Breast MRI of ductal carcinoma in situ: Is there MRI role?

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Background. *The purpose of this study is to report our personal experience of 22 cases of ductal carcinoma in situ (DCIS) studied with magnetic resonance imaging (MRI).*

Patients and methods. *From September 1995 to December 2001, 22 women diagnosed with DCIS lesions underwent contrast enhanced MRI within 7 days after mammographic examination.*

Dynamic MRI was performed with a 1 T system, using a three dimensional fast low angle shot (FLASH) pulse sequence before and after contrast media administration. We evaluated the morphologic features of the enhancement, the enhancement rate and the signal time intensity curve. Pathology was obtained in all cases.

Results. *The results of histopatological examination included: 15 DCIS and 7 DCIS with associated microinvasive component or microfoci of invasive ductal carcinoma (IDC).*

On MRI, 21 of 22 (95%) DCIS lesions showed contrast enhancement. Fourteen out of 15 pure DCIS lesions demonstrated respectively a low (3), undeterminate (5), and strong (6) enhancement. Morphologically, the enhancing lesion was focal in 7, segmental in 4, and with linear branching in 3 cases. Wash out was found in 4 cases, plateau curve in 8 and Type I curve in 2 cases. Multifocality was present in 5 cases.

All DCIS with associated microinvasion demonstrated contrast enhancement: 1/7 cases showed a low enhancement, 2/7 showed an indeterminate enhancement and 4/7 showed a strong enhancement. Morphologically, the enhancing lesion was focal in 3/9, segmental in 5 and with linear branching in 1 case. The wash out was demonstrated in 3/7 cases, plateau curve in 3 and Type 1 curve in 1case. Multifocality was present in 3 cases.

Conclusions. *In conclusion, the sensitivity of MRI for DCIS detection is lower than that achieved for invasive breast cancer; however, contrast-enhanced MRI can depict foci of DCIS that are mammographically occult. The MRI technique is of complementary value for a better description of tumor size and detection of additional malignant lesions.*

Key words: breast neoplasms; carcinoma, ductal, noninfiltrative; carcinoma in situ, minimally invasive breast cancer; magnetic resonance imaging

Introduction

Ductal carcinoma in situ (DCIS) is histologically not considered as a single entity, but as a heterogeneous group of lesions that differ in their histopathologic features, growth pattern, clinical presentation and biological behavior. Before the advent of widespread mammographic screening, DCIS was rarely detected and accounted for only 0.8%-5.0% of all breast cancers.[1] With the introduction of mammographic screening, DCIS accounted for 15-20% of all detected breast cancers, and for 25%-56% of all clinically occult cancers.[1,2]

Seventy percent of DCIS presents as a cluster of microcalcifications; therefore, mammography is the primary and most sensitive technique to identify DCIS. Nevertheless, in many cases, it is not accurate either in assessing the real cancer's extent (underestimation of 46% of cases) or detecting multifocal lesions.[3]

The potential of magnetic resonance imaging (MRI) in the detection of DCIS is well documented in many recent trials,[4-6] where encouraging data about the role of MRI have been shown. Unfortunately, these data are not always concordant with others in different studies, reporting of varying in sensitivities. The explanation is likely related to the extreme variability in histologic features of a tumor, tumor size, tumor grade, different MRI parameters used, different technical factors involved in performing breast MR imaging and image interpretation.

The purpose of this study is to report our personal experience on 22 cases of DCIS studied with MRI.

Patients and methods

We retrospectively reviewed the MRI and mammographic (Mx) examinations performed from September 1995 to December 2001on 22 women (aged between 75 and 43 years, mean 53 years) affected by DCIS.

Bilateral mammograms (mediolateral oblique and craniocaudal views) were obtained on a standard mammographic unit (Mammo DIAGNOST UC, Philips medical Systems Inc., Best Netherlands). In most cases, additional mammograms (e.g. spot views) were obtained in both projections.

The following mammographic features were specifically assessed in each examination:
- Focal nodular mass;
- Microcalcifications: distribution, characteristics, size, association with mass (suspicious of malignancy if: clustered, pleomorphic, mixed density or associated with mass or area of architectural distortion);
- Associated features: architectural distortion, parenchymal distortion.

