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The study of micrometastasis detection in sentinel lymph node of breast cancer

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Background: Although sentinel lymph node biopsy (SLNB) has become the method of choice for axillary staging, the extent of the pathological examination (HE or IHC, the number or intervals of sections) described in the literature differed considerably between studies, particularly for the detection of micrometastases (MMs). Our aim was to evaluate the optimal methods and intervals for the detection of SLN macrometastases, MMs and isolated tumor cells (ITCs).

Material and Methods: Ninety-eight continuous breast cancer patients with 200 SLNs identified "negative" with standard HE stain carried on initial 4 levels were retrospectively analyzed. All SLNs were step sectioned (SS) at 100μm interval, and for each level both HE and IHC with AE1/AE3 were performed. Then HE and IHC detection rates were analyzed at 100-, 200-, 300-, 400-, and 500μm intervals for the detection of macrometastases, MMs and ITCs.

Results: In 98 cases with original SLN negative cases, 18 (18.4%), 25 (25.6%) and 27 (27.6%) cases were found to had metastases with SS HE, SS IHC, and SS HE + IHC, respectively (SS HE + IHC vs. SS HE, $p = 0.004$). In all the 2175 sections, metastases were found in 79 sections (3.6%) by SS HE, and 127 (5.8%) by SS HE + IHC ($p = 0.000$). The metastases included macrometastases 16.7%, MMs 50.0%, and ITC 33.3%. The detection rates of MMs were 9.2%, 15.3%, and 16.3%, respectively (SS HE + IHC vs. SS HE, $p = 0.03$). The detection rates of ITCs were 6.1%, 7.1%, and 9.2%, respectively ($p > 0.05$). The detection rates of metastases at 100-, 200-, 300-, 400-, and 500-μm intervals by SS HE were 18.4%, 14.3%, 13.3%, 12.2%, and 12.2%, respectively. No significant differences were found between 100- and 200-μm intervals ($p = 0.125$), and between 100- and 300-μm ($p = 0.063$), while $p < 0.05$ between 100-μm and other intervals. The detection rates of metastases at 100-, 200-, 300-, 400-, and 500-μm intervals by SS HE + IHC were 27.6%, 23.5%, 18.4%, 20.4%, and 19.3%, respectively. No significant difference was found between 100- and 200-μm intervals ($p = 0.125$), while $p < 0.05$ between 100-μm and other intervals.

Conclusion: SS HE could significantly increase detection rate of SLN metastasis compared to our routine 4 levels HE pathological examination. SS HE + IHC could further significantly improve the detection of SLN metastases, mostly due to the detection of MMs. The optimal interval was 300 μm for SS HE, and 200 μm for SS HE + IHC. Our data will be updated to 244 cases with 4yrs follow-up at the meeting.

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Intraoperative frozen section examination of sentinel lymph node in breast cancer – always, never, sometimes

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Background: Intraoperative frozen section examination of sentinel lymph node (IFSESLN) in breast cancer is controversial and increases the operating time. Partial IFSESLN requests a delayed axillary lymph-node dissection (DALND) in false negative cases increasing costs and psychological distress for patients. The aim of this study is to identify a subset of breast cancer patients candidates for sentinel lymph node biopsy (SLNB) in which IFSESLN can be avoided increasing the number of daily operations, without increasing DALND.

Materials and Methods: 1205 IFSESLN consecutively performed at our department from 2001 to 2007 were reviewed and distribution of positive lymph nodes was considered according to tumor size and results of IFSESLN. IFSESLN was performed as follows: quick freezing was performed with a cooled flat weight to obtain a flat surface and 4 consecutive frozen sections were cut at a microtome setting of 4 microns. Care was taken to waste only the minimum lymph node material when cutting.

Results: Sensitivity of IFSESLN has been 41.9% and in 20.1% of patients a DALND was performed. In T1mic, T1a, T1b breast cancers (427 pts) 71 pts were N+ (16.6%). With IFSESLN the DALND were 51 i.e. 11.9%, with a reduction of 20 DALND (4.7%). In T1c, T2, T3-T4 breast cancers (778 pts) 347 pts were N+ (44.6%). With IFSESLN the DALND were 192 i.e. 24.6%, with a reduction of 155 DALND (19.9%) (Tab1).

