

EA-NSM with the conventional method and a large clinical trial with long-term follow-up are needed to accept its safety and complications.

516

Poster

# Excision of Breast Cancer Followed by Radiofrequency Ablation of Margins Decrease the Need for a Second Surgery for Close or Positive Margins

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**Background:** Excision of breast cancer followed by radiofrequency ablation (e-RFA) is a technique designed to increase the margin in breast conservative surgery (BCS) by heat generated from high frequency alternating currents. The objective of this study is to analyze the impact of the e-RFA in avoiding a second surgery for close or positive margins after BCS.

**Material and Methods:** From February 2008 to May 2010, 20 patients with a diagnosis of stage I invasive ductal carcinoma of the breast and planned BCS were included in the study after signing an informed consent. After lumpectomy, the RFA probe was deployed in the lumpectomy cavity and heated at 100° during 15 minutes. After the RFA, biopsies from each margin from the radial ablated cavity walls were obtained. The biopsies were sent fresh to Pathology and placed in the Triphenyltetrazolium chloride (TTC) vitality stain for assessment of the ablation zone width and tumor viability. Lumpectomy and sentinel nodes were analyzed by standard pathologic examination. All patients received radiation therapy to the breast as part of the BCS treatment.

**Results:** e-RFA was successful in 19 patients. Mean age was 66.9 years (range, 46–76 years). The mean pathologic size of tumor was 14.7 mm (range, 4–28 mm). In all patients the devitalized tissue extended beyond the 5–10 mm radial depth of the biopsy sample. Six patients (26%) had margins <2 mm in the final pathology, 4 of them with <1 mm margin. All the 6 patients had the incisional biopsies from the cavity wall with no tumor viability after stained by TTC. The other 13 patients had negative margins although in one patient, a small ductal in situ carcinoma was found at the edge of the cavity biopsy following the coagulative necrosis. She underwent a mastectomy. There were no complications from the RFA. Six patients (25%) developed a lipid cyst in the mammogram at one year after the RFA. At a median follow-up of 28 months (range, 12–43 months), no local recurrences have occurred.

**Conclusions:** This study supports the feasibility of radiofrequency lumpectomy cavity treatment to extend final negative tissue margins by approximately 1 cm. The e-RFA has spared 25% of patients to undergo a re-excision surgery for close or focally positive margins and in long term it may reduce local recurrences.

517

Poster

# Presence of Symptoms and Timing of Surgery Do Not Affect the Prognosis of Patients with Primary Metastatic Breast Cancer

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**Background:** Though most studies on surgical resection of the breast tumor in patients with primary distant metastatic breast cancer indicated that surgery is associated with prolonged overall survival, some state that this effect has been confounded by indication for an operation and the timing of surgery. In this study we analysed these possible confounders and their relation to overall survival.

**Methods:** The Eindhoven Cancer Registry of the Comprehensive Cancer Centre South records data on all newly diagnosed patients with cancer in the south of the Netherlands. With these data we already performed a study on 728 patients with primary distant metastatic breast cancer. The current study includes a selection of the patients, derived from four large

teaching hospitals in the south of the Netherlands, resulting in 318 eligible patients diagnosed between 1995 and 2005 for whom extensive analysis was possible.

**Results:** The median survival in patients treated with surgery of the breast tumor was 39 months, compared to 15 months for those without surgery ( $p < 0.0001$ ). The median survival of patients with symptomatic metastatic disease ( $n = 112$ ) was 19 months, compared to 22 months for those without symptomatic disease ( $n = 167$ ) ( $p = 0.15$ ). Patients who received surgery and whose metastases were detected before surgery of the breast tumor had taken place ( $n = 40$ ) had a median survival of 38 months, compared to 40 months for patients in whom the metastatic disease was diagnosed after surgery ( $n = 43$ ) ( $p = 0.81$ ).