Breast MRI was performed within 7 days from the Mx, with a 1 T system (Magneton Impact Siemens, Erlangen Germany), with a dedicated bilateral breast surface coil. A three-dimensional fast low-angle shot (FLASH) pulse sequence was used: 14 ms repetition time (TR), 7 ms echo time (TE), 25° flip angle, 2.5 mm effective slice thickness, 192x256 matrix, and 84 sec acquisition time. Images were acquired in coronal plane, with rectangular FOV (4/8). The entire breast was imaged before and five times after intravenous injection of 0.1-mmol of Gd-DTPA/Kg body weight (Magnevist; Schering Berlin, Germany).

The post-processing procedures included:
- Digital image subtraction: subtraction of pre-contrast from the second acquisition of the post-contrast images. The subtraction enables to obtain the signal suppression of fat tissue and to identify the enhancing areas (malignant lesions with neoangiogenetic activity);
- Maximum intensity projection (MIP) permits to obtain a 3D-image rotating on axial and on sagittal plane, based on the subtracted images;

- Multiplanar reconstruction (MRP) permits to obtain axial images, based on the coronal acquisition.

Semi-quantitative analysis of the signal intensity to time relation was performed with the region of interest technique. The region of interest (ROI) (2-5 pixel) was placed within the tumoral area, where the highest signal intensity enhancement was seen.

The percentage of signal intensity increase was defined as:

SI Increase lesion = (SI post-SI pre)/SI pre x 100

SI = signal intensity; »pre« and »post« mean before and after contrast administration.

With respect to enhancement kinetics, the enhancement rate that is referred to as a relative signal intensity increase that occurs in a certain period of time (usually identified in the first contrast minute) was calculated.

The optimal threshold value above which the enhancement level should be considered suggestive of malignancy is still debated. According to recent studies, a relative signal increase below 70% is usually considered as an index of no or minimal enhancement; a relative signal increase ranging between 70% and 140% is considered as intermediate, and a relative signal increase over 140% is considered as strong.[4]

The three types of time-intensity curve, which have been previously described,[7,8] were used:
- Type 1 (continuous signal intensity increase): a persistent increase in SI was present beyond 2 minutes after the contrast media injection;
- Type II (plateau): the maximum signal intensity was achieved in the first 2 minutes and then remained fairly constant;
- Type III (wash out): the maximum signal intensity was achieved in the first 2 minutes and went decreasing over time

The morphology of the enhancement[7] was classified as:
- Focal enhancement corresponding to a well-defined mass;
- Ductal enhancement corresponding to a linear/linear branching configuration, which can be related to a single enhancing duct (»galactogram«);
- Segmental enhancement usually present in the lesions confined to the territory of a duct or of a ductal system, of a triangular shape with the tip pointing toward the nipple;
- Regional or diffuse enhancement corresponding to the areas of confluent enhancement that do not respect the borders of ductal system.

In 6 patients, the histological diagnosis was obtained by surgical biopsy, following the placement of a mammorep under Mx or US guidance, while in the other 16 patients, histological diagnosis was provided by core needle biopsy. The patients underwent definitive surgical treatment within 14 days after MRI. Finally, in all patients, the definitive histological diagnosis was made from the pathologic specimen (mastectomy or breast-conservative surgery).

Results

Pathology demonstrated the presence of DCIS in 15 cases (68%), and of DCIS with associated microinvasive component or microfoci of invasive ductal carcinoma (IDC) in 7 cases (32%). In 12 patients an isolate focus was diagnosed. Twenty-one out of 22 lesions (95%) showed enhancement after contrast media administration at MRI.

DCIS

The diagnosis of pure DCIS was made by histopathology in 15 lesions; 2 lesions were

classified as comedo type and 13 as non-comedo type DCIS.

Mammography demonstrated clusters of exclusively pleomorphic round and branching microcalcifications in 12 cases (3 associated with mass) (86%), and achitectural distortion or opacity in 2 (14%). One patient had negative mammograms, but ultrasonography (US) revealed abnormal findings.

