Cancer Science
The official journal of the Japanese Cancer Association

Comparison of core needle biopsy (CNB) and surgical specimens for accurate preoperative evaluation of ER, PgR and HER2 status of breast cancer patients

Kentaro Tamaki,[1,2,3,4] Hironobu Sasano,[2] Takanori Ishida,[1] Minoru Miyashita,[1] Motohiro Takeda,[1] Masakazu Amari,[1] Nobumitsu Tamaki[3] and Noriaki Ohuchi[1]

[1]Department of Surgical Oncology, Tohoku University Graduate School of Medicine, Miyagi; [2]Department of Pathology, Tohoku University Hospital, Miyagi; [3]Department of Breast Surgery, Nahanishi Clinic, Okinawa, Japan

(Received January 26, 2010/Revised May 8, 2010/Accepted May 18, 2010/Accepted manuscript online May 25, 2010/Article first published online June 15, 2010)

The roles of core needle biopsy (CNB) have become well established as an important preoperative diagnostic method for breast lesions. We examined the concordance of histological types, nuclear grades, hormone receptors, and human epidermal growth factor receptor 2 (HER2) status between CNB and surgical specimens in 353 cases. In addition, we analyzed the correlation between the number of CNB specimens obtained and accuracy of histological factors in order to explore the optimal number of CNB specimens. Between CNB and surgical specimens, concordance rates of histological type, nuclear grade, estrogen receptor (ER), and progesterone receptor (PgR) status (cut-off 0–<1%, 1–10%, and 10%<), and HER2 were 84.4%, 81.3%, 92.9%, and 89.3%, respectively. In 52 of 353 patients who were histopathologically diagnosed as ductal carcinoma *in situ* (DCIS) by CNB, final diagnosis was changed in to invasive ductal carcinoma (IDC) in surgical specimens. Statistically significant differences were detected in the discrepancy of the following factors between CNB and subsequent surgical specimens: histological types, nuclear grade, and PgR, between patients who received four or more cores and those who had received three or less cores. In addition, a similar tendency was also detected in estrogen receptor (ER) and HER2 as in the above, and the cases that received four cores reached to 100% concordance in diagnosis between CNB and surgical specimens. Therefore, the optimal numbers of CNB were considered four at least in assessing the histological type, invasion, nuclear grade, hormone receptor status, and HER2 status of individual patients in the preoperative setting. (*Cancer Sci* 2010; 101: 2074–2079)

The incidence of breast cancer is increasing worldwide, which is partly considered to be due to mass screening programs resulting in the discovery of clinically occult breast lesions.(1) In these lesions, relatively a more cautious approach is required to obtain appropriate tissue samples for preoperative pathological analysis. Roles of core needle biopsy (CNB) have become well established as an important diagnostic tool for both palpable and non-palpable breast lesions and it is considered the method of choice for tissue sampling.(2,3) In addition, CNB is less invasive than excision biopsy and generally provided more reliable information compared to fine needle aspiration biopsy cytology (FNAC), especially for providing architectural or histological information. For instance, an absolute sensitivity of ultrasound guided FNAC was 83.1% and that of CNB was 96.7%.(4) Accurate preoperative diagnosis of a breast lesion has recently considered essential for designing an optimal treatment algorithm in order to achieve a definite diagnosis without delay and with minimal biopsies.

The cases receiving preoperative systemic therapy have increased in order to reduce the tumor volume and eliminate possible micrometastasis for the patients with locally advanced breast carcinoma. Therefore, clinical demands on pathologists to provide not only histological diagnosis but also prognostic information for patients, including the determination of estrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2) for treatment planning, have markedly increased for clinicians in institutions of many parts of the world.(2) The information obtained from CNB may be the only information available for determining the candidates for preoperative or neoadjuvant treatment.(2) However, the information obtained from CNB must reasonably reflect that in the whole tissue for determining a treatment strategy for these patients. Results of previous studies demonstrated that the concordance rate between CNB and surgical specimens were 61.7–99% for ER, 61.5–97.1% for PgR, and 80–96% for HER2, respectively.(1,2,5–7) However, it is also true that these studies evaluated only 100 cases at most with a limited statistical power to detect discordance, and results differed significantly between these studies.(5,6) Therefore, in this study, we examined the concordance rate of nuclear grades, hormone receptors, and HER2 status between CNB and surgical specimens in 353 Japanese patients with breast carcinoma.

