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Nipple-centered Radiate MPR Images of MDCT for Evaluation of Breast Cancer Extent

—— Correlation with Mammography and Pathologic Specimen ——

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Background & Aims: Evaluation of the extent of breast cancer lesions is important for selecting the appropriate surgical procedure or to determine the surgical margin. We aimed to assess the diagnostic accuracy of nipple-centered radiate multiplanar reconstruction (NRMPR) images using multidetector row helical computed tomography (MDCT), comparing it with conventional mammography. **Methods:** Our subjects were 26 breast cancer patients with a total of 29 lesions who sequentially received contrast-enhanced MDCT imaging for preoperative evaluation. We measured the maximum diameter of the breast cancer in the direction toward the nipple on NRMPR images and mammography. All data were correlated with histopathological mapping of the specimens. **Results:** The tumor extent measured on NRMPR images and in pathological examinations ranged from 12.4 to 66.0 mm (average, 28.0 mm) and 10 to 70 mm (average, 27.9 mm), respectively. The correlation coefficient of the two measurements was 0.898. On mammography, two lesions were not clearly identified. The correlation coefficient of mammography and pathological measurements was 0.554. **Conclusions:** The addition of NRMPR images to mammography provides more information to evaluate breast cancer extension toward the nipple. Potentially, it provides a clue for selecting the appropriate surgical procedure or surgical resection margin for breast cancer. (Kitakanto Med J 2009；59：123～129)

Key Words： multidetector row helical CT, breast cancer, mammography, tumor extent

Introduction

Evaluation of the extent of breast cancer lesions is important for selecting the appropriate surgical procedure or to determine the surgical margin, contributing to attain adequate local control.[1] CT has been one of the modalities used for the accurate determination of the local extension of breast cancer.[2–11] Advances in imaging work stations have led to various image processing techniques for acquired CT image data. The frequently used CT image processing methods to evaluate the extent of breast cancer are reconstructed coronal images or sagittal images using multiplanar reformations (MPR), maximum intensity projections (MIP), and volume rendering (VR). Though these methods are useful to identify the location of the lesion on the chest wall, it is not easy to recognize the location relative to the nipple, because the nipple and tumor do not always appear on the same image using sagittal MPR, and the slab thickness and reconstructed angle sometimes lead to misinterpretations or diagnostic confusion regarding the nipple tumor distance (NTD) and tumor extent in the direction of the nipple. We supplementarily use nipple-centered radiate MPR (NRMPR) images of multidetector row helical computed tomography (MDCT) to evaluate breast cancer, especially for the evaluation of the tumor extent in the direction toward the nipple and consequent NTD. NRMPR images can show the nipple and tumor in the same image, as well as provide information regarding lesion extension toward the nipple. The reformatting of NRMPR images is performed semi-automatically using an image workstation.

The aim of this study was to evaluate the diagnostic accuracy of NRMPR images for assessing the extent of breast cancer in the direction toward the nipple, comparing the accuracy with the histopathological

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mapping of breast cancer and conventional mammography.

Materials and Methods

Patients

Between July 2004 to December 2004, 28 consecutive patients underwent contrast-enhanced CT for preoperative breast cancer evaluation in our institution. Among them, 26 patients with a total of 29 focal breast masses were included in our study. We excluded two patients from this study because we could not sufficiently examine the CT-pathological correlation due to unsuitable slice preparations of the pathological specimens.

Of these 26 patients, one had bilateral cancer, operated on the same time. Two patients showed two focally-enhanced masses on ipsilateral breast CT, and each mass was independently measured. All patients underwent surgery for breast cancer in our hospital. Eleven patients underwent total mastectomy, and 15 patients (including one patient with bilateral cancer) underwent breast-conserving surgery. Histopathologic types are summarized in Table 1.

Table 1 Histopathologic types of carcinoma.