On MRI, 14/15 (93%) lesions revealed the uptake of contrast media, while 1 (7%) lesion was not identified at MR imaging. Nevertheless, Mx demonstrated microcalcifications typical for malignancy in this false negative at MRI. In five out of the 14 enhancing lesions patients were affected by multiple foci of DCIS.

Among the 14 enhancing lesions, 3 (21%) showed a low, 5 (36%) an indeterminate, and 6 (43%) a strong enhancement (Table 1a). Morphologically, the enhancing lesion was focal in 7 (50%), segmental in 4 (27%) and with linear branching in 3 (21%) cases (Table 1b). Wash out was found in 4 (29%) cases, a plateau curve in 8 (57%), and type I curve in 2 (14%) cases (Table 1c).

In detail, the 2 comedo type DCISs showed a morphological pattern (ductal or segmental) and a enhancement behavior, strong typical for malignancy.

DCIS + DCI

In 7/22 lesions (32%), histology detected DCIS with associated minimally invasive carcinoma.

Mx was abnormal in all these patients (100%) who were suspicious for microcalcifications present in all cases (in one case, microcalcifications were associated with opacity).

All lesions demonstrated contrast enhancement at MRI: 1/7 (14%) showed a low enhancement, 2/7 (29%) an indeterminate enhancement, and 4/7 (57%) a strong enhancement (Table 1a).

Morphologically, the enhancing lesion was focal in 3/7 (43%) cases, segmental (Figure 1) in 3 (43%), and with linear branching in 1 (14%) case (Table 1b) (Figure2). Wash out was demonstrated in 3/7 (43%) cases, plateau curve in 3 (43%), and type I curve in 1 (14%) case (Table 1c).

Three out of 7 cases (43%) presented multiple foci of DCIS with associated microinvasion (Figure 3).

Table 1a. Enhancement rates in14 DCIS and 7 DCIS with associated minimum invasion.

Percentage of signal intensity increase	DCIS	DCIS+DCI	Total
<70%	3 (21%)	1(14%)	19%
70%-140%	5 (36%)	2 (29%)	33%
>140%	6 (43%)	4 (57%)	48%

Table 1b. Enhancement configuration in 14 DCIS and 7 DCIS with associated minimum invasion.

Configuration			
Focal mass like	7 (50%)	3 (43%)	48%
Segmental	4 (27%)	3 (43%)	33%
Linear-branching	3 (21%)	1 (14%)	19%

Table 1c. Signal intensity curve types in 14 DCIS and 7 DCIS with associated minimum invasion.

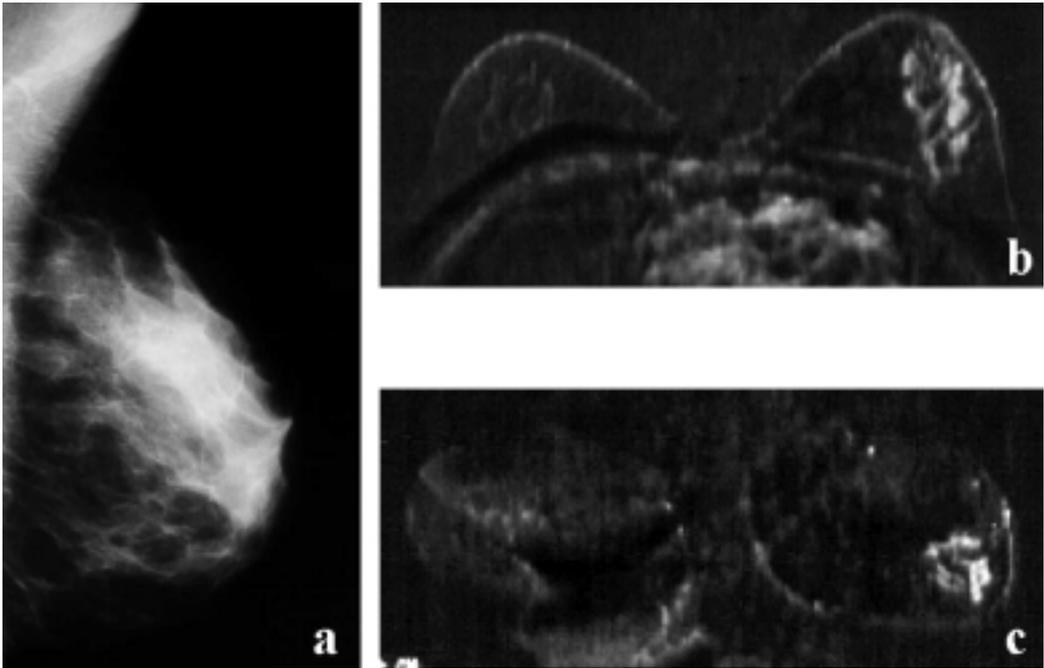| Signal intensity curve			
Type i	2 (14%)	1 (14%)	14%
Type ii	8 (57%)	3 (43%)	52%
Type iii	4 (29%)	3 (43%)	33%