There have been controversies as to the optimum number of the CNB specimens to be taken from the patients in order to obtain accurate information of whole carcinoma tissues. Three or four cores were initially recommended as the most appropriate or optimum number of the specimens in a pioneer stereotactic study, employing needles of different calibers and excursion.(8) Another study also demonstrated relatively a high correlation of histological parameters between CNB and surgical specimens with only two cores.(9) To the best of our knowledge, no studies have reported the correlation between the number of cores obtained and the status of hormone receptors and HER2 status in the whole specimens. Therefore in this study, we examined the correlation between the number of cores and the accuracy of histological types, nuclear grade, hormone receptors, and HER2 status, and attempted to establish the optimal number of cores taken from the patients in preoperative settings.

Materials and Methods

We examined 353 Japanese female patients with breast carcinoma without neoadjuvant chemotherapy who underwent CNB and surgical resection from January 2002 and June 2009 at the Department of Breast and Endocrine Surgery, Tohoku University Hospital in Sendai, Japan. We received informed consents from all the patients and the protocol for this study was

[4]To whom correspondence should be addressed.
E-mail: nahanisikenta@yahoo.co.jp

doi: 10.1111/j.1349-7006.2010.01630.x

approved by the Ethics Committee at Tohoku University Graduate School of Medicine. The median age of the patients was 57 years (range, 27–85 years). All the core biopsies were performed under ultrasound guidance using a 16-gauge true-cut needle with an automated biopsy device.

We performed staining with hematoxylin–eosin (H&E) and immunohistochemicals for ER, PgR, and HER2 at the Department of Pathology, Tohoku University Hospital. After CNB and surgical resection of the primary tumors, the specimens were fixed in 10% formalin, embedded in paraffin, cut into 4-μm thick sections, and placed on the glue-coated glass slides. For determining the hormone receptor status, we employed the avidin–streptavidin immunoperoxidase method using the clone 6F11 antibody (Ventana, Tucson, AZ, USA) for ER and the clone 6 antibody (Ventana) for PgR in an automated immunostainer (Benchmark System; Ventana). A standardized immunohistochemistry kit (HercepTest for Immunoenzymatic Staining; Dako, Copenhagen, Denmark) was used for HER2 staining. Hematoxylin–eosin (H&E) and IHC staining were performed by a single and experienced technician. Positive controls for ER, PgR, and HER2 were breast carcinoma, whereas negative controls for immunostaining were hepatocellular carcinoma.

Two of the authors independently evaluated CNB samples and surgical specimens twice on different days. They were also blinded to the findings of CNB and surgical specimens, respectively. If there were discrepancies, they reached a final decision using evaluations from the third experienced pathologist. Olympus BX 50 and 20 X objectives (Tokyo, Japan) were used for the analysis. We examined the comparison between CNB samples and surgical specimens for the following parameters: histological types, nuclear grades, ER, PgR, HER2, correlation between the number of cores and status of hormone receptors, and HER2 status in operative specimens. Histopathological evaluations were based on World Health Organization (WHO) histological classification of tumors of the breast[10] and Rosen's Breast Pathology.[11] The nuclear grade was evaluated according to the Japan National Surgical Adjuvant Study of Breast Cancer (NSAS-BC) protocol.[12] By combining the nuclear atypia and mitotic counts, nuclear grades were defined as the summation of scores for the nuclear atypia (1 for low degree atypia; 2 for intermediate-degree atypia; 3 for high-degree atypia) with the scores for the mitotic counts per 10 high-power fields (×40 objective lens) (1 for 0–4 mitoses; 2 for 5–9 mitoses; 3 for 10 mitoses).[12] The nuclear grade was 1, 2, and 3 when the summation of scores for the nuclear atypia and those for mitotic counts were 2–3, 4, and 5–6, respectively.[12] Estrogen receptor (ER) and PgR were determined by nuclear staining graded from 0 to 8 using the Allred score.[13] The results were categorized as positive when the total score (TS), expressed as the sum of the proportion score (PS) and immunointensity score (IS),[13] was 3 or more.[13] In addition, we also evaluated the number of ER- and PgR-positive tumor cells according to the following criteria: cut-off 0–<1%, 1–10%, and 10%<, which was demonstrated by Arihiro *et al.*[14] We also defined the positive hormone receptor status as follows: cut-off 1%≤, discussed at the 11th St Gallen (Switzerland) expert consensus meeting on the primary treatment of early breast cancer in March 2009,[15] and cut-off 10%≤, defined by the J-score system.[14,16] In addition, with regard to HER2 evaluation of 225 cases excluding ductal carcinoma *in situ* (DCIS) diagnosed by CNB or surgical specimen, membranous staining was graded as the following: score 0–1+, 2+, and 3+.[2,6] A score of 0 was defined as no staining observed or membrane staining in <10% of tumor cells, and 1+ as faint/-barely perceptible membrane staining detected in more than 10% of the tumor cells.[2,17] Scoring of 2+ was assigned when there was weak to moderate complete membrane staining in >10% tumor cells; whereas 3+ consisted of uniform, intense membrane staining of >10% tumor cells.[2,17]

