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Reliability of Detecting Macrometastases in Sentinel Lymph Node in Breast Cancer Patients by Bivalved Section in Comparison to Serial Section

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Abstract

Objectives: **The aim of this study was to compare the reliability of bivalved section with serial section to detect the macrometastases in sentinel lymph node in breast cancer patients.**

Materials and Methods: **A total number of 40 patients were involved in the reliability study to detect the macrometastases in sentinel lymph node (SLN) in breast cancer patients in the Department of Surgery, Phramongkutklao Hospital & College of Medicine, between January 2000 and June 2004.**

Results: **Of 76 sentinel lymph nodes, 28 were positive and 48 were negative. In detecting SLN by dye direct injection with isosulfan blue, 42 out of 45 cases were identified, with an identification rate of 93.3% and with false negative (skip metastases) in 2 cases (4.76%). The negative SLN by bivalved section was then studied by serial section at 1 mm interval and dyed with H & E, whereby 1 node of micrometastases was encountered. However, when compared with previous slide, the micrometastases already existed. No additional metastases were encountered in other lymph nodes as well as in false negative lymph nodes.**

Conclusions: **This study revealed that there was no difference in detecting macrometastases of SLN by bivalved section and serial section. The reliability in detecting the macrometastases by bivalved section in this study is 100%. However, the numbers of the sample are too small for conclusion and further studies with more sample size are required.**

Breast cancer is the most common cancer in women worldwide and accounts for 18% of women's cancer. In Thailand breast cancer is the second most common cancer in women after cervical cancer. The spread of the cancer to the lymph node is the main factor which affects the diagnosis and the treatment. Axillary lymph node dissection (ALND) helps to detect whether the cancer has spread to the lymph node.

Cancer spread to the axillary lymph node increases according to the size of the primary tumor[1]. Hence, ALND in some patients with small primary tumor does not work and may result in serious complications. Most common complications are paresthesia, seroma and lymphedema[2].

Usually the spread of breast cancer to the axillary lymph node is divided into 3 stages, i.e. from level I to

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II and III respectively. Skip metastatic rate has been reported to be 4%[3]. This leads to Sentinel Lymph Node (SLN) biopsy to identify the cancer spread to the axillary lymph node based on the principle that SLN is the first lymph node that the lymphatic drainage from the primary tumor occurs before spreading to other lymph nodes.

The current standard pathological examination of SLN is the serial section of 2 mm/section and dyed by Haematoxylin and Eosin (H & E) along with immunohistochemistry study (CK-IHC)[4] by which the micrometastases can be detected in 6-8%[5,6].

At Phramongkutklao Hospital SLN biopsy has not been introduced until recently. In addition, SLN has been pathologically examined by bivalved section which can give false negative results. Hence, this study was to compare the reliability of the bivalved section with serial section to detect the macrometastases.

Table 1 Primary tumor, staging & grading

Invasive Ductal Carcinoma	Number of Patients
T stage	
T1a	2
T1b	5
T1c	11
T2	19
T3	1
Grading	
I	6
II	23
III	9
Total	**38**
DCIS	**Number of Patients**
High grade with comedo	3
Low grade non-comedo	1
Total	**4**

Materials and Methods

In this study, SLN biopsy was performed in all patients with breast cancer between January 2000 and June 2004. Serial section at an interval of 1mm/section was performed on all SLN in paraffin block and dyed by H & E. The results were reviewed by a pathologist and classified into micrometastasis and macrometastasis (micrometastasis less than 2 mm, macrometastasis greater than 2 mm).

Analysis is conducted based on basic statistics in %, frequency and mean to determine the reliability.

Results

Between January 2000 and June 2004, SLN biopsy was performed in 45 patients. Each patient received a dye-directed lymphatic mapping with peritumoral injection of 1 ml isosulfan blue at 4 spots. The SLN identification rate was 93.3% (42/45). The total number of identified SLN was 76 (a mean of 1.8 nodes / patient).

Of 42 patients who underwent SLN biopsy, ALND was performed in 40 patients. Two patients received no ALND, one patient had DCIS and the other patient had a negative SLN result and consequently were excluded.

Of the primary tumor, invasive ductal carcinoma was encountered in 38 patients; including T1a in 2 patients, T1b in 5 patients, T1c in 11 patients, T2 in 19 patients and T3 in 1 patient. If categorized according to grading, grade I was encountered in 6 patients, grade II in 23 patients and grade III in 9 patients. DCIS was observed in 4 patients; high grade with comedo in 3 patients and low grade non-comedo in 1 patient (Table 1).

