

原著 The Efficacy of Breast Specimen MR Imaging in the Evaluation of Tumor Characteristics and Surgical Margins.

Eleni Testempassi, Toru Sakuma, *Hiroyuki Kato, *Masafumi Suzuki,
Junta Harada, Shimpei Tada

Department of Radiology and *Department of Pathology,
The Jikei University School of Medicine

Abstract

Purpose : To determine the correlation between appearances at Magnetic Resonance and the pathologic diagnoses. To evaluate the surgical margins of the specimens and the evidence of coexistent multicentric tumor.

Materials and Methods : A serial Magnetic-resonance-pathologic correlation of breast specimens was performed on 48 consecutive breast lesions. Specimens were examined at 1.5 MR unit. Coronal and axial T1-weighted images were obtained. Paraffin sections were done in the same direction as MR axial images.

Results : 27 of the lesions were scirrhous carcinomas, 4 papillotubular carcinomas, 4 solid tubular carcinomas 2 apocrine carcinomas, 2 medullary carcinomas, 2 fibroadenomas, 2 cases of mastopathy, 1 nipple adenoma, 1 case of intraductal papillomatosis, 1 of sclerosing adenosis and 1 of post-operative panniculitis. The size of the lesions ranged from 5 to 60mm in the pre-operative MR study and from 5 to 100mm in the post-operative MR study. The size of the lesions, that was measured by pathologists, ranged from 5 to 100mm. The borders and the intensity of the lesions were also estimated on MR images and pathological sections and they were correlated. Four cases had multifocal tumors in other site than the main tumor.

Conclusion : Magnetic Resonance images of breast specimens can depict the tumor, differentiate malignant from benign lesions, and clearly show the evidence of tumor at the surgical margins or a synchronous tumor in other sites.

Key words : Breast Tumors - Breast Specimen - Magnetic Resonance Imaging

Introduction

The development of specimen radiography has paralleled that of mammography and apecimen radiography has become an established part of the pathologist armamentarium for the study of mammary lesions^{1,2)}. Many previous reports have emphasized in the use of breast specimen mammography for the definition of occult or non-palpable, calcified or non-calcified breast lesions^{3,4,5)}. In spite all these, to our knowledge there has been no report concerning serial correlation of magnetic resonance imaging of breast specimens with specific histologic diagnoses and features. This prospective study was undertaken to compare specimen MR findings with histologic findings in gross and paraffin sections, to describe the spectrum of the MR appearance of breast lesions and to determine the accuracy of specimen MR in predicting the presence or absence of a multifocal tumor and the

evidence of tumor at the surgical margins.

Materials and Methods

48 female patients ranging in age from 30 to 78 years (mean 48 years) had breast lesions diagnosed by MR mammography (MRM). The method that we have used in the pre-operative MR study was as follows: Trans-axial T1-weighted images of the entire breast were obtained by using a spin-echo sequence (TR500/TE25). Slice thickness was 7.5mm with 0.5mm interval gap. FOV was 22cm and matrix 256 × 256. Then 0.2mmol/kg Gd-DTPA was administered at a rate of 2mL/sec (bolus injection). After the intravenous injection of Gd-DTPA images were taken every minute for a period of 10 min. The dynamic study was performed by using a T1-weighted spin-echo sequence (TR200/TE25). The pre-contrast images were then subtracted from the corresponding post-contrast images. After the

dynamic study, T1WI spin-echo sequences (TR500/TE25) were performed in the axial plane. Time intensity curves were also obtained.

From the 48 patients, 36 patients had mastectomy, 9 patients initially had lumpectomy and thereafter mastectomy, because of the frozen section suggestive of malignancy, and 3 patients (2 with fibroadenoma and 1 mastopathy case) had lumpectomy only. The excised mastectomy specimens and the excised lumps were examined at 1.5 T MR unit (Hitachi Medical, Japan), with a surface coil. The specimens were labelled with sutures by the surgeon to describe their orientation within the breast, they were covered with a cellophane wrap and then they were placed in the magnetic field. Spin-echo T1WI (TR500/TE23, 24, 25) were obtained, in both coronal and transverse planes. FOV was 200, matrix 512×512 and slice thickness 3mm without interval gap. 39 specimens were examined after formalin fixation, 6 before and after formalin fixation and 3 only before formalin fixation. The specimens were sliced in the same direction as the MR sections in order to obtain as much as possible perfect anatomical correlation between MR and histological slices.