Statistical analysis, such as the one-factor ANOVA and simple regression analysis, were performed using StatMate III for Windows version 3.18 (ATMS, Tokyo, Japan). The agreement on the histological types, nuclear grade, hormone receptors, and HER2 status was tested using the kappa test.[18] Results obtained were considered significant at $P < 0.05$.

Results

Concordance of histological type between CNB samples and surgical specimens. The concordance rate of histological types between CNB and surgical specimens was 84.4% (298 of 353 cases) with a kappa value of 0.70 (Table 1). Concordance rates, defined as the number of CNB samples divided by surgical specimens of the following histological types, invasive ductal carcinoma (IDC), DCIS, invasive lobular carcinoma (ILC), and mucinous carcinoma, were as follows: 99.5% (196/197), 58.6% (75/128), 92.9% (13/14), and 100% (14/14), respectively (Table 1).

Concordance of nuclear grades. The concordance rate of nuclear atypia was 76.8% (271/353), including 41 cases with a score of 1, 191 cases with 2, and 39 cases with 3, with a kappa value of 0.55 (Table 2a). The concordance rate of mitotic counts was 82.2% (290/353), including 191 cases of with a score of 1, 57 cases with 2, and 42 cases with 3, with a kappa value of 0.69 (Table 2b). In addition, the concordance rate of nuclear grades was 81.3% (287/353), including 209 cases of with a score of 1, 38 cases with 2, and 40 cases with3, with a kappa value of 0.64 (Table 2c).

Comparison of ER and PgR status between CNB and surgical specimens. The agreement of ER status defined by the following criteria: cut-off 0–<1%, 1–10%, and 10%< was 92.9% (328/353), including 58 cases of cut-off 0–<1%, 12 cases of cut-off 1–10%, and 258 cases of cut-off 10%<, with a kappa value of 0.82 (Table 3a). The agreement of ER-positive or -negative status was as follows: 94.1% (332/353) for the Allred Score, 94.9% (335/353) for the proportion; cut-off level of 1%≤ and 96.0% (339/353) for the proportion; cut-off level of 10%≤, respectively. Sensitivity was 95.2% (279/293) for the Allred Score, 95.8% (277/289) for the cut-off level of 1%, and 96.8% (271/280) for the cut-off level of 10%≤, respectively. However, specificity was 88.3% (53/60) for the Allred Score, 90.6% (58/64) for the cut-off level of 1%≤, and 93.2% (68/73) for the cut-off level of 10%≤, respectively. In addition, positive predictive values (PPV) were 97.6% (279/286) for the Allred Score, 97.9% (277/283) for the cut-off level of 1%≤, and 98.2% (271/276) for the cut-off level of 10%≤, respectively.

The agreement of PgR status was 77.9% (275/353), including 105 cases of cut-off 0–<1%, 40 cases of cut-off 1–10%, and 125 cases of cut-off 10%<, with a kappa value of 0.66 (Table 3b). The concordance ratio of positive and negative was as follows: 86.1% (304/353) for the Allred Score, 89.5% (316/353) for the cut-off level of 1%≤, and 88.7% (313/353) for the cut-off level

Table 1. Analysis of the concordance of histological type between CNB and surgical specimens

		Surgical specimens			
		DCIS	IDC	ILC	Mucinous
CNB	DCIS	75	52	0	1
	IDC	0	196	1	0
	ILC	0	1	13	0
	Mucinous	0	0	0	14

CNB, core needle biopsy; DCIS, ductal carcinoma *in situ*; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; mucinous, mucinous carcinoma.