**Conclusion:** Presence of symptomatic metastatic disease and the timing of surgery were no significant prognostic factors for breast cancer patients with distant metastasis at diagnosis. Therefore, it is unlikely that the prolonged survival after surgery is explained by these two potentials confounders.

Table 1. Characteristics of patients who had surgery before or after the diagnosis of the metastases ( $n = 83$ )

	Number of patients with surgery		P-value
	Before diagnosis of metastases (n = 43)	After diagnosis of metastases (n = 40)	
<b>Age at diagnosis (years)</b>			0.53
<50	15	10	
50–69	17	16	
≥ 70	11	14	
Median age [range]	54.6 [32.6–88.7]	64.8 [27.1–92.1]	
<b>T-classification</b>			0.0001
T1–2	32	13	
T3–4	5	21	
Unknown	6	6	
<b>Hormone receptor status</b>			0.01
ER and/or PR positive	30	38	
ER and PR negative	11	2	
ER/PR unknown	2	0	
<b>Site of metastases</b>			
Bone	24	30	0.07
Liver	14	6	0.06
Lung/pleural	3	5	0.39
Cutaneous	2	1	0.30
CNS	0	1	0.60
Other/unknown	3	3	0.93
<b>Number of metastatic sites</b>			0.52
1	39	35	
≥2	3	5	
Unknown	1	0	
<b>Symptomatic metastases</b>			<0.0001
Yes	2	16	
No	41	24	
<b>Margin status</b>			0.86
Complete resection	33	28	
Positive margins	7	8	
unknown	3	4	

518

Poster

# Sentinel Lymph Node Biopsy in Breast Cancer: the Approach in Day Surgery Under Local Anaesthesia for Quality-of-life and Effective Cost Reduction

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**Background:** Sentinel lymph node biopsy (SLNB) is widely used in the management of breast cancer patients without axillary metastases and inflammatory breast cancer.

Purpose of this study is to investigate the approach in day surgery (DS) under local anaesthesia (LA) for quality of life and cost reduction.

**Materials and Methods:** From Jan. 1<sup>st</sup> 2006 through Apr. 30<sup>th</sup> 2011 we performed 265 SLNB at St. M. Goretti Hospital. Mammary carcinoma was diagnosed as malignant by cytology and/or biopsy. Quadrantectomy and SLNB were performed at the same time in cases of positive cytology or biopsy. All patients underwent pre-operative lymphoscintigraphy

and surgical treatment 3–12 h. later. SLNB and quadrantectomy were performed in DS and LA without ever using vital blue dye. Axillary incision was 3–4 cm. This study was approved by an ethics committee, discussed with all patients and informed consent was obtained.

**Results:** Four patients underwent pre-operative lymphoscintigraphy, the radiotracer did not show any sentinel lymph node (SLN), we directly performed axillary dissection. In these cases the axilla was positive. In three other cases of multifocal (MF) and two of multicentric (MC) invasive breast cancer the SLN was identified and SLNB was performed. Only one case of MC cancer the SLNB was positive. In three other cases of multifocal (MF) and two of multicentric (MC) invasive breast cancer the SLN was identified and SLNB was performed. Only one case of MC cancer the SLN was positive. Four patients classified T4b with negative axilla to clinical examination and Positron Emission Tomography (PET) were treated with neoadjuvant chemotherapy (NC). After completion of NC, lymphatic mapping was able to identify SLN and we performed SLNB. In these patients SLN was negative. Two cases of male cancer with negative axilla to clinical examination had SLN positive for macrometastases. Four cases showed isolated tumor cells, sixteen micrometastases and twenty-nine macrometastases. In one case of negative SLN there was a positive second palpable lymph node. Another case showed a double SLN in the axilla and internal mammary chain, but only the internal mammary SLN was positive. The SLN identification rate was 99%. After surgery we distributed a questionnaire to the patients about the acceptability of this approach.

