

596

Poster

Recurrence Rate After Skin Sparing Mastectomy and Immediate Reconstruction

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Background: We present local recurrence (LR), systemic recurrence (SR) & disease-free survival (DFS) after Skin-sparing mastectomy (SSM – removal of all breast tissue including nipple-areola complex with preservation of breast skin) in operable breast cancer as there is relative lack of evidence in recent literature regarding its safety in light of increase in in-situ disease and advances in adjuvant hormone therapy (especially aromatase inhibitors).

Materials and Methods: Prospectively recorded database of 95 patients who had SSM over 4 years period (April 2006-July 2010) were reviewed. 13 patients were excluded as they had either risk-reducing (for high-risk family history) or prophylactic (after contra-lateral cancer) SSM.

Results: 81 patients with median age of 51.7 (31.5–66.1) years had 82 SSM with immediate reconstruction (58 implant based; 23 LD flap). Decision for SSM was based on tumour size relative to breast size, multi-focality (n=12), unclear margin at conservation surgery or simply patient choice. Tumor quadrants involved were multi-quadrant (34%), upper outer (21%), central (17%), upper inner (11%). Tumour types were invasive ductal (37.8%), invasive lobular (7.3%), DCIS alone (37.8%). Median tumour size was 22 (1–86) mm including pure in-situ disease of 20 (1–85) mm. Median clear distance was 5 (0–45) mm including pure in-situ disease of 5 (0–40) mm. Sentinel node was positive in 18.3% (excluding pure in-situ disease). Median NPI was 3.54 (2.1–6.98), ER positive (84%, pure in-situ-70.6%), HER2 positive (8.5%). 17.1% patients received Radiotherapy to breast & 37.8% patients received hormone therapy (tamoxifen-24.4%, upfront AI-4.9%, switch regime-8.5%, tamoxifen to exemestane at 2 years). 8 (9.6%) patients had infection/wound healing problems with loss of implant in 3 (3.6%). At a median Follow-up of 23.8 (8–64) months, there were no LR and 2 SR following invasive disease (brain & liver-1; liver-1) with a median DFS of 24.4 (6.1–61.9) months (26.9, 10.8–61.9 in pure in-situ disease).

Conclusions: The LR and SR rates are lower than current literature (minimum 6% LR & 7% SR) for T1-T2 tumors. It also confirms that immediate reconstruction does not compromise adjuvant therapy and that adjuvant radiotherapy does not compromise immediate reconstruction. Therefore, SSM with immediate reconstruction appears to be even safer option both surgically and oncologically in light of advances in adjuvant therapies.

597

Poster

Partial Mastectomy Reconstruction During Breast-conserving Surgery – Classification of Oncoplastic Techniques

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Background: Most patients presenting with breast cancer are treated by breast-conserving therapy (BCT). Some of these patients present with poor cosmetic results after surgery. To avoid partial defects after BCT a wide spectrum of reconstructive techniques have been published during the last years – a concept termed oncoplastic breast surgery. To improve clinical utility of oncoplastic breast-conserving surgery we developed a classification of oncoplastic techniques with standardization of indications and surgical performance.

Materials and Methods: We prospectively defined five major principles in oncoplastic breast surgery (Krämer et al., Breast Care 2007; 2: 299–306) based on the localization, size of the segmental resection defect, size of the breast and the necessity for skin resection during breast-conserving therapy. These major principles are: BCT-glandular rotation, BCT-dermoglandular rotation, BCT-tumoradapted reduction mammoplasty, BCT-thoracoepigastric flap, BCT-latissimus dorsi flap. We analyzed the clinical practicability and the cosmetic results. All patients received adjuvant postoperative radiotherapy. Systemic adjuvant treatment was applied according to international guidelines. 35% of the treated patients received neoadjuvant chemotherapy. A tumor-free resection margin was mandatory and achieved in 91% during first surgery, while in 5% secondary mastectomy was required.

Results: Between November 2008 and November 2011 we performed 952 breast-conserving operations in 913 patients. For reconstruction of the partial resection defect during segmental resection the defined five oncoplastic principles were used as follows: glandular rotation (n=549; 58%), dermoglandular rotation (n=149; 16%), tumoradapted reduction

mammoplasty (n=135; 14%), thoracoepigastric flap (n=27; 3%) and latissimus dorsi flap (n=92; 9%). Partial mastectomy defects could be reconstructed during BCT with these five oncoplastic principles in 97%. The cosmetic results were good or excellent in 95%.

Conclusion: The use of five defined oncoplastic principles allows the reconstruction of segmental resection defects during breast-conserving therapy with highest clinical applicability and results in favourable esthetic outcomes. This approach might be useful in extending the indications for breast-conserving therapy.