Table 2. Analysis of the concordance of (a) nuclear atypia, (b) mitotic counts, and (c) nuclear grade between core needle biopsy (CNB) and surgical specimens

(a)

		Surgical specimens			
		Low	Intermediate	High	Total
CNB	Low	41	37	4	82
	Intermediate	11	191	26	228
	High	0	4	39	43
	Total	52	232	69	353

(b)

		Surgical specimens			
		Score 1	Score 2	Score 3	Total
CNB	Score 1	191	18	1	210
	Score 2	13	57	17	87
	Score 3	1	13	42	56
	Total	205	87	60	353

(c)

		Surgical specimens			
		Grade 1	Grade 2	Grade 3	Total
CNB	Grade 1	209	21	4	234
	Grade 2	12	38	20	70
	Grade 3	1	8	40	49
	Total	222	67	64	353

Table 3. Analysis of the concordance of (a) ER and (b) PgR between CNB and surgical specimens

(a) ER

		Surgical specimens			
		0–<1%	1–10%	10%<	Total
CNB	0–<1%	58	7	5	70
	1–10%	0	12	9	21
	10%<	0	4	258	262
	Total	58	23	272	353

(b) PgR

		Surgical specimens			
		0–<1%	1–10%	10%<	Total
CNB	0–<1%	106	21	5	132
	1–10%	0	40	23	63
	10%<	0	29	129	158
	Total	106	90	157	353

CNB, core needle biopsy; ER, estrogen receptor; PgR, progesterone receptor.

of 10%≤, respectively. Sensitivity was 84.6% (219/259) for the Allred Score, 88.7% (211/238) for the cut-off level of 1%≤, and 89.4% (185/207) for the cut-off level of 10%≤, respectively. However, specificity was 90.4% (85/94) for the Allred Score, 91.3% (105/115) for the cut-off level of 1%≤, and 87.7% (128/146) for the cut-off level of 10%≤, respectively. In addition, PPV were 96.1% (219/228) for the Allred Score, 95.5% (211/221) for the cut-off level of 1%≤, and 91.1% (185/203) for the cut-off level of 10%≤, respectively.

Concordance of HER2 status between CNB and surgical specimens. Agreement of the HER2 status defined by the following criteria: cut-off 0,1+, 2+, and 3+ was 89.3% (201/225 invasive carcinomas) including 182 cases of cut-off 0,1+, seven cases of cut-off 2+, and 12 cases of cut-off 3+, with a kappa value of 0.64 (Table 4).

Table 4. Analysis of the concordance of HER2 status between CNB and surgical specimens

		Surgical specimens			
		0–1+	2+	3+	Total
CNB	0–1+	182	6	0	188
	2+	4	7	10	21
	3+	0	4	12	16
	Total	186	17	22	225

CNB, core needle biopsy; HER2, human epidermal growth factor receptor 2.

Analyses of discordant cases. The discordance of histological types was 55 of 353 cases. Among 52 cases which were originally diagnosed as DCIS by CNB, and subsequently changed to IDC by surgical specimens, 63.5% (33 of 52) were T1mic and T1a. The discordance of nuclear grade, ER, PgR, and HER2 was 66 of 353, 25 of 353, 78 of 353, and 24 of 225 cases, respectively (Tables 1–4). We defined major discordance as the discordance of two grades or two scores, and minor discordance as the discordance of one grade or one score. Major discordance of nuclear grade, ER, and PgR accounted for 5 of 66, 5 of 25, and 5 of 78 cases, respectively (Tables 2,3). As for HER2 status, all of 24 discordant cases corresponded with minor discordance (Table 4). Some of these discordances were due to technical problems, for instance, there was only one core and insufficient sample volume caused difficulty in histopathological diagnoses. In the case of only one sampling core that was 100 μm in diameter with a very small amount of carcinoma tissue, accurate diagnosis was difficult. Five discordant cases of histological types, four major and two minor discordant cases of nuclear grades, three major and two minor discordant cases of ER and PgR, and two discordant cases of HER2 status were due to the technical problem described above. On the other hand, all of the other cases were due to intratumoral heterogeneity.