Type	n
Papillotubular carcinoma	15
Solid-tubular carcinoma	2
Scirrhous carcinoma	9
Mucinous carcinoma	1
Apocrine carcinoma	2
Total	29

The time intervals between CT examinations and surgery were 1 to 62 days (average, 14.9 days). The time intervals between mammography and surgery were 1 to 50 days (average, 18.3 days). All subjects provided a written informed consent, and this study was approved by our institutional review board.

CT facilities, data acquisition, and image processing

The CT scanner used was a 16-slice CT system (Aquilion, Toshiba, Tokyo, Japan). CT examinations were performed using the following parameters: 0.5 seconds per rotation, 16-detector rows, 0.5-mm collimation, 5-mm table increments, and a slice thickness of 1 mm with 0.8 mm intervals. Contrast media (2 ml/kg of body weight; maximum amount of 100 ml) was injected via the antecubital vein over a period of 60 seconds, and the CT scan delay time after the start of injection was 80 seconds. These injection rates and scan delay times were determined based on previous reports.[4–7] Axial slices were reconstructed with the reconstruction field-of-view limited to the area around the breast.

Images were post-processed using a work station (Advantage Workstation 4.0, General Electric, Fairfield, CT, USA). NRMPR images perpendicular to the chest wall were created with 2-dimensional images, at a 2-mm thickness, with one slice every 5 degrees, a total range of 180 degrees, and total 36 slices, which included the focally-enhanced mass.

Evaluation of tumor extent by CT

Based on previous reports, the length of tumor extension was measured on the CT images according to the following criteria: a nodule within the breast showing greater attenuation than the normal mammary glands on enhanced CT was defined as a tumor, and symmetric enhancement was defined as negative (normal or mastopathy).[3,4] Referring to some previous reports, we set the range of the appropriate window level and width as 200–250 and 40–60 HU, respectively.[4,7]

The extent of each breast cancer was measured on a NRMPR image which showed the maximum diameter of the focally-enhanced mass (Figs. 1a and 2a). For the determination of the lesion depth, we evaluated other sectional images including source axial images and coronal reformatted or sagittal reformatted images. In cases in which the tumor reached the nipple, the point of measurement was determined as under the center of the nipple.

All images were examined by two experienced radiologists (A.K. and N.K.) retrospectively without knowledge of the pathological and mammographic findings. They were well-trained and certified as specialists by the central committee on quality control of mammographic screening, a non-profit organization. In cases in which the 2 radiologists disagreed, a consensus was reached through discussion.

Mammography equipment

Mammography was conducted using a mammography machine (Senographe DMR, General Electric, Fairfield, CT, USA). The radiological technologists, who were trained and certified by the central committee on quality control of mammographic screening, a non-profit organization, performed mammography in all subjects.

Evaluation of tumor extent by mammography

Breast cancer evaluation based on mammography was performed by one radiologist (M.M.) who was trained and certified by the central committee on quality control of mammographic screening, a non-profit organization. We diagnosed the lesion extent based on the descriptions in the official textbooks and

