reporting local recurrence rates following skin sparing mastectomy (chronological order of publications)

<table>
<thead>
<tr>
<th>Authors et al.</th>
<th>SSM/vs. Mx (n); FU(follow up) in months (m)</th>
<th>LR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newman et al., 1998</td>
<td>372 SSM; median FU = 26m</td>
<td>6.2%</td>
</tr>
<tr>
<td>Toth et al., 1999</td>
<td>50 SSM; median FU = 51.5m</td>
<td>0%</td>
</tr>
<tr>
<td>Medina-Franco et al., 2002</td>
<td>173 SSM; median FU = 73 m</td>
<td>4.5%</td>
</tr>
<tr>
<td>Carlson et al., 2003</td>
<td>539 SSM; median FU = 61.6 m</td>
<td>5.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[0.6, 3.0, 10.4, 11.1, 0% in Stage 0, I, II, III, IV respectively]</td>
</tr>
<tr>
<td>Drucker-Zertuche et al., 2007</td>
<td>105 SSM; mean FU = 51 m</td>
<td>1%</td>
</tr>
<tr>
<td>Vaughan et al., 2007</td>
<td></td>
<td>5.3%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(9 of 11 in the index quadrant)</td>
</tr>
<tr>
<td>Lanitis et al., 2010</td>
<td>825 SSM vs. 2518 Mx; Median FU for studies = 37.5-101 m</td>
<td>5.7% SSM (3.8-10.4) vs. 4.0% Mx (1.7-11.5) OR = 1.14 (95% CI, 0.78-1.68) [Systemic recurrence = 8.3% SSM vs. 12.1% Mx; OR = 0.63, 95% CI, 0.43-0.92]</td>
</tr>
<tr>
<td>Meta-analysis of 7 studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kinoshita et al., 2011</td>
<td>73 SSM vs.129 Mx; mean FU = 30 m</td>
<td>2.7% SSM vs. 3.9% Mx</td>
</tr>
<tr>
<td>Nava et al., 2011</td>
<td>77 SSM; median FU = 36 m</td>
<td>0.5%/year</td>
</tr>
<tr>
<td>Sheikh et al., 2011</td>
<td>177 SSM vs. 249 Mx; mean FU = 28 m</td>
<td>1.1% SSM vs. 0.8% Mx (non-significant); [positive or close margin, 29% SSM vs. 12% Mx; p &lt; 0.01]</td>
</tr>
<tr>
<td>Peled et al., 2012</td>
<td>126 SSM; median FU = 28 m</td>
<td>2.4%</td>
</tr>
<tr>
<td>Romics et al., 2012</td>
<td>207 SSM; median FU = 119(14-163) m</td>
<td>2.9%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(8.2% loco-regional, 10.6% systemic recurrence)</td>
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</table>
NAC saving mastectomy + Latissimus dorsi flap
ORIGINAl ARTICLE

Oncological Safety and Quality of Life Associated with Mastectomy and Immediate Breast Reconstruction with a Latissimus Dorsi Myocutaneous Flap

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*Center for Breast Cancer, Research Institute and Hospital, National Cancer Center, Goyang, Korea; †Graduate school of Kyung Hee University, Seoul, Korea; ‡Division of Cancer Control, National Cancer Control Research Institute, National Cancer Center, Goyang, Korea; and §Department of Surgery, Medical College, Korea University, Seoul, Korea

Abstract: To determine the quality of life (QoL) of breast cancer patients who underwent mastectomy and immediate breast reconstruction with a latissimus dorsi myocutaneous flap (LD), and the oncological safety of the procedure. Between May 2001 and March 2007, 2,566 patients had breast cancer surgery at the National Cancer Center, Korea. Of the 2,566 patients, 1,699 had breast-conserving surgery (BCS) and 120 had a mastectomy with an immediate LD. We retrospectively compared the oncologic safety of the two techniques. We also assessed the QoL using the EORTC QLQ BR-23 and Zung’s self-rating depression scale in 52 LD patients, 104 age- and stage-matched patients who underwent BCS, and 104 age-matched healthy women. The LD group had earlier stage disease than the BCS group at baseline, but following surgery, the groups did not differ in the rates of local recurrence or systemic metastases. Compared with the healthy group, the patient groups had poorer functioning and more depression (p < 0.001). Among the patient groups, the LD group reported lower scores for body image (p = 0.007) and future perspective (p = 0.023) than the BCS group. In the LD group, patients who received neoadjuvant chemotherapy reported lower scores for future perspective and higher scores for depression than those who did not receive neoadjuvant chemotherapy (p < 0.001). The BCS and LD groups did not differ in oncological outcome, and the QoL of patients in the LD group was not always good. Mastectomy with immediate reconstruction should be considered carefully and tailored to the patient’s needs and characteristics.