Figure 1. Segmental enhancement. A 54 year-old asymptomatic woman. Mammogram of the left breast, in medio-lateral oblique view, did not show abnormalities (a). MRI revealed an area of segmental enhancement, well visible both in the coronal and in the MPR images (b,c). Histology proved DCIS with a focal area of minimally invasive component.

Discussion

Ductal carcinoma in situ is a heterogeneous group of histopathologic lesions, traditionally classified in two main subgroups, non-comedo (cribriform, micropapillary, clinging and solid), and comedo type, on the basis of the architectural growth pattern and cell type, and the presence or absence of comedo type necrosis within the ducts.

Recently, the new pathologic classifications proposed by Holland et al.[9] distinguish among well-, intermediately-, and poorly differentiated DCIS subtypes on the basis of cytonuclear differentiation and architectural growth pattern. Silverstain et al[10] have introduced the so-called Van Nuys classification in which the presence or absence of high nuclear grade and the presence or absence of comedo type necrosis is considered.

A new pathologic classification, consider-ing the biological behavior of DCIS and playing an important role in recognizing more aggressive lesions for an optimal management of DCIS, should be recommended.

The value of mammography is well known seeing that 70% of DCIS become evident as a cluster of microcalcifications (usually linear, with linear branching or granular; Le Gal type IV-V), and that, in well-differentiated lesions, mammography is also very useful.

Several investigations demonstrated that contrast enhanced MRI has a very high sensitivity in invasive breast cancer detection, with the values reaching 100%, whereas the sensitivities for the identification of DCIS on MR images have been reported to be variable, ranging from 33 to 100%.[4] There are many potential explanations for the wide variability in reported sensitivities; according to one, it may be due to the differences in the size of DCIS lesions studied. It is obvious that MRI is
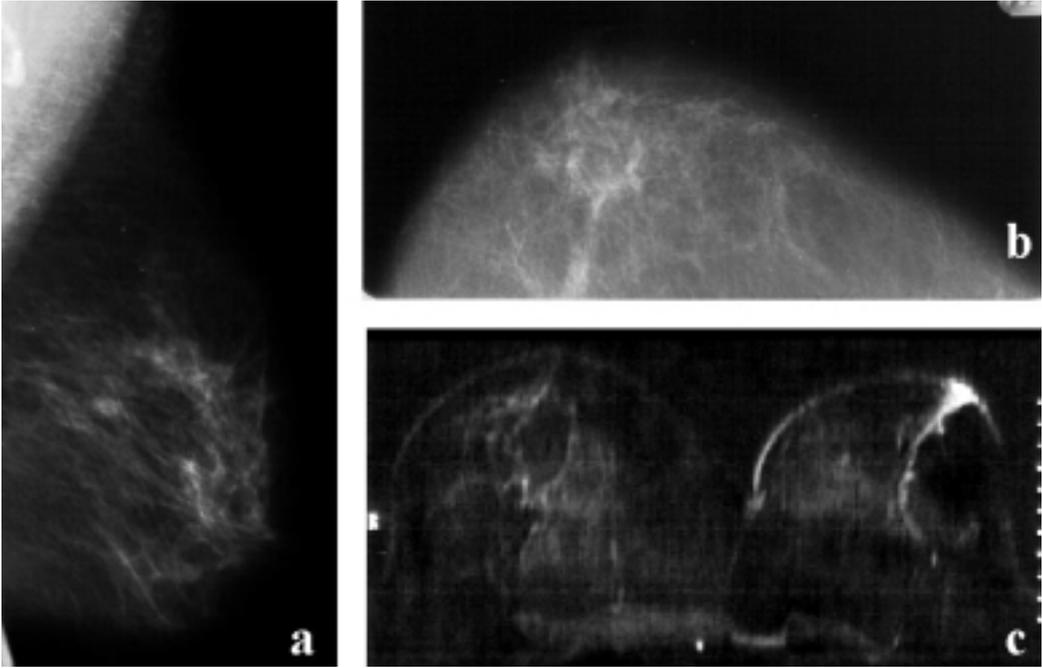
Figure 2. Linear branching enhancement. Images of a 58-year-old woman with a retracted mammary nipple on the left side. Mammography, in medio-lateral oblique and cranio-caudal views, demonstrated an area of subtle architectural distortion, better seen in the second projection (a, b). MPR image on axial plane revealed a typical linear branching enhancement pattern (c). Histology proved a pure DCIS.