**Conclusions:** This approach is safe, well accepted by patients who reported better quality of life (99%). The oncological results are absolutely reliable. As regards hospital logistics, operations in DS and LA can be easily managed leading to an effective cost reduction of 42.15%, less expensive than the same operation performed under general anaesthesia.

519

Poster

#### Intraoperative One-step Nucleic Acid Amplification Assay(OSNA) to Detect Sentinel Lymph Node(SLN) Metastasis in Breast Cancer – an Evaluation of 703 Cases in a Single Institution

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**Background:** One-step nucleic acid amplification assay (OSNA) is a semi-automated lymph node examination method with semi-quantitative result reflecting the volume of metastatic foci by measuring the amount of CK19 mRNA in sentinel lymph node (SLN). Recent studies have revealed that OSNA method is as accurate as conventional histological examination for the detection of SLN metastasis. The aim of the study was to evaluate the ability of OSNA to predict SLN metastases, as well as to validate the semi-quantitative range of CK19 mRNA in detecting or excluding metastases.

**Material and Methods:** From August 2009 to March 2011, 703 breast cancer patients without clinical lymph node metastasis had undergone SLN biopsy during breast cancer operation. Both 99mTc and blue dye were injected into the dermis of the areola before surgery. All nodes stained with blue dye and/or those with high radioactive counts were defined as SLNs. The result of OSNA was classified by the amount of CK19 mRNA  $<2.5 \times 10^2$  copies/ $\mu$ L,  $2.5 \times 10^2$ – $5.0 \times 10^3$ , and  $>5.0 \times 10^3$  as –, + and ++, respectively. OSNA+ and ++ were defined as metastasis of SLN. OSNA+ and ++ patients received axillary dissection (ALND) while OSNA– patients were avoided. All the nodes acquired from ALND and those removed as non-SLN were examined by routine histological examination after the operation.

**Results:** From 703 patients, 870 SLNs were examined with an average 1.24 nodes in each patient. The average time to obtain the result of OSNA was 36 minutes. Among the 703 patients, 581 patients (82.6%) were OSNA–, while 56 (8.0%) were +, 66 (9.4%) were ++. The total median number of axillary nodes removed for both OSNA and histological examination was as follows: OSNA–/+ /++: 3 (1–15)/9 (2–22)/14 (4–35). The total median number of metastatic nodes was identified in OSNA–/+ /++: 0 (0–3)/1 (1–6)/2 (1–28). There appeared a correlation between tumor size and the frequency of OSNA result, with T0 (n=104): OSNA–/+ /++: 101 (97.1%)/2 (1.9%)/1 (1.0%) vs T1 (n=314): 269 (85.7%)/21 (6.7%)/24 (7.6%) vs T2 (n=262): 197 (75.2%)/30 (11.5%)/35 (13.4%); vs T3 (n=18): 10 (55.6%)/2 (11.1%)/6 (33.3%) vs T4 (n=5): 4/1/0. Non-SLN metastasis were identified in 1.5% (9/581) in OSNA–, as compared to 17.9% (10/56) in OSNA+ and 57.6% (38/66) in OSNA++ patients respectively. Positive predictive value of OSNA++ for non-SLN metastasis (38/66, 57.6%) was significantly higher than that of OSNA+ (10/56, 17.9%) ( $p=0.0001$ ).

**Conclusions:** OSNA is an accurate tool for intraoperative assessment of SLN status and could reduce the burden on pathologists. The semi-quantitative result of OSNA–/+ /++ was a strong predictive factor indicating

additional non-SLN involvement, which suggests that further axillary procedure may be potentially avoided in OSNA-patients, but considered for OSNA++ patients. In addition, for patients with OSNA+, consideration could be made for pickup of selected suspicious nodes instead of ALND.

520

Poster

#### Lymphoscintigraphy – is It Important for Accurate Sentinel Lymph Node Biopsy?

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**Aim of the study:** to determine the value of lymph-nodes (LN) scintigraphy as a part of sentinel LN (SN) biopsy in patients (pts) with breast cancer.