Correlation between the concordance rates and number of consecutive cores. One to five cores were obtained in clinical settings as follows: one core in 158 cases, two cores in 119 cases, three cores in 33 cases, four cores in 17 cases, and five cores in 26 cases. The concordance rate of histological types from one core to five cores was 82.3% (130/158), 83.2% (99/119), 84.8% (28/33), 88.2% (15/17), and 100% (26/26), respectively (Fig. 1a). The concordance rate of nuclear grades from one to five cores was 74.7% (118/158), 84.9% (101/119), 81.8% (27/33), 88.2% (15/17), and 100% (26/26) (Fig. 1b). The concordance rate of ER status was 91.1% (144/158) for one core, 95.8% (114/119) for two cores, 97.0% (32/33) for three cores, 100% (17/17) for four cores, and 100% (26/26) for five cores, respectively (Fig. 2a). The concordance rate of PgR was 88.6% (140/158) for one core, 87.4% (104/119) for two cores, 93.9% (31/33) for three cores, 100% (17/17) for four cores, and 100% (26/26) for five cores, respectively. In addition, the concordance rate of HER2 was 85.6% (83/97) for one core, 88.4% (61/69) for two cores, 91.3% (21/23) for three cores, 100% (15/15) for four cores, and 100% (21/21) for five cases, respectively (Fig. 2b). As for histological types, nuclear grades, and PgR, there were statistically significance between patients who received four or more cores and those who had received three or less cores ($P = 0.035$, $P = 0.012$, and $P = 0.020$, respectively). A similar tendency was also detected in ER and HER2 but did not reach statistical significance ($P = 0.087$ and $P = 0.053$, respectively).

doi: 10.1111/j.1349-7006.2010.01630.x

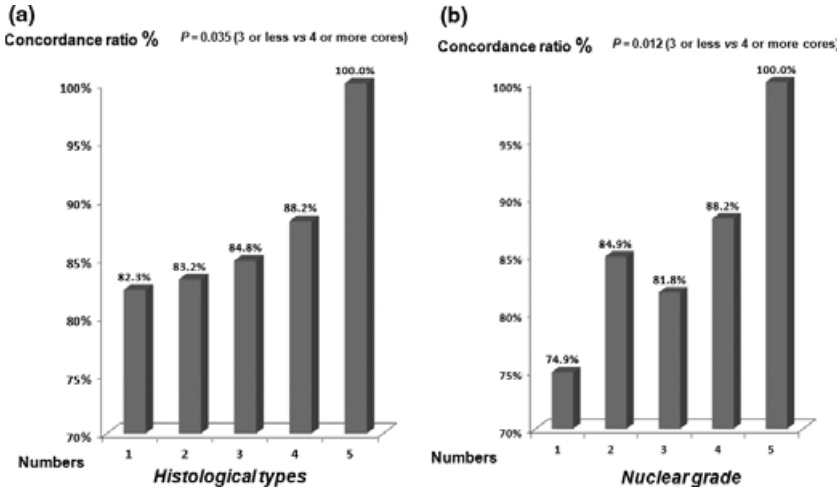

Fig. 1. Analysis of concordance rate of (a) histological type and (b) nuclear grade according to the number of core needle biopsies (CNB).

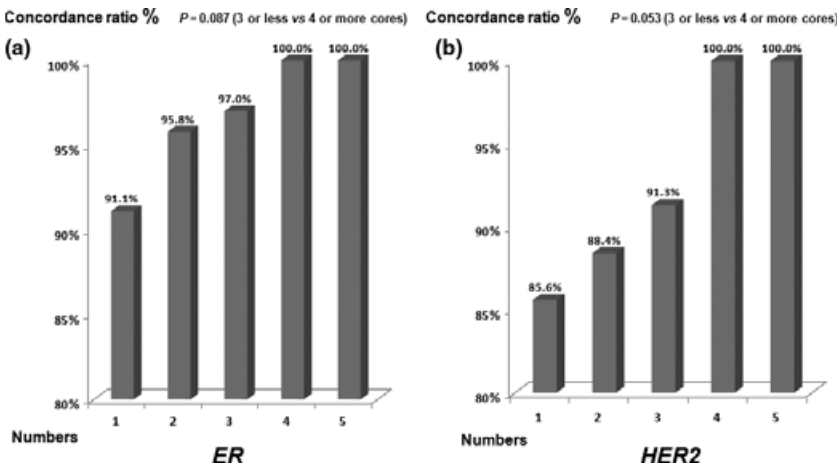

Fig. 2. Analysis of concordance rate of (a) estrogen receptor (ER) and (b) human epidermal growth factor receptor 2 (HER2) according to the number of core needle biopsies (CNB).