not able to visualize tumors smaller than the slice thickness due to partial volume effect. Nevertheless, the size of lesions does not seem to be the only explanation for the variable detection of DCIS with MR imaging. In fact, false-negative results with tumor sizes ranging from 2 mm to 9 cm have been reported.

Another factor that could affect the sensitivity of MRI in DCIS detection is the histological type of the tumor. However, the histological subtype by itself is not sufficient to explain the presence or absence of contrast enhancement on MR images because false negative cases of both comedo type and noncomedo type DCIS have been reported. The degree of tumor angiogenesis is another histological variable that could influence the sensitivity of MRI in the depiction of DCIS. It is well known that malignant lesions release angiogenetic factors (e.g. vascular endothelial growth factor, VEGF) that induce sprouting and growth of pre-existing capillaries, and the ex novo formation of new vessels (angiogenetic activity). In dynamic breast MR imaging, invasive breast cancer is detectable due to its strong enhancement, whereas a certain degree of angiogenetic activity seems to be a prerequisite for tissue invasion, and it is not needed as long as the tumor stands in the preinvasive state (in situ). While invasive growth is almost invariably associated with contrast enhancement, this is not necessarily true for the in situ cancers. In fact, a weak tumor angiogenesis, found in the stroma and around the ducts involved in DCIS, can explain the lack of a significant enhancement behavior.

In addition to the size of the lesion, histological subtype and neoangiogenesis, differences in MRI technique (2D section selected sequence, 3D volume sequence, 3D volume
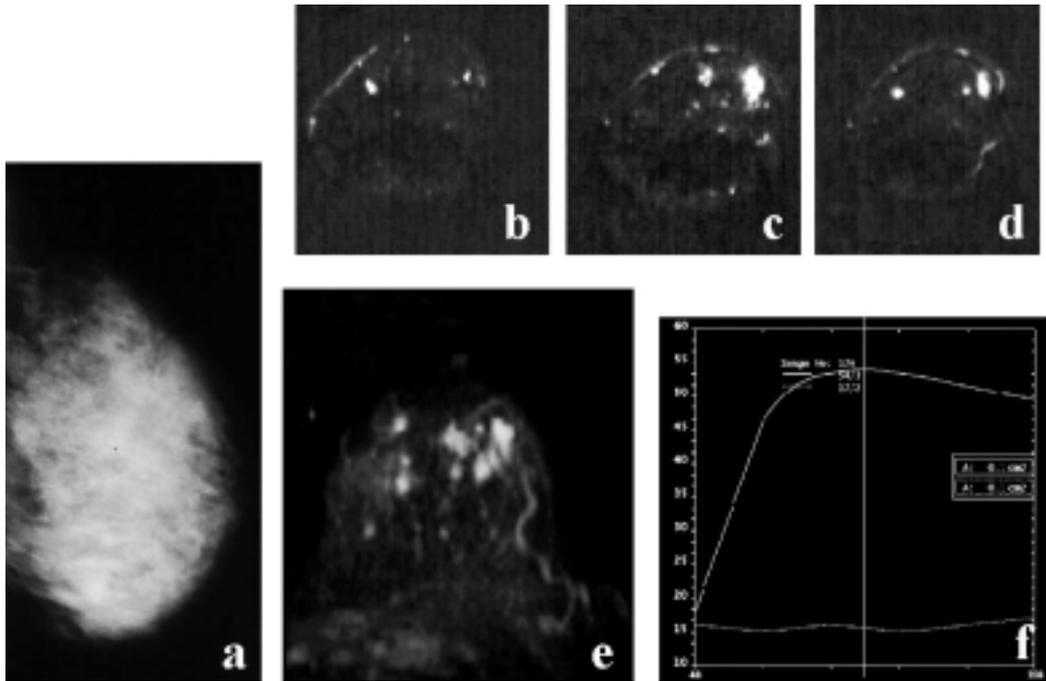
Figure 3. Multifocal, multicentric enhancement. Images of a 47-year-old woman. Mammogram of the left breast, in the medio-lateral oblique view, did not show any abnomality (a). MIP and several coronal MR images revealed multifocal and multicentric enhancement (b,c,d,e). The SI/T curve, relative to the lesion, presents a plateau-type curve (f). Histology proved DCIS with associated microinvasion.