Paraffin sections were examined by two pathologists for the establishment of the histologic diagnosis. The size of the tumor and the distance between the borders of the tumor and the surgical margins to the nearest site were measured. Following the protocol of the Department of Pathology a grossly free-tumor margin of 10 to 20mm is considered significant for the incidence of local recurrence. The co-existence of multi centric tumor was also investigated.

All specimen MR images were reviewed by two radiologists without knowing the histologic analysis. The size, the intratumoral structure, the intensity (high, low or iso-intense to the surrounding normal breast tissue), the borders (clear, lobulated, spiculated or indeterminate) were considered. The evidence of a synchronous tumor in other site and the distance between the tumor margins and the surgical margins were measured to the nearest site. The MR parameters were then correlated with the same pathological parameters. The MR

ultrastructural characteristics of the tumors were correlated with the histologic appearance of the tumors.

Results

The histologic diagnosis of the 48 (39 malignant and 9 benign) lesions were as follow: (Fig.A), scirrhus carcinoma in 27 (Fig.1), papillotubular carcinoma in 4, solid tubular carcinoma in 4, medullary carcinoma in 2, apocrine carcinoma in 2, fibroadenoma in two, mastopathy in 2, nipple adenoma, intraductal papilloma, intraductal papillomatosis, sclerosing adenosis and post-operative panniculitis in one, respectively.

Tumor was present in 35 cases. From the remaining 13 cases there was no tumor in 4 cases and in the 9 cases that performed lumpectomy and mastectomy, we have examined only the specimen and not the tumor lump, and there was no evidence of residual tumor in the mastectomy specimen. Two cases of fibroadenomas had only lumpectomy and the excised lump was also examined. In both cases of mastopathy, the diagnosis was negative for tumor in pre-operative MR study and there was also no evidence of tumor in the MR study of the breast specimen.

The texture of the tumor was homogeneous in 27 lesions and inhomogeneous in 8 lesions. The histology of the inhomogeneous lesions was as follow: 1 benign lesion, that was nipple adenoma and 7 malignant (4 scirrhus, 1 medullary, 1 papillotubular and one solid tubular carcinoma). The medullary carcinoma and the two scirrhus

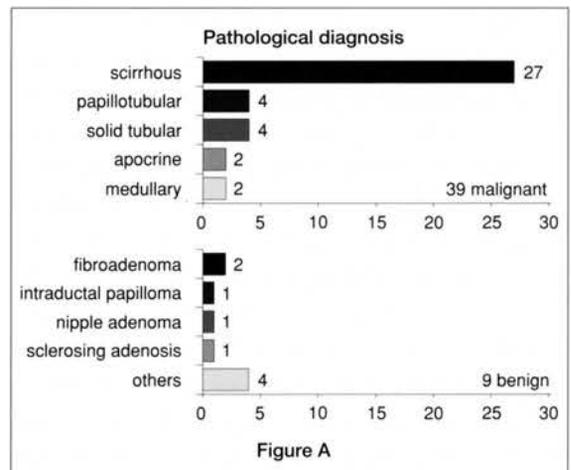


Figure A

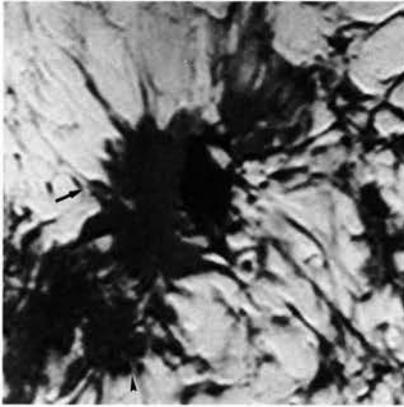


Figure 1. a

MR of breast specimen in a patient with scirrhous carcinoma. Slice on the coronal plane (TR500/TE24). Mass is visible as low intensity with spiculations (arrow). Normal breast tissue (arrowhead).