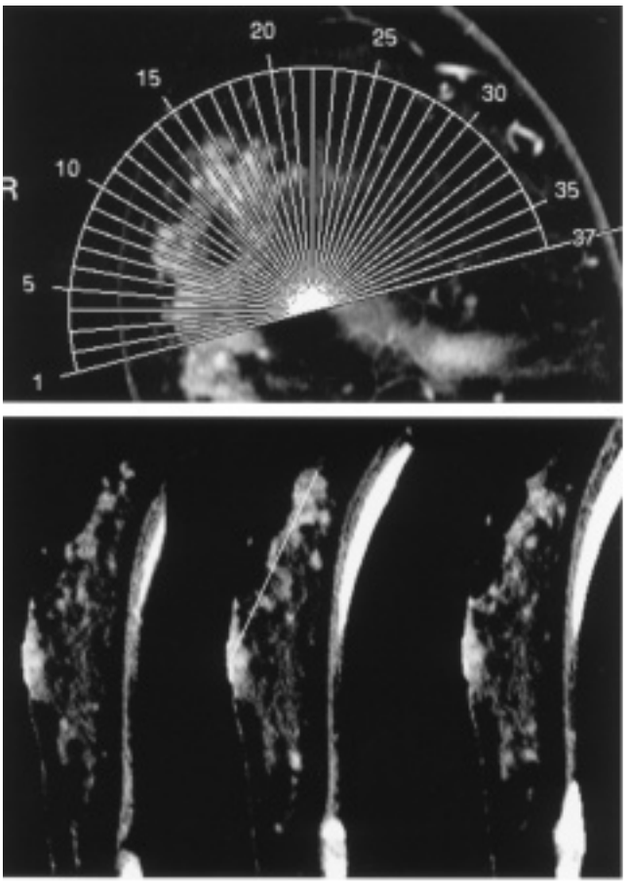


Fig. 1a Reconstruction setting image and NRMPR images with lines to measure the breast cancer extent. They showed scattered, multiple, spot-enhanced lesions in the upper portion of the mammary gland toward the nipple.

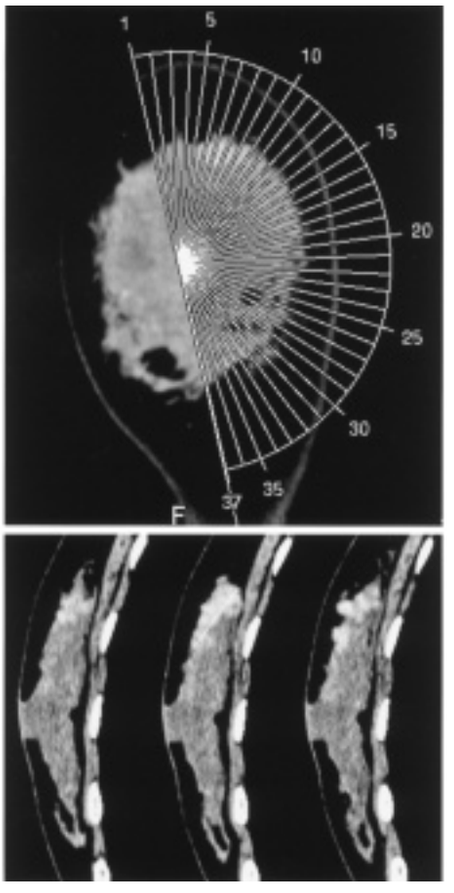


Fig. 2a Reconstruction setting image on a workstation and NRMPR images with a line to measure the breast cancer extent. An ill-defined mass with spotty enhancement toward the nipple is shown.

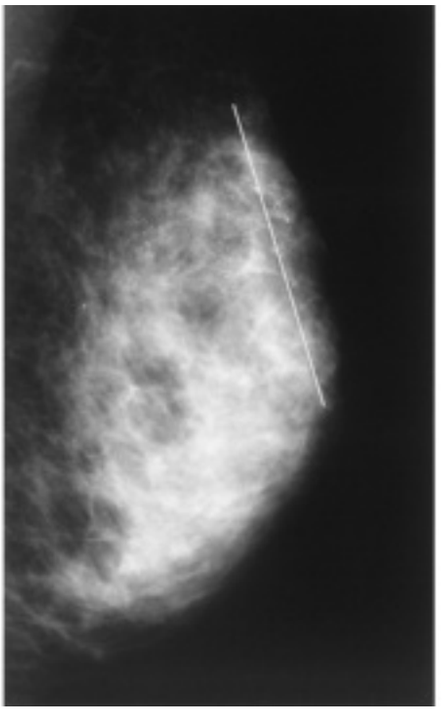


Fig. 1b Mammography with a line for lesion measurement. In this case, wide spread, multiple microcalcifications can be seen from the upper portion of the breast to underneath the nipple.