Discussion

Core needle biopsy (CNB) has been performed using a variety of devices to evaluate the nature of breast lesions. Core needle biopsy (CNB) has become the gold standard because of its lower inconclusive rate and the histological information it can provide.[19] The histological type of the lesions obtained by CNB was reported to be correlated closely with that of the excision specimen in 87 of 105 (83%) of cases.[5] In our present study, we demonstrated that the concordance rate of histological types between CNB and surgical specimens was 84.4% (298/353), which is very consistent with the results of report above. When the lesions are malignant, the presence or absence of invasion can be documented and the grade and type of tumor present can be assessed by histopathological evaluation of CNB.[19] It is also possible to examine ER, PgR, and HER2 status using immunohistochemistry in CNB specimens.[15] Therefore, information obtained from CNB greatly helps clinicians to determine a treatment plan for individual patients with regard to conservative management or primary chemotherapy.[19] However, some complications of CNB have been also reported in previous studies,[20–23] including postbiopsy pain,[20] hematoma,[21] infection[22] and seeding of carcinoma cells,[23] although such complications are considered rare if done in appropriate institutions by qualified staff. These indicate above all that CNB is a reliable and safe measure to diagnose breast disorders in a preoperative setting.

In our present study, 52 cases diagnosed as DCIS by CNB were subsequently diagnosed as IDC by surgical specimens; however, among these cases, 63.5% (33/52) were T1mic and T1a, and the tumor size was smaller than 2 cm. As for nuclear grades including nuclear atypia and mitotic counts, the concordance rates were almost 80%. In addition, more than 90% of discordant cases were within one grade discrepancies. In Table 2, we also demonstrate the tendency of nuclear atypia, mitotic counts, and nuclear grade of CNB to be lower compared to those of surgical specimens. This phenomenon is considered to be caused by the differences in methodologies employed between CNB and surgical specimens. We examined the higher atypical and mitotic area in surgical specimens, whereas we examined the narrow and limited area in CNB specimens. Therefore, the nuclear factors of surgical specimens tended to be worse than those of CNB. As for ER and PgR expression, results of previous studies demonstrated that the absolute concordance of ER and PgR between CNB and surgical specimens were 61.7–99% and 61.5–97.1%, respectively.[1,2,5–7] We demonstrated that the concordance rate of ER and PgR was 94.1–96.0% and 86.1–89.5%, respectively. The concordance of PgR was lower than that of ER, due to the fact that PgR immunoreactivity was weaker and more heterogenous than ER. We examined ER expression by Allred score and proportions of immunoreactive tumor cells were scored as follows: cut-off ≤1%[15] and 10%≤,[14,16] but there were no statistically significant differences. In addition, the concordance rate of HER2 status was 64–96%.[1,2,5–7] Recently, there have been increasing reports evaluating the use of HER2-targeted agents in neoadjuvant therapy for both primary operable and primary inoperable HER-positive breast cancer.[24,25] It is therefore important to achieve

a more definitive diagnosis of HER2 status in pre-operative CNB. We also demonstrated that there was discordance in judgments of ER, PgR, and HER2 between CNB specimens and surgically resected specimens in some cases. However, many of these discordant cases were detected more frequently in equivocal or borderline categories (Tables 3,4). In Table 4, it can be seen that four cases of HER2 score 2+ for CNB were changed to 1+ for surgical specimens, and four cases of CNB 3+ were changed to surgical 2+. We detected the strongest HER2 expression area in these tumors by CNB. Therefore, HER2 scores from surgical specimens were lower than those from CNB in these cases. We demonstrated that the disagreements were due to technical problems and intratumoral heterogeneity. If there were discrepancies between two evaluators, the evaluation of the third experienced pathologist was selected. In addition, histopathological staining was performed by a single and experienced technician. Two authors independently evaluated CNB samples and surgical specimens twice on different occasions. Therefore, these findings suggest that interobserver difference, different immunohistochemical technique, and different pre-analytical conditions were not the causes of discordance in the judgment of these factors. It is important for diagnostic accuracy to be established more definitively, and if possible, an increment of the number of CNB specimens may be considered more important because of intratumoral heterogeneity.