Conclusions: According to the results above our future policy will be not to perform IFSESLN in T1mic, T1a, T1b breast cancers and to reoperate N+ patients of this group. On the basis of this experience if we had applied this policy, we would have performed IFSESLN in T1c, T2, T3-T4 breast cancers and DALND in 21.8% (263/1205). This would have increased of 1.7% the number of DALND performed and decreased of 35.4% (427/1205) the number of IFSESLN, allowing to reduce the waiting list by increasing the number of operations per day. On the basis of these data we will follow this policy.

Table 1. Distribution of breast cancer patients according to tumor size, positive lymph nodes and IFSESLN

Tumor size	No. of pts	%	N+	%	IFSESLN +	Sensitivity %	False negatives	%
T1mic	28	2.3	5	17.8	0	0	5	100
T1a	90	7.4	10	11.1	4	40	6	60
T1b	309	25.6	56	18.1	16	28.6	40	71.4
T1c	551	45.6	224	40.6	84	37.5	140	62.5
T2	222	18.4	120	54.1	68	56.6	52	23.4
T3–T4	5	0.4	3	60	3	100	0	0
All	1205	100	418	34.68	175	41.9	243	20.1

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The frozen section is superior to imprint cytology for intraoperative diagnosis of sentinel node biopsy for breast cancer

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Background: Sentinel lymph node biopsy (SNB) has become the preferred alternative to identify or exclude axillary nodal metastasis in breast cancer. Two procedures, intraoperative frozen section (Fs) analysis and imprint cytology (Cy) of sentinel lymph node (SLN) have been to shown to be reliable for detecting breast cancer metastases in SLN. Recently, several techniques such as histo- and cytopathologic methods, immnohistochemistry or molecular biology have been introduced, however, available in not all institutions as routine procedures. In the present study, we compared Fs and Cy to clarify which will be more reliable for intraoperative SLN diagnosis.

Materials and Methods: A total of 118 patients of primary breast cancer, who received SNB treatment at Niigata University Hospital between 2003 and 2006, were entered. The intraoperative SLN diagnosis was performed by Fs, Cy or both. The result of intraoperative diagnosis was compared with postoperative histological diagnosis (Hx). The sensitivity (ST), specificity (SP), accuracy (AC) and false negative rate (FNR) of each method was compared.

Results: SLNs were successfully identified in all 118 patients (100%), and SLN metastases were detected in 30 cases by intraoperative Cy and/or Fs. However, postoperative Hx revealed metastatic SLNs in further 2 cases (ST 93.8%, AC 98.3% and FNR 6.3%). Among 368 removed SLNs, metastases were detected in 48 nodes by intraoperative Cy and/or Fs. However, postoperative histological diagnosis revealed metastatic SLNs in further 2 nodes (ST 96%, AC 99.5%, FNR 4%). The intraoperative Cy diagnosis was performed in 117 cases, and metastatic SLNs was detected in 26 cases, however, postoperative Hx revealed metastatic SLNs in further 3 cases (Cy: ST 89.7%, AC 97.4%, FNR 10.3%). The intraoperative Fs diagnosis was performed in 90 cases, and meatstases were detected in 26 cases, however, postoperative Hx revealed metastatic SLNs in further 2 cases (Fs: ST 92%, AC 97.6%, FNR 8%). In the 89 cases of both Cy and Fs was done simultaneously, metastases were detected in 23 cases by postoperative Hx. Among 23 metastatic cases, metastasis was detected in 19 cases by Cy and in 22 cases by Fs. Among a total of 268 SLNs, metastases were detected in 35 nodes by postoperative Hx. Among 35 metastasic nodes, Cy detected 31 nodes and Fs detected 34 nodes.

Conclusions: Our study suggests that Fs is more accurate and useful method than Cy for the intraoperative diagnosis of SLN metastasis.

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Comparative study of long-term morbidity in patients with breast cancer after sentinel lymph node biopsy and axillary sampling versus axillary dissection

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Background: Intraoperative examination of the sentinel lymph node biopsy may correctly detect axillary node metastases in more than 90% of the