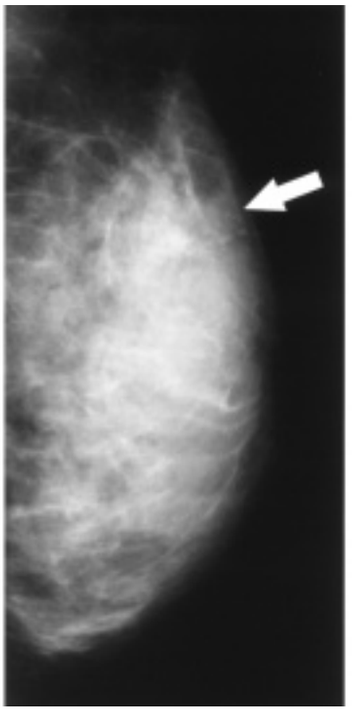


Fig. 2b Mammography shows focally increased density in the upper area of the breast (arrow).

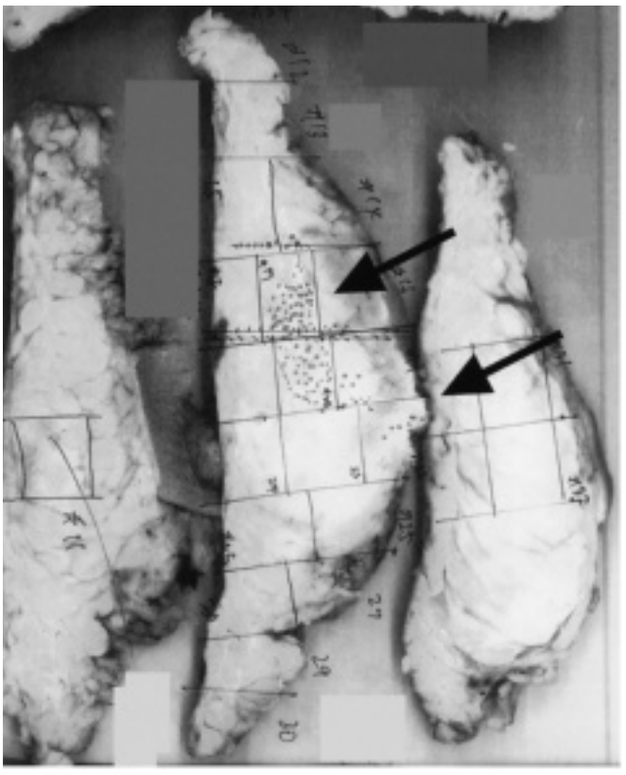


Fig. 1c Pathological map of mastectomy for breast cancer, drawn on the photograph of the macroscopic specimen. The gray dots represent the extension of breast cancer (arrows). Pathological examination revealed invasive ductal carcinoma, predominantly of the intraductal type, and papillotubular carcinoma with Pagetoid spreading in the areola. A correlation was noted between the multiple, enhanced nodular lesions on NRMPR and multiple microcalcifications on mammography.

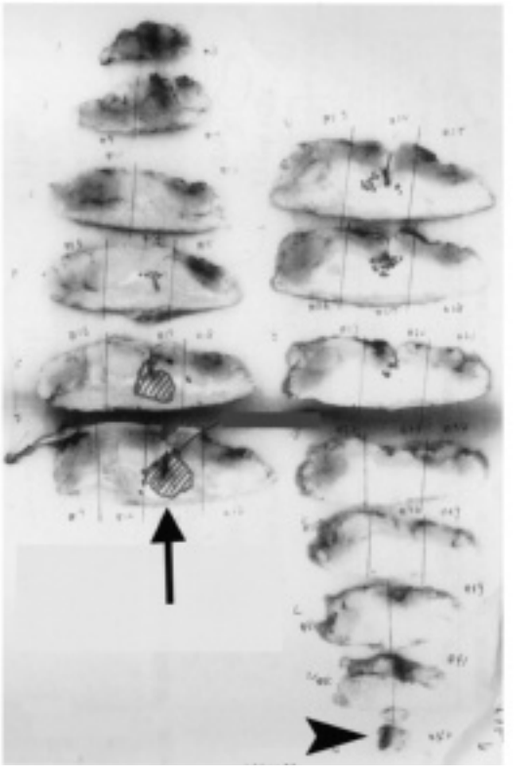


Fig. 2c Pathological map for the breast-conserving surgery for breast cancer drawn on the photograph of the macroscopic specimen. The gray lines and dots represent the extension of breast cancer (arrow). Pathological examination revealed invasive ductal carcinoma and papillotubular carcinoma with intraductal spread. The main tumor shows a multinodular shape and it extends mainly with intraductal spread. The breast tissue also presents a wide variety of fibrocystic changes. It shows a good relationship with the focal mass of mulinodular shape and the enhanced area toward the nipple on NRMPR (arrowhead ; nipple side).