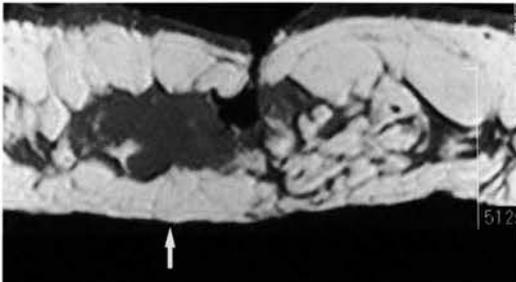


Figure 1. b

Same specimen. MR slice on the transverse plane. The low intensity mass lesion is visible. There is no evidence of tumor at the surgical margins (arrow).

carcinoma were of the pure type but all the other cases were of the mixed type with preponderance of the scirrhous, papillotubular or solid tubular component.

The intensity of the lesions compared with the surrounding normal breast tissue was as follows: Fibroadenomas were of high intensity. Nipple adenoma was of low intensity. From the 24 visible scirrhous carcinomas 12 were of low intensity, 5 were iso-intense and 7 were of high intensity. From the 3 visible papillotubular carcinomas 2 were of low intensity and 1 of high intensity. From the 3 visible papillotubular carcinomas 2 were of low intensity and 1 of high intensity. From the 3 visible solid tubular carcinomas 2 was of low and 1 of high intensity. The apocrine and the medullary carcinomas were of low intensity (Fig.B).

As far as it concerns the borders of the lesions from the 24 visible scirrhous carcinomas 6 had clear



Figure 1. c

Low-power photomicrograph shows a spiculated mass lesion (original).



Figure 1. d

High power photomicrograph shows the tumor cells (scirrhous carcinoma), (magnification X100).

borders, 14 had spiculation and 4 had indeterminate borders. 2 solid tubular had lobulated borders and one has indeterminate. Two papillotubular carcinomas had indeterminate borders and one lobulated. The apocrine carcinoma showed spiculation and the medullary carcinomas had lobulated borders. The nipple adenoma had indeterminate borders and was misdiagnosed as carcinoma (Fig.C).

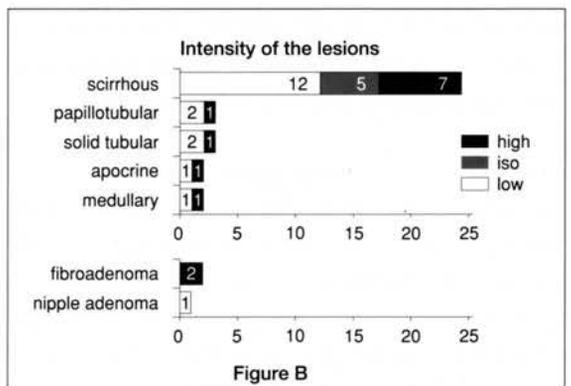
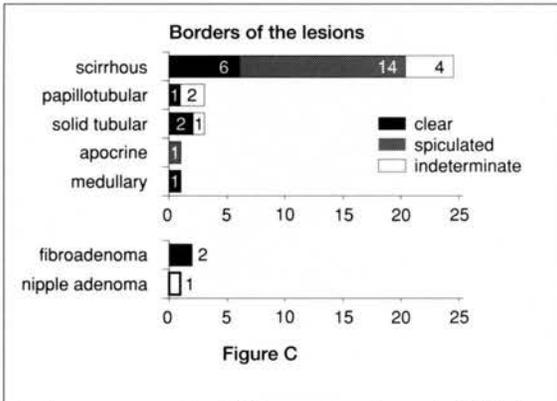


Figure B



In the pre-operative MR examination only 28 lesions were visible on T1WI. 26 were hypointense to the surrounding breast parenchyma, 1 isointense and 1 lesion was evident just simply as architectural distortion. In 1 papillotubular carcinoma pseudocapsule was also visible. Both fibroadenomas were not visible on T1WI.

In four of the 48 breast specimens, there were two lesions. In three cases there were multi-centric tumors and the additional lesion had the same characteristics with the main tumor. The histology of the multi-centric lesions was as follow: 2 were scirrhou carcinomas and 1 was solid tubular carcinoma. Only one of these lesions was visible in the pre-operative MR study. In one case the additional lesion was capillary hemangioma and the main tumor was scirrhou carcinoma, and that was also not detected in the pre-operative MR examination.

The size of the lesions ranged from 10 to 60mm in the pre-operative MR study of the breast and from 5 to 100mm in the MR study of the specimen. The pathological size of the lesions ranged from 5 to 100mm. The correlation coefficient of the pre-operative and pathological size of the lesions was as follows: $y=1.227x+2.148$, $r=0.892$. The correlation coefficient of the post-operative and pathological size was as follows: $y=1.005x+0.096$, $r=0.991$.