**Material and Methods:** LN visualisation was performed before SLN biopsy in 92 primary pts with breast cancer. Scintigraphic images were acquired 1–15, 30, 240 and 480–720 min after intratumoural injection of 75–150 MBq (0.5–1 ml) of 99mTc-nanocolloids (d <80 nm). Delayed images (obtained 1–2 hr before operation) more precisely visualised hot nodes which can be detected by gamma probe during biopsy. SLN were determined according to the following criteria: first appeared LN in the area, the only visualised LN, LN connected with tumour by the 'the road of lymph flow'. All other LN were considered as second-echelon nodes.

**Results:** SLN were successfully visualised in 86 of 92 evaluated pts (98%). Axillary LN detected in 83 pts: in 38 (41.3%) pts it was the only region of lymph flow from tumour, in 45 (52.1%) cases – it was accompanied by drainage to internal mammary and/or sub-supraclavicular LN. In 3 pts all SLN were localised outside axillary region: subclavicular – in 1 and internal mammary – in 2 cases.

Second echelon LN detected in 64 of 83 (77.1%) pts with 'hot' nodes in the axillar. 'Hot' nodes revealed in sub-supraclavicular region were SLN only in 4 of 34 (11.7%) cases. On the contrary, visualised internal mammary LN were considered SLN in all 27 observations.

**Conclusion:** LN scintigraphy must be obligatory done before SLN biopsy in order to differentiate SLN from second echelon axillar LN (77.1% of cases) and because visualisation help to detect SLN outside the axillary region in 36.1% of pts.

521

Poster

#### The Predictive Factor of Non-sentinel Lymph Nodes Metastases for Breast Cancer Patient with Micrometastasis and Macrometastasis in Sentinel Lymph Node Only

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**Background:** Sentinel lymph node(SLN) biopsy is considered the gold standard technique for axillary staging in early stage breast cancer. Tumor-positive SLN suggests a risk of non-SLN metastases in breast cancer. This risk is lower after micrometastasis in SLN, and recent studies suggest that completion axillary lymph node dissection (ALND) might not improve outcome in these patients. So, we analyzed the clinicopathological factors of the primary tumor with micrometastasis in SLNs that can influence the risk of additional metastasis in the non-SLNs.

**Material and Methods:** We retrospectively reviewed the results of 622 consecutive SLN biopsies for breast cancer performed in Hallym University Sacred Heart Hospital from January 2006 to June 2011. We selected 140 patients with positive SLN followed by ALND for invasive ductal carcinoma. In 10 patients, isolated tumor cells were found in SLN and were not included in the study. The study population included that 10 patients with negative SLN after H&E stain had micrometastasis in SLN after IHC, eventually underwent completion ALND. All of the patients had breast cancer with T1 or T2 stage and negative axilla clinically. 69 patients (group 1) had only one of positive SLN after ALND, 71 patients (group 2) had more than 2 positive lymph node including positive SLN. We analyzed group 1 and 2 with clinicopathological factors to predict non-SLN metastasis.

**Results:** There were no significant differences in clinicopathological factors between patients with micrometastasis and the others with macrometastasis in group 1. Compared with group1 and group2, tumor size more than 2 cm was associated with non-SLN metastases ( $p=0.039$ ). In addition, histologic grade ( $p=0.032$ ) and lymphatic invasion ( $p=0.002$ ) were significant factor to predict non-SLN metastases. Only 1 of 10 patients with micrometastasis in SLN had non-SLN metastasis. The patients had risk factor-tumor size ( $\geq 2$  cm), high histologic grade(3) and lymphatic invasion.

**Conclusions:** Nonsentinel node metastases are rare with micrometastasis in SLN. Although data from randomized controlled trials are lacking, we suggest SLN dissection is recommended as preferred care for SLN-negative patients and selected patients with SLN-micrometastasis. Despite this, ALND remains the standard management in breast cancer patients