training supervised by the organization. Before we started the evaluation in this study, test of mammography examinations were performed in 5 trial subjects who had breast cancer and were operated on in our facility. Two experienced radiologists (N.K. and M. M.) independently assessed the mammographic findings. For trial subjects, we confirmed the area of the breast cancer lesion and measured the maximum diameter on a straight line connecting the center of the nipple and the center of the breast cancer lesion on a medio-lateral-oblique (MLO) mammographic view using a ruler. The correlation coefficient of the extent of breast cancer in the 5 trial subjects measured by the two radiologists was statistically analyzed. After the evaluation of the 5 trial subjects, one radiologist (M. M.) assessed the breast cancer extent in the 26 study subjects (Figs. 1b and 2b).

Statistical analysis

Correlations between NRMPR images of MDCT and pathological results, and mammographic findings and pathological results regarding the breast cancer extent, were statistically analyzed using Pearson's correlation coefficient. The cases whereby the lesion could not be detected or confirmed by mammography were excluded in the correlation analysis between mammographic findings and pathological results. Statistical analyses were performed using StatView software 5.0 (SAS Institute Inc., Cary, NC, USA).

Pathological evaluation of tumor extent

All pathological mappings and evaluations were performed based on the general rules for the clinical and pathological recording of breast cancer, issued in June 2004 (The 15th edition, The Japanese Breast Cancer Society). In patients who underwent total mastectomy, the specimens were sliced into continuous 10-mm sections parallel to the line connecting the nipple to the center of the focal mass. In patients who underwent breast-conserving surgery, the specimens

were sliced into continuous 5-mm sections perpendicular to the line connecting the nipple to the center of the focal mass. The sections were examined microscopically by one experienced pathologist, and a pathological map was generated to show the distribution of breast cancer (Figs. 1c and 2c). Based on this pathological map, the range of the tumor extent on the line connecting the nipple to the center of the focal mass was assessed retrospectively. Since the specimens were sliced at 5-mm intervals perpendicular to the line connecting the nipple to the center of the focal mass in patients receiving breast-conserving surgery, the minimum unit evaluated regarding the pathological extent was 5-mm in patients who underwent breast-conserving surgery.

Results

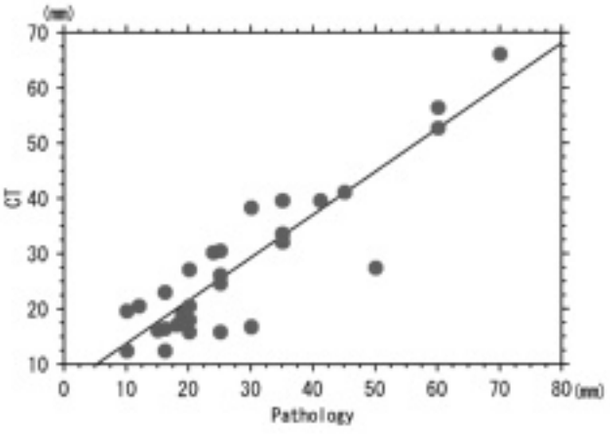
CT and pathological measurement of tumor extent