Discussion

In comparison with the past, more patients with early stage breast cancer undergo breast-conserving surgical procedures followed by irradiation and the results are the same with those treated by mastectomy. If conservation surgery

undertaken the specimen margins must be clear of carcinoma^{6,7}. It has been reported by many authors that there is higher rates of local recurrence in patients with diseased margins⁸. Besides, assurance that a potentially malignant lesion has been excised makes mandatory the intra-operative use of specimen imaging⁹. Since there is no high degree of resolution between carcinomas and the surrounding normal breast tissue in specimen mammography, we undertook this prospective study to show the efficacy of specimen MR mammography in depicting the tumor and differentiating this from normal structures and the possibility to use this modality intra-operative in cases that undergo breast conservation surgery.

Since MR mammography has established as a modality of great specificity and sensitivity¹⁰ in the diagnosis of breast tumors its increasing utilization has also intensified the need for better understanding of the MR features of breast lesions. This serial specimen MR study with pathologic correlation can also improve our understanding of the appearance of breast carcinomas and breast lesions in general, and minimize the unnecessary surgical biopsies.

A sufficient tissue characterization was possible in all cases that underwent specimen MRM by evaluating tissue signal intensity parameters. Even calcifications are not visualized by MR the visualization of the lesion is possible because of the change of signal intensity at the site of the lesion. Fibroadenomas had relatively high intensity to the surrounding normal breast tissue and their inner texture is homogeneous. Usually breast carcinomas are of lower signal intensity to the surrounding normal breast tissue and usually have homogeneous intensity. The inhomogeneous lesions were those called mixed types of intraductal carcinomas. There were solid tubular and scirrhou components or scirrhou and papillotubular components. This inhomogeneity was probably due to the mixed histologic pattern of the tumor. Although in our study only few benign lesions were included, we conclude that most of carcinomas show low intensity on T1WI and have spiculated or indeterminate borders while fibroadenomas are of

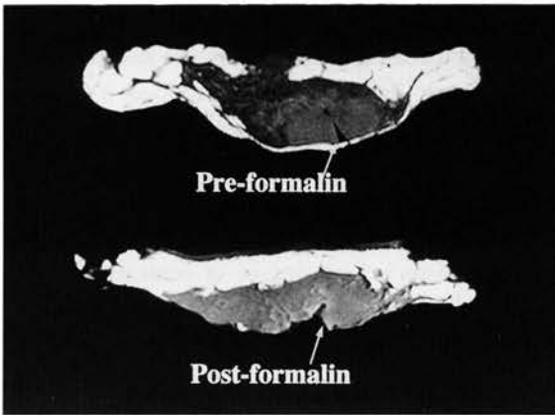


Figure 2.

MR of breast specimen in a patient with scirrhous carcinoma.

a) Before formalin. Slice on the transverse plane. Well-circumscribed mass lesion of high intensity compared to the surrounding normal parenchyma is visualized (arrow).

b) After formalin. The mass lesion is also visualized, almost isointense to the surrounding normal parenchyma (arrow).

relatively high intensity and have clear borders.

There was no correlation with the type of the tumor and the borders of the tumor. There were scirrhous carcinomas with clear borders and with indeterminate borders. Solid tubular carcinomas which are considered to have better prognosis than other types of carcinomas had also lobulated or indeterminate borders. Spiculation was also evident in some lesions without any preponderance according to the type of the lesion. The halo sign which is a characteristic of benign lesions and especially of fibroadenomas was also present in one case of papillotubular carcinoma. The nipple adenoma had also indeterminate borders. Stomper et al has also reported that well-circumscribed lesions with round or lobulated borders are not necessarily associated with favorable histologic findings such as medullary and mucinous carcinomas but may represent infiltrating intraductal carcinomas⁵⁾. Our study also showed similar results. This serial MR-pathologic correlation of tumor margins showed similar appearance of tumor borders on both MR slices and pathologic sections. Well-defined lesions seen on specimen MR were associated with well-circumscribed lesions

seen on histologic examination and irregular or spiculated masses were associated with irregular or spiculated margins seen on histologic examination.