Key Words: breast cancer, immediate reconstruction, latissimus dorsi flap, oncological safety, quality of life
Reconstructive method in NCC, Korea
Trends and Variation in Use of Breast Reconstruction in Patients With Breast Cancer Undergoing Mastectomy in the United States

Reshma Jagsi, Jing Jiang, Adeyiza O. Momoh, Amy Alderman, Sharon H. Giordano, Thomas A. Buchholz, Steven J. Kronowitz, and Benjamin D. Smith

J Clin Oncol 32. © 2014 by American Society of Clinical Oncology
Bilateral Risk Reduction Mastectomy

NCCN Guideline
Risk reduction : at least 90%
✓ in moderate- and high- risk women
✓ in known BRCA1/2 mutation carriers

Recommendation
✓ For carefully selected women at high risk of breast ca. (BRCA1/2, TP53, PTEN mutation)
✓ Who desire prophylactic mastectomy

Meijers-Heijboer et al. NEJM 2001; 345: 159-164
Rates of ipsilateral-breast tumor recurrence and contralateral breast cancer in series of BRCA1/2 mutation carriers treated with breast-conserving surgery

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>BRCA 1/2 mutation carriers (N)</th>
<th>Control/noncarrier (N)</th>
<th>Median F/up (yr)</th>
<th>IBTR</th>
<th>CBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robson et al.</td>
<td>1999</td>
<td>28</td>
<td>277</td>
<td>10</td>
<td></td>
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<tr>
<td>Pierce et al.</td>
<td>2000</td>
<td>71</td>
<td>213</td>
<td>5</td>
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<tr>
<td>Haffty et al.</td>
<td>2002</td>
<td>22</td>
<td>105</td>
<td>12</td>
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<tr>
<td>Seynaeve et al.</td>
<td>2004</td>
<td>26</td>
<td>174</td>
<td>6</td>
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<tr>
<td>Robson et al.</td>
<td>2005</td>
<td>87</td>
<td>-</td>
<td>6</td>
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<tr>
<td>Kirova et al.</td>
<td>2005</td>
<td>27</td>
<td>261</td>
<td>9</td>
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<td>Pierce et al.</td>
<td>2006</td>
<td>160</td>
<td>445</td>
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<tr>
<td>Garcia-Etienne et al.</td>
<td>2009</td>
<td>54</td>
<td>162</td>
<td>4</td>
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</tr>
<tr>
<td>Kirova et al.</td>
<td>2010</td>
<td>29</td>
<td>271</td>
<td>5.4</td>
<td></td>
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</tbody>
</table>

- **IBTR**
  - Carriers (%): 22, 49, 30, 24, 27, 44
  - Control/noncarriers (%): 7, 21, 16, 19, 4, 31
  - p-value: 0.25, 0.007, 0.005, 0.47, 0.03, 0.33

- **CBC**
  - Carriers (%): 27, 42, 14, 14, 37, 25
  - Control/noncarriers (%): 9, 9, 6, 6, 9, 1
  - p-value: 0.002, 0.001, 0.06, 0.0003, 0.0001, 0.03
BRCA1/2 mutation carriers treated with breast-conserving surgery

**IBTR**  
Inconsistent findings  
Several matched studies: no significant difference

**CBC** (Contralateral breast cancer)  
Consistent findings: Significantly higher incidence of CBC in BRCA1/2 carriers

Kirova et al. Bresat Cancer Res Treat 2010; 120:119-126
Personal experience of risk reducing surgery

- **BRRM**: 2 cases who had BRCA1 mutation and benign papillary lesions

- **CRRM**: 14 patients who had BRCA1,2 mutation or strong family history (179 BC patients who had BRCA1,2 mutation or strong family history, 11 patients already bilateral cancers from 2012-2014)

- Not Covered by Governmental insurance
Image guided therapy, non surgical method
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Radiofrequency Ablation</th>
<th>Laser Irradiation</th>
<th>Microwave Irradiation</th>
<th>High-Intensity Focused Ultrasound</th>
<th>Cryoablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Requirement for percutaneous insertion of one or more needles of probes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Preferred imaging guidance</td>
<td>Ultrasound</td>
<td>Ultrasound</td>
<td>Ultrasound</td>
<td>MRI</td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Required conscious sedation or general anesthesia</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Procedure time (min)</td>
<td>&lt; 30</td>
<td>&lt; 30</td>
<td>&lt; 30</td>
<td>≤ 120</td>
<td>&lt; 30</td>
</tr>
<tr>
<td>Target temperature (°C)</td>
<td>95</td>
<td>60</td>
<td>90</td>
<td>60–90</td>
<td>–40</td>
</tr>
<tr>
<td>Specific complications</td>
<td>Burns</td>
<td>Burns</td>
<td>Burns</td>
<td>Burns</td>
<td>Frostbite</td>
</tr>
<tr>
<td>Real-time monitoring (and possible adjustment) of the progress of the ablation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cost of equipment</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Very high</td>
<td>Low</td>
</tr>
</tbody>
</table>
Surgical evolution in breast cancers

- Clonal evolution in the **ERBC** inferred from single cell exome and CNVs data

![Diagram of ERBC clonal evolution]

- Clonal evolution in the **TNBC** inferred from single cell exome and CNVs data

![Diagram of TNBC clonal evolution]

Y. Wang et al., 2014, Nature