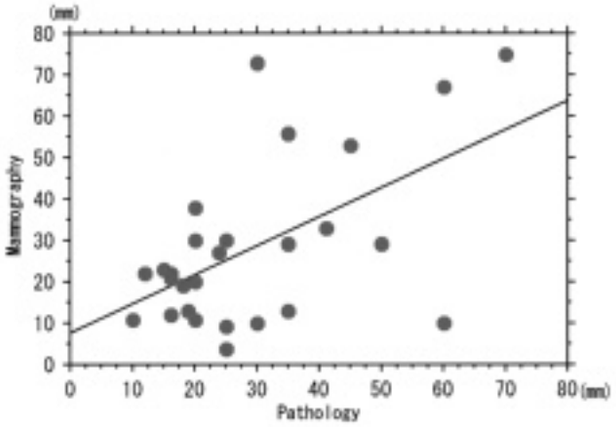
In all 26 patients, sufficient NRMPR images of MDCT could be produced to evaluate the tumor extent in the direction toward nipple. Two cases that showed two focally-enhanced masses in the unilateral breast showed the same pathological findings. One case which was diagnosed as scirrhous carcinoma showed sequential, minimally invasive cancer between the two masses in areas AC and C. The other case was diagnosed as papillotubular carcinoma with the lesions in areas C and A, and there was intraductal spread between the two masses. We considered that each of the two cases had two masses, and measured each mass independently because the NRMPR images showed the two focally-enhanced masses on separate images. For this reason, we analyzed them as four independent lesions in these two cases. The size of the tumor extent on NRMPR images and pathological examinations ranged from 12.4 to 66.0 mm (average, 28.0 mm) and from 10 to 70 mm (average, 27.9 mm), respectively. The difference between CT and pathologic measurements of the tumor extent ranged from 0.1 to 22.4 mm (average, 4.94 mm). The correlation between the distance of the tumor extent measured in NRMPR images and pathological examination was good, with a correlation coefficient of 0.898. Scatter diagram with a regression line of the tumor extent measured on pathological examinations and NRMPR was showed in Fig. 3a. Two cases showed more than a 10 mm difference within the two measurements. In one of the two cases, the nipple and tumor were not shown on the same image, even using NRMPR images. This case had a focally-enhanced mass with spotty enhancement, but not all the lesions were shown on the same MPR image where the focal mass was delineated. This was thought to reflect a limitation in the measurement of the tumor extent using only one slice for NRMPR images. The other case also had an extensive intraductal component, which could not be identified, and we could not evaluate the tumor extent as an enhanced lesion on MDCT. This case had two focally-enhanced masses in the ipsilateral breast, which were pathologically identified as the same lesion and connected with an extensive intraductal component.

Mammography and pathological measurement of tumor extent

The mean size, the range, and the correlation coefficient of the extent of the breast cancer in the 5 trial mammography measured by the two radiologists was 14.8 mm, 13 to 18 mm, r=0.90, respectively.

Of all the 26 subjects, lesions in 2 cases could not be detected on mammography. One case had dense breast tissue, and the other case had mucinous cancer which was obscured due to surrounding normal breast tissue. These cases were excluded from statistical analyses of the correlation between CT and mammography. Both cases showed two mass shadows in the unilateral breast on nipple-centered MPR images,





Figs. 3a and 3b Scatter diagrams with a regression line of the tumor extent measured on pathological examinations and NRMPR (Fig. 3a, n=29, r=0.898) and mammography (Fig. 3b, n=27, r=0.554).

noted as two mass shadows on mammography. We analyzed them as 4 independent lesions in these two cases in this study. The measurement of the tumor extent on mammography ranged from 9 to 75 mm (average, 28.1 mm). The difference between mammography and pathologic measurements of the lesions ranged from 0 to 50.0 mm (average, 12.4 mm). The correlation between the distance of the tumor measured on mammography and pathological examination was intermediate, with a correlation coefficient of 0.554. Scatter diagram with a regression line of the tumor extent measured on pathological examinations and mammography was showed in Fig. 3b.