598

Poster

Single Center Experiences with Intraoperative Radiotherapy as a Boost During Oncoplastic Breast-conserving Surgery

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Background: Breast-conserving surgery followed by external beam radiation therapy (EBRT) to the whole breast in combination with external boost radiation therapy has become the standard of care for most patients with localised early breast cancer. Breast-conserving surgery (BCS) is performed in an oncoplastic approach with tumor-specific immediate reconstruction of the partial mastectomy defect (Krämer et al., Breast Care 2007; 2: 299–306). In the attempt to further improve local outcome in breast-conserving therapy we introduced intraoperative radiotherapy (IORT) with low-kilovoltage X-rays as a boost during oncoplastic BCS followed by EBRT.

Material and Methods: Between February 2010 and July 2011, a total of 100 patients were treated with IORT as a boost (20 Gy, 50 kV x-rays; Intrabeam System, Carl Zeiss Surgical, Oberkochen, Germany) during primary oncoplastic breast-conserving surgery, followed by whole-breast radiotherapy. After segmental resection of the tumour during oncoplastic BCS and frozen-section analysis to reveal tumor-free resection margins the adequate size of the bowel-applicator for IORT-boost was evaluated. After mobilisation of glandular tissue the segmental resection borders were narrowed to the applicator using purse-string sutures. Resection defects were definitely reconstructed after IORT-boost using the predefined oncoplastic principles to achieve optimal esthetic results after BCS.

Results: Median age was 61.8 (range 30–74) years. There were T1 and T2 tumours in 76 and 24 patients, respectively, and N0, N1 and N2 disease in 69, 21, and 10 patients, respectively. The used radiation applicator-sizes ranged between 25 and 40 mm in 79% of the patients. The mean radiation time was 21 (range 18–32) minutes. IORT boost radiotherapy was combined with oncoplastic principles for partial mastectomy reconstruction: glandular rotation (n=86), dermoglandular rotation (n=7), tumoradapted reduction mammoplasty (n=7). With a median follow-up of 7.6 months 1 patient had a chronic skin toxicity with percutaneous fistula, while 2 patients developed liponecrosis and 3 patients a seroma which was punctured.

Conclusion: IORT as a tumour bed boost with low-kilovoltage x-rays is clinically applicable with low toxicity and complication rates. The method supports the close interdisciplinarity between radiation therapy and breast surgery and can be combined with oncoplastic principles in BCS.

599

Poster

Lymph Node Metastases Detection by FDG-PET and Sentinel Node Biopsy in Breast Cancer Patients: Clinical and Biological Meaning

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Background: Sentinel node (SN) biopsy has become the reference method for the evaluation of axillary involvement in breast cancer (BC), for decision of the need of axillary surgery and/or adjuvant treatment. Positron Emission Tomography (FDG-PET) is a non-invasive tool able to evaluate the regional nodes in BC by a metabolic-dependent, bio-molecular related way. In 1999, after our previous PET experience on nodal involvement in BC we started a prospective non randomised study in order to compare the two methods in terms of sensibility, accuracy and predictive value. The main aim was to evaluate the prognostic information given by PET, due to the work

hypothesis that PET results may directly be influenced by the bio-molecular characteristics of primary BC.

Methods: 145 T1N0 BC patients were studied from 06 1999 to 11 2006. FDG-PET was performed no later than 48 hours before surgery. Lymphoscintigraphy was performed within 6 hours before surgery. SN biopsy was followed in all cases by a complete ALND. Pathologic involvement of the SN and the other non-SNs was evaluated on definitive sections and represented the basis of the comparison between PET imaging and SN biopsy.

Results: The median age was 54 years (range 24–70). All patients had pT1 BC except 3 pts with pT2 BC. The average histological tumor size was 16 mm (range 1–35 mm). All lymph nodes detected by lymphoscintigraphy were in axilla, and the detection rate was 100%. All patients underwent complete ALND. 62 patients out of 145 had nodal metastases (42.7%) and 29 had one positive axillary node.

PET results showed 45 true positive and 17 false negative, whereas SN biopsy resulted false-negative in 7 cases and true-positive in 55 cases. The negative predictive value of PET and SN biopsy was 80.5% and 92.2% respectively. However, if micrometastasis detected in SN biopsy may explain in part the PET results, the analysis of clinical, pathological and bio-molecular factors on the primary tumor showed two different patients' population inside PET evaluated N+ patients. A subgroup of more aggressive tumors (ER-, GII, Her2+) were mainly in the PET true-positive patients, whereas in PET false-negative patients, LumA, Mib1 low rate BC were statistically significant detected ($p=0.005$). Overall, the Kaplan Meier survival estimates on the entire patients' population showed a significant worse curve in N+PET+ patients respect to all the other after a median 7 years follow-up; N+PET- and N-PET+/- curves were overlapped ($p=0.017$).

Conclusions: Intrinsic biologic features of primary tumor are probably determinant of FDG-PET results and on clinical meaning of nodal metastases in term of prognostic value and therapeutic planning. PET false negative cases may identify less aggressive indolent metastasis. Removal of these axillary nodes may be facultative without the risk of understaging the disease.

600

Poster

Is a Clinicopathological Scoring System Valid in Selecting Patients for Sentinel Lymph Node Biopsy?