Of all 76 SLN, 28 were positive SLN in 18 patients and 48 were negative SLN in 24 patients. The total number of patient was 42. ALND was performed in 40 patients. One patient had DCIS by frozen section and 1 patient had SLN negative for malignancy by frozen section in which ALND was performed. In these 40 patients, 2 negative SLN (3 SLN nodes) were encountered. There was 4.76% positive ALND (false negative).

Results of pathological examination of SLN and axillary lymph nodes, classified based on primary tumor are shown in Table 2.

A serial section at 1 mm interval was performed on SLN which had undergone a bivalved section and dyed by H&E with negative result. One lymph node was encountered at the 1 mm micrometastasis. However, compared to the previous slide, micrometastasis had already existed but was not reported. Also a serial section was performed on the other 2 SLN with false negative result but no metastases were encountered.

In these procedures the paraffin block was lost in

Table 2 Pathological results of SLN and axillary lymph node classified according to primary tumor

Primary Tumor	SLN Negative	Axillary LN		SLN Positive	Axillary LN	
		Negative	Positive		Negative	Positive
DCIS	3	3	-	-	-	-
T1a	1	1	-	1	1	-
T1b	3	2	1*	1	-	1
T1c	5	5	-	5	4	1
T2	10	9	1*	10	2	8
T3	-	-	-	1	-	1
Total	**22**	**20**	**2**	**18**	**7**	**11**

**false negative*

3 patients which accounted for 6 lymph nodes (5 negative and 1 positive).

Discussion

Studies on the reliability of detecting SLN have been conducted in other countries by using H&E dye only. When the negative SLN from this technique was dyed by CK-IHC, it was found that 6-8%, although negative by H & E, was positive by CK-IHC[5,6]. However, the CK-IHC dyeing technique was to determine the micrometastasis and isolated tumor cell.

It was reported that the chance of SLN micrometastases spreading to non-SLN was slim[7-9]. Also local recurrence in SLN micrometastases with no ALND is unlikely and has no impact on disease free survival.

In this study the focus is thus only on macrometastases SLN which can be found by H & E dye technique and not only by bivalved section. In other countries the interval was 2 mm but in this study a section interval of 1 mm was performed to avoid any failure.

In this study it was found that the reliability rate of SLN identification was 93.3% which is close to many other reports[10,11]. Hence, the incorrectness in detecting SLN has no effect on this study. In 2 patients where serial section was performed on the false negative SLN (3 nodes) followed by H & E dye, the result was still negative and therefore categorized as skip metastases which accounted for 4.76%. This was in accordance with the report of Noguchi M[4], which reported approximately 4% as well.

Of all 40 nodes found in other negative SLN cases, 1 micrometastatic node was encountered after the serial section examination. However, when compared to the previous slide it was found that the micrometastasis had already existed although not reported in the initial pathological result and hence not regarded as new positive SLN. As for the other 39 nodes, no metastases were found. It was concluded that the reliability rate of bivalved section is 100% (42/42) and there was no difference in detecting macrometastases by serial section at 1 mm interval as shown in Table 3.

Table 3 Details of SLN and pathological results

Total SLN: 76 nodes
- Positive - 28 nodes
- Negative - 48 nodes
  - False negative - 3 nodes
  - True negative - 45 nodes *

*No paraffin block - 5 nodes
*Misinterpreted metastases in the initial pathological report - 1 node
Total negative SLN of 42 were included in this study
- Negative SLN in bivalved section 42 nodes
- Negative SLN in serial section with 1 mm interval 42 nodes

In this study there was no difference in detecting macrometastases by bivalved and serial section. However, this is only a pilot study due to the small number of samples and hence further study is required to confirm absolute reliability.

If there were no difference in reliability of these 2 sectioning methods, bivalved sectioning could be adopted for clinical use, as it would help shorten the biopsy procedure, reduce diagnostic cost and time

necessary for determining the pathological result, which will be useful in treating patients in the future.

Conclusion

No difference in detecting macrometastases by the two sectioning methods was found in this study. The reliability in detecting macrometastases by bivalved section is 100%.

However, due to small number of patients and the loss of some paraffin blocks, this study may not be completely correct and hence further study is required.

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