Discussion

Our study suggested that NRMPR images of MDCT help to evaluate the extent of breast cancer in Japanese female patients. They showed a better concordance with pathological measurement than mammography. There have been several reports that CT is useful to evaluate the breast cancer extent.[2–11] The margin status is an important prognostic factor for local recurrence after breast-conserving therapy for breast cancer,[14] and many studies have been conducted on local recurrence control, such as the surgical margin status, use of systemic therapy, and irradiation therapy.[1,15,11] Cabioglu et al. reported on multivariate analysis for an age $>$ 50, presence of negative surgical margins, and the use of adjuvant hormonal therapy were independent predictors of an improved 5-year ipsilateral breast tumor recurrence-free survival rate after breast-conserving therapy.[15] Thus, we need to diagnose the tumor margins to determine the surgical margin before the operation, especially for patients who choose breast-conserving therapy associated with optimal local control. Since positive surgical margins were often recognized toward the nipple,[8] our study specifically focused on the breast cancer extent toward the nipple on NRMPR images using MDCT. This image reconstruction method was considered useful for assessing the breast cancer extent, because the nipple and tumor could be shown in the same image in most cases. Frequently used image processing methods for breast cancer extension evaluation are reconstructed coronal images or sagittal images using MPR, MIP, and volume rendering. Although these methods are useful to identify the location of the lesion on the chest wall, the location in relation to the nipple is sometimes difficult to observe using them, because the nipple and tumor do not always appear in the same image using the sagittal MPR technique, and the slab thickness and reconstructed angle lead to a misunderstanding or diagnostic confusion regarding NTD and tumor extension toward the nipple. We supplementarily used the NRMPR images of MDCT to evaluate breast cancer, and our results showed that these reconstructed images well-visualized the extent of the tumor toward the nipple.

In this study, two lesions could not be detected on mammography. The cause in one case was a dense breast, and the other case might have been obscured by normal breast tissue. However, CT could delineate these lesions clearly. In cases showing dense breasts, the lesions are likely to be obscured by normal breast tissue on mammography. In that sense, MDCT is considered superior in the evaluation of dense breast cases, because we can evaluate tomographic images of multidirectional access with source axial images and MPR images, as well as with contrast media enhancement.

Our study had some limitations. One was retrospective nature, so we could not analyze the preoperative clinical usefulness of CT diagnosis. The other limitation was that, in some cases, the nipple and the entire tumor were not always shown in the same image even using NRMPR images. In this study, two cases showed more than a 10 mm difference in the measured distance between CT and pathology. Both cases had a focal mass and intraductal extension, and, in one case, the entire intraductal component could not be visualized on the same MPR image slice in which the focally-enhanced mass was represented at its maximal size. Thus, we could not measure the tumor extent accurately. For this reason, we should be aware that NRMPR images provide information to supplement axial or MIP images of MDCT. In the other case in which cancer lesion spread was underestimated, its wide intraductal component could not be identified. The case had two main tumors in the ipsilateral breast, and these were related by way of the wide-spreading intraductal component, although we could not identify the component on MDCT as an enhanced lesion. This may have been due to lack of hypervascularity.

NRMPR images of MDCT were reconstructed with a 2 mm thickness, at 5 degrees per slice, with a total range of 180 degrees, and a total of 36 slices, including the lesion. It means the entire breast can not be covered with NRMPR images. For this reason as well, NRMPR images should be used to supplement axial or MIP images of MDCT. We suggest this method adds more information to basic routine MDCT images, and it is easy to reconstruct on workstations.

We acknowledge that the sample size was relatively small. Nevertheless, our results do show significant differences between NRMPR images of MDCT and conventional mammography on comparing tumor extension toward the nipple.

Recently, many studies have been reported regarding the accuracy of MR images in the diagnosis of breast cancer extension, and some reported that MR images could be used to diagnose breast cancer accurately.[10,11,17–19] CT has the clinical advantage that it can also show the presence of axillary lymph node swelling and lung or liver metastasis. We believe that MDCT examination with the addition of NRMPR images is valuable as a preoperative study for breast cancer.

In conclusion, with NRMPR images of MDCT, we were able to clearly and easily visualize breast cancer for assessment of the tumor size, especially regarding tumor extension toward the nipple, superior to the MLO view of mammography.

We recommend the addition of NRMPR images to routine MDCT examination for the evaluation of breast cancer extension toward the nipple.

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