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Background: Sentinel lymph node biopsy is widely used as an alternative to axillary clearance in early breast cancer. However, selecting those patients most likely to require axillary clearance from initial investigations can be difficult. Carmichael et al. outlined a clinicopathological scoring system to select patients for sentinel node biopsy versus axillary clearance in 2006. This was prospectively assessed favourably by Pinkney et al. in 2007. A retrospective validation series in our unit also supported the implementation of this scoring system. We now present our experience of the prospective use of this scoring system for stratifying patients for sentinel node biopsy versus axillary clearance.

Materials and Methods: Carmichael's 10-point scoring system was calculated for all invasive breast cancer patients at the pre-operative multidisciplinary team meeting over an 18 month period between 2007 and 2009. The score was used with clinical information and patient preference to decide on the nature of the axillary surgery undertaken. The lymph node status from either sentinel node or axillary clearance results was then compared with the pre-operative Carmichael score.

Results: 190 patients with a mean age of 61 years were assessed using Carmichael's scoring system. The accuracy of the scoring system was 62% with a false positive rate of 25% and a false negative rate of 12%. A low score reflected a 20% node positive rate (21% in validation series) whilst a high score reflected a 45% node positive rate (85% in validation series).

Conclusions: Despite the results from our validation series, this test has not shown sufficient accuracy when used prospectively. The scoring system appears to overestimate the need for axillary clearance. Whilst there is a place for a clinicopathological test in a sub-group of patients, the requirement for this is likely to be superseded by intra-operative sentinel node assessment techniques. Until these techniques are broadly implemented, the decision regarding axillary surgery in breast cancer patients remains a clinical judgement in our unit.

601

Poster

Factors Influencing Requirement for Re-excision in Breast Conservation for Ductal Carcinoma in Situ

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Background: Previous results from the UK National Breast Cancer Screening Programme have highlighted that there were a higher proportion of women with ductal carcinoma in situ (DCIS) only undergoing more than one procedure for complete excision in our region than in other regions in Scotland. While an internal review of those individual cases was performed for audit purposes, we sought to determine any causative or predictive factors to improve the numbers of patients with DCIS completing treatment with one operation.

Methods: All patients undergoing breast conserving surgery for DCIS from February 2010 for a twelve month period were identified from the local cancer audit database. Patients undergoing mastectomy as first operation for DCIS, and patients with microinvasive or invasive disease were not included.

Results: In the twelve month period from Feb 2010, forty-three patients were diagnosed with DCIS. Of 35 patients that had breast conserving surgery for DCIS, 26 required only one operation, 8 required two procedures and one required three procedures. There was no difference in age or mode of presentation between those that required one or more operations for disease control. Tumour size on final pathology was significantly greater in those that had more than one operation ($p=0.03$). In those who had one operation, in no case was the disease extent underestimated on mammography by greater than 10 mm, and in 5 cases the disease was overestimated by >10 mm. In those that had more than one operation, the disease was underestimated in 3 cases (>10 mm) and not overestimated in any case ($p=0.01$). Initial excision specimens from those that required more than one procedure were of similar mean weight as those with more than one procedure, but had a significantly greater volume (mm^3 ; $p<0.0001$), despite overall pathological size after all treatment being larger in this group. In 88% of those undergoing one operation DCIS was diagnosed on core biopsy (B5a), whereas only 55% of those who required more than one procedure were B5a on core biopsy ($p=NS$). Grade of DCIS (low, intermediate or high) was not a factor in determining need for re-excision.

Conclusion: Factors influencing complete excision of DCIS with a single procedure were smaller tumour size, underestimation of extent of disease on mammography (by >10 mm), larger volume excision at first procedure, and core biopsy not showing DCIS pre-operatively.

602

Poster

Sentinel Lymph Node Micrometastases. How to Act?

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Background: Complete axillary node dissection (ALND) is the standard surgical treatment for women with sentinel lymph node (SLN) micrometastases of breast cancer. In recent years, some studies have compared SLN and ALND, and even if more data is necessary, it appears that SLN alone do not result in inferior survival. However, patients with ALND are more likely to suffer from morbidities such as paresthesias, shoulder pain and lymphedema.

We analyze the rate of axillary micrometastases found in our patients as well as the clinical and histopathological features and current status of these women.

Materials and Methods: Retrospective observational study including 26 patients with breast cancer and nodal micrometastases diagnosed in the period 2007–2010 in our multidisciplinary unit.

Results: From January 2007 to November 2011 we have obtained a positive result for micrometastases in 26 patients. We used hematoxylin eosin staining intraoperatively between 2007 and 2009. From 2010 we are using the OSNA method (detection of CK19 copy number), making the 65.38% of this determinations by this technique. Average age of these patients: 60.99 years. Average tumor size after surgery: 20 mm. We found infiltrating ductal carcinoma in 22 patients (84%) and infiltrating lobular carcinoma in four of them (7.69%). 22 women had hormone-sensible carcinomas. 13 of them luminal A and 9 of them Luminal B. 4 tumors overexpress erb-2. There was no triple-negative phenotype. 61% of the tumors were grade II tumors, 27% of them were grade III tumors and 3.8% of them were grade I tumors.