There was also increased signal intensity of the lesions in the specimen compared with the in vivo study. In those cases where examinations were done before and after formalin fixation of the specimen, the lesion was better visualized in the study before the formalin fixation and its intensity was also higher compared to the study after formalin fixation (Fig.2). This higher intensity and better visualization of the tumor we consider that to some extent must due to the edema and the increased intracellular water compared to the post-formalin study where we have dehydration of the whole breast tissue. There were 3 cases with multicentric lesions 7.6% of all detected carcinomas. Only one of these three lesions was detected in the pre-operative MR study. The remaining two lesions were not detected because the size of the multicentric lesion was very small and on the other side dynamic studies were not done at the site of the additional lesion. These lesions were also not detected by the other imaging modalities such as mammography and ultrasonography. The incidence of multifocality in breast specimens range from 9% to 37%⁶⁾. Patients with tubular carcinomas are more likely to have multicentric invasive carcinomas but the patients with ductal carcinomas in situ less than 25mm diameter are unlikely to have multicentricity. The women with multi-focal carcinomas have a significantly worse mortality rate than those in which the carcinomas are not multifocal^{6,11,12)}. There is also a sharp contrast with the infrequency which multifocal tumors are detected clinically and by the imaging modalities and the frequency which those are detected in the specimen examination¹³⁾. For that reason to detect a multi centric lesion during the operation is very important and of great significance for the prognosis of the patient. In one of our cases the second lesion was very closed to the surgical margins and this distance was less than 10mm of the specimen margins. According to our pathologists the distance of the lesion from the surgical margins must not be less than 10mm. When this distance is less than 10mm, the risk of

local recurrence is higher.

There was no discrepancy in the objective size of the lesions measured by radiologists and the histologic size of the tumor. There was a discrepancy in the size of the lesion in the pre-operative MR study and the specimen MR study. The smaller size of some lesions in the specimen was a result that these smaller lesions were not discovered in the pre-operative study.

In the one case with post-operative panniculitis there was diffuse strong enhancement of the breast tissue similar to that of carcinoma. On the subtraction images same diffuse pattern of enhancement was visible, but no tumor was evident in the specimen MR examination. Mammogram and US suggested also the diagnosis of a recurrent carcinoma. The clinical diagnosis was also suspicious of recurrent carcinoma and for that reason underwent mastectomy. Because of the increased use of radiation therapy for breast cancer many physicians encounter patients with post-radiation panniculitis¹⁴. Radiologists must always be aware of this entity and suspect it when irradiation treatment has been performed.

The case, which was histologically proven sclerosing adenosis, was misdiagnosed as carcinoma in the pre-operative MR study. It has been previously reported the resemblance of mammographic appearance of solid tubular carcinoma and sclerosing adenosis as well as the superficial histologic resemblance which causes difficulties in the differential diagnosis of those two entities¹⁵.

We evaluated the usefulness of breast specimen MR images and the efficacy of them to depict the tumor. There was perfect correlation between MR images and pathological gross sections. In all cases specimen MR images could clearly depict the tumor and differentiate it from the surrounding normal breast tissue, in spite that the tumor was not visible

in some pre-operative T1WI. We consider that specimen MR images can inform the surgeon if the entire breast lesion has been removed, if there is and additional lesion and if the surgical margins are free of disease. Even if the examination time is longer than the plain radiography, since we can obtain images of the whole specimen in two planes because there is high degree of contrast between normal and abnormal tissue, we can accurately confirm the evidence or absence of tumor. There are not any artifacts of overlapping tissue and there is no need of compression or the use of water bath mainly for the estimation of surgical margins^{16,17,18,19}. We consider that this modality can be used within the operation and the surgeon can be informed of the specimen results while still in the operating room, and if necessary removal of additional tissue can be performed immediately²⁰. We would like to recommend breast specimen MR images in cases with impalpable lesions and when specimen radiography fails to depict the lesion to reduce the uncertainty of the surgeon and the anxiety of the patient.

Specimen MR examination can also be useful as a guide to the gross examination of a mastectomy specimen^{21,22}. The MR images can be used to guide selection of blocks for histologic study. This procedure may be useful in large breasts with small occult or impalpable lesion.

In conclusion specimen MR images are useful in the confirmation of the excised tumor, depiction of tumor at the surgical margins (**Fig.1b**) of the specimens or depiction of additional tumors in the same breast, which are not diagnosed in the pre-operative MRM studies. The evidence of more than one lesion may change the operative technique during the operation time which is very important for the further treatment and survival of the patient.

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