Several previous studies have tried to determine the optimum number of specimens to be obtained for ultra sound (US)-guided CNB to accurately diagnose histological subtypes.[26–29] One study demonstrated that among 73 lesions, cells indicating the diagnosis were present in the first specimen in 51 (70%), in the second specimen in 67 (92%), in the third specimen in 70 (96%), and in the fourth specimen in all 73 (100%) of cases.[27] This result suggested that a minimum of four specimens should be obtained with 14-gauge US-guided breast biopsy.[27] However, a study by Melotti *et al.*[29] examined the comparison of the quantity and quality of tissue harvested from breast biopsy when using 14-, 16-, and 18-gauge long-throw needles. The results in that study clearly demonstrated that when comparing 14-, 16-, and 18-gauge needles, accuracy rose with needles of increasing size.[29] These results also suggested that diagnostic accuracy of CNB increased with the increase of harvested specimens.[27,29]

To the best of our knowledge, this is the first study to evaluate the correlation between the number of core biopsies obtained and an accuracy of histological types, nuclear grades, hormone receptors, and HER2 status. Statistically significant differences were detected between patients who received four or more cores and those who had received three or less cores in the discrepancy of the following factors between CNB and subsequent surgical specimens: histological types, nuclear grade, and PgR. In addition, a similar tendency was also detected in ER and HER2 as above, and the cases that received four cores reached to 100% concordance in diagnosis between CNB and surgical specimens. Therefore, the optimal numbers of CNB may be considered four cores, which represent sufficient volume for histopathologic diagnosis. Core biopsy can provide reliable information on histological types, invasion, nuclear grade, hormone receptors, and HER2 status of patients.

Acknowledgments

We appreciate Yayoi Takahashi, MT, for her excellent technical assistance. This work was partly supported by grants from the Ministry of Health, Labour and Welfare of Japan for Research on Intractable Diseases, Risk Analysis Research on Food and Pharmaceuticals, and Development of Multidisciplinary Treatment Algorithm with Biomarkers and Modeling of the Decision-making Process with Artificial Intelligence for Primary Breast Cancer. This work was also partly supported by a Grant-in-Aid for Scientific Research (18390109) from the Ministry of Education, Culture, Sports, Science and Technology of Japan, and the Yasuda Medical Foundation.