fat suppressed technique, dynamic technique,...), and the differences in image interpretation (morphologic criteria to establish the degree of suspicion, threshold value of enhancement above which a lesion should be considered suggestive for malignancy) may also explain the variability in reported sensitivities.

Mammography, whose morphologic criteria of suspicion in a detected lesion are well known, does not use any criteria similar to those used in MR imaging. The enhancement configuration of DCIS is variable: DCIS lesions can present a focal, mass-like enhancement with ill-defined borders or can exhibit a linear or linear branching enhancement (duct-like configuration) or even a segmental enhancement with a configuration corresponding to a ductal system.[2,7]

In a recent study reported by Viehweg et al.[4], MRI detected 96% of DCIS lesions that exhibited at least some week enhancement. Only 4% of DCIS lesions did not show enhancement at all. The morphology of enhancement was focal (73%), diffuse (10%) or ductal (17%). In 65% of cases, the speed of enhancement was considered as delayed. In high-grade DCIS lesions (according to Van Nuys classification), comparing comedo subtype to non-comedo subtype, the behavior of enhancement was more often ill defined (83% vs. 43%), ductal (29% vs. 12%), and rapid (50% vs. 29%). Significant differences in the enhancement behavior were not found between high-grade and low-grade DCIS, nor were there any between comedo and non-comedo subtype lesions. Although 96% of DCIS showed the contrast enhancement on MRI, only 50% of DCIS lesions showed a »typical« enhancement behavior suspicious for malig-

nancy characterized by a strong and early enhancement, focal ill-defined enhancement or an enhancement with ductal configuration. Moreover, in the same work, MRI allowed the detection of 25 additional foci of DCIS.

In our study, the majority (95%) of DCIS lesions demonstrated at least some enhancement. The only false negative lesion at MRI was a pure non-comedo DCIS. On the other hand, MRI identified additional foci of DCIS that were mammographically occult in 8 cases. However, using the usual diagnostic algorithm, the enhancement rate was considered typical of malignancy, e.g. strong or at least indeterminate in 79% of pure DCIS and in 86% of microinvasive DCIS.

The configuration of DCIS was variable: linear branching enhancement, which is considered to be an important feature of malignancy, was present in only 21% of pure DCIS and in 14% of microinvasive DCIS. Early wash out, known as a typical feature of invasive malignancy was present in 29 % of pure DCIS and 43% of microinvasive DCIS. The non-enhancing DCIS was mammographically identified by the presence of microcalcifications. MR imaging, however, may contribute to the diagnosis of DCIS by detecting the lesions not visible on mammography.

In conclusion, the sensitivity of MRI for DCIS detection is lower than that achieved for invasive breast cancer; however, contrast enhanced MRI can depict mammographically occult foci of DCIS. Mammography remains the main diagnostic technique for breast examination. The MRI technique is of complementary value for better description of tumor size, in the detection of additional malignant lesions, and in the study of the dense breasts, poorly visible by mammography.

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