References

1 Sutela A, Vanninen R, Sudah M *et al.* Surgical specimen can be replaced by core samples in assessment of ER, PR and HER-2 for invasive breast cancer. *Acta Oncol* 2008; **47**: 38–46.
2 Arnedos M, Nerurkar A, Osin P *et al.* Discodance between core needle biopsy (CNB) and excision biopsy (EB) for estrogen receptor (ER), progesterone receptor (PgR) and HER2 status in early breast cancer (EBC). *Ann Oncol* 2009; **20**: 1948–52.
3 Pettine S, Place R, Babu S *et al.* Stereotactic breast biopsy is accurate, minimally invasive, and cost effective. *Am J Surg* 1996; **171**: 474–6.
4 Britton PD. Fine needle aspiration or core biopsy. *The Breast* 1999; **8**: 1–4.
5 Usami S, Moriya T, Amari M *et al.* Reliability of prognostic factors in breast carcinoma determined by core needle biopsy. *Jpn J Clin Oncol* 2007; **37**: 250–5.
6 Cavaliere A, Sidoni A, Scheibel M *et al.* Biopathologic profile of breast cancer core biopsy: is it always a valid method? *Cancer Lett* 2005; **14**: 22–7.
7 Park SY, Kim KS, Lee TG *et al.* The accuracy of preoperative core biopsy in determining histologic grade, hormone receptors, and human epidermal growth factor receptor 2 status in invasive breast cancer. *Am J Surg* 2009; **197**: 266–9.
8 Dronkers DJ. Stereotaxic core biopsy of breast lesions. *Radiology* 1992; **183**: 631–4.
9 Brenner RJ, Fajardo L, Fisher PR *et al.* Percutaneous core biopsy of the breast: effect of operator experience and number of samples on diagnostic accuracy. *Am J Roentgenol* 1996; **166**: 341–6.
10 Tavassoli FA, Devilee P. *World health organization classification of tumors. Tumor of the breast and females gentia organs*. Lyon: IARC Press, 2003.
11 Rosen PP. *Rosen's Breast Pathology*, 3rd edn. Philadelphia, PA, USA: Lippincott Williams & Wilkins, 2009.
12 Tsuda H, Akiyama F, Kurosumi M *et al.* Establishment of histological criteria for high-risk node-negative breast carcinoma for a multi-institutional randomized clinical trial of adjuvant therapy. Japan National Surgical Adjuvant Study of Breast Cancer (NSAS-BC) pathology section. *Jpn J Clin Oncol* 1998; **28**: 486–91.
13 Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer by immunohistochemical analysis. *Mod Pathol* 1998; **11**: 155–68.
14 Arihiro K, Umemura S, Kurosumi M *et al.* Comparison of evaluations for hormone receptors in breast carcinoma using two manual and three automated immunohistochemical assays. *Am J Clin Pathol* 2007; **127**: 356–65.
15 Goldhirsch A, Ingle JN, Gelber RD *et al.* Threshholds for therapies: highlights of the St Gallen International Expert Consensus on the primary therapy of early breast cancer 2009. *Ann Oncol* 2009; **20**: 1319–29.
16 Kurosumi M. Immunohistochemical assessment of hormone receptor status using a new scoring system (J-score) in breast cancer. *Breast Cancer* 2007; **14**: 189–93.
17 Chivukula M, Bhargava R, Brufsky A *et al.* Clinical importance of HER2 immunohistologic heterogenous expression in core-needle biopsies vs resection specimens for equivocal (immunohistochemical score 2+) cases. *Mod Pathol* 2008; **21**: 363–8.
18 Fleiss JL. *Statistical Methods for Rates and Proportions*. New York: John Wiley & Sons, 1981; 212–36.
19 Shannon J, Douglas-Jones AG, Dallimore NS. Conversion to core biopsy in preoperative diagnosis of breast lesions. Is it justified by the results? *J Clin Pathol* 2001; **54**: 762–5.
20 Frank SL, Frank JL, March D *et al.* Does therapeutic touch ease the discomfort or distress of patients undergoing stereotactic core breast biopsy? A randomized clinical trial. *Pain Med* 2007; **8**: 419–24.
21 Somerville P, Seifert P, Destounis SV *et al.* Anticoagulation and bleeding risk after core needle biopsy. *AJR Am J Roentgenol* 2008; **191**: 1194–7.
22 Witt A, Yavuz D, Walchetseder C *et al.* Preoperative core needle biopsy as an independent risk factor for wound infection after breast surgery. *Obstet Gynecol* 2003; **101**: 745–50.
23 Liberman L, Vuolo M, Dershaw DD *et al.* Epithelial displacement after stereotactic 11-gauge directional vacuum-assisted breast biopsy. *AJR Am J Roentgenol* 1999; **172**: 677–81.
24 Buzdar AU, Ibrahim NK, Francis D *et al.* Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: results of a randomized trial in

doi: 10.1111/j.1349-7006.2010.01630.x

human epidermal growth factor receptor 2–positive operable breast cancer. *J Clin Oncol* 2005; **23**: 3676–85.
25 Baselga J, Semiglazov V, Manikhas GM *et al.* Efficacy of neoadjuvant trastuzumab in patients with inflammatory breast cancer: data from the noah (Neoadjuvant Herceptin) phase iii trial [abstract 2030]. *Eur J Cancer* 2007; **5**: 193.
26 Dagrada GP, Mezzelani A, Alasio L *et al.* HER-2/neu assessment in primary chemotherapy treated breast carcinoma: no evidence of gene profile changing. *Breast Cancer Res Treat* 2003; **80**: 207–14.
27 Fishman JE, Milikowski C, Ramsinghani R *et al.* US-guided core-needle biopsy of the breast: how many specimens are necessary? *Radiology* 2003; **226**: 779–82.
28 Kaplan SS, Racenstein MJ, Wong WS. US-guided core biopsy of the breast with a coaxial system. *Radiology* 1995; **194**: 573–5.
29 Melotti MK, Berg WA. Core needle breast biopsy in patients undergoing anticoagulation therapy: preliminary results. *AJR Am J Roentgenol* 2001; **174**: 245–9.