Detection of pure ductal carcinoma in situ (DCIS) at diffusion-weighted imaging (DWI)

Poster No.: C-1472
Congress: ECR 2015
Type: Scientific Exhibit
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Keywords: Breast, MR, Staging, Cancer
DOI: 10.1594/ecr2015/C-1472

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Aims and objectives

Ductal carcinoma in situ (DCIS) is an abnormal proliferation of malignant epithelial cells that line duct without invasion of the basement membrane.

With the advent of mammographic screening the incidence of DCIS varied from $1.9 \times 10^5$ to $32.5 \times 10^5$ and currently it represents the 15-20% of malignant breast lesions and the 25-56% of mammographically detected cancers.

Even thought DCIS represents an heterogeneous disease in terms of biological behavior, there is evidence that about 30-50% of all DCIS progresses to an invasive cancer.

In the detection of DCIS, Breast MRI shows sensitivity up to 93%. In particular, the diagnostic performance of this modality is higher in the identification of high and intermediate grade DCIS (98% and 91% respectively) than in low grade disease (80%). Moreover, Breast MRI is more accurate than mammography in the local staging of DCIS (identification of multifocal/multicentric disease 42-90% vs 26-40%). Breast MRI DCIS features may vary. However, it appears as abnormal non mass enhancing lesion in 60-81% of the cases. By adopting the MR BIRADS (Breast Imaging Reporting and Data System) lexicon, several studies identified descriptors characterized by a higher predictive value for DCIS. With regards to morphologic descriptors, more frequently the enhancement of DCIS tends to show linear, segmental or focal distribution, heterogeneous or clumped internal pattern and asymmetry with respect to the contralateral breast. On the other hand no specific functional features have been identified.

Diffusion Weighted Imaging (DWI) is a MR technique, which detects random motion of water molecule in a tissue. In particular, malignant lesions are characterized by restricted diffusion and appear as hyperintense at DWI. The role of DWI in breast diseases is still under investigation. This technique has been evaluated in terms of characterization of breast lesions, showing potential in improving the diagnostic performance of DCE-MRI. More recently, a few studies evaluated its role in the identification of breast cancer, demonstrating a good cancer detection rate (up to 78%), especially for invasive disease.

The purpose of this work is to assess the diagnostic performance of DWI in comparison to Dynamic Contrast-Enhanced MRI (DCE-MRI), in both detection and diagnosis of pure DCIS.

Methods and materials
The series retrospectively included the 19 patients (averaged age 53y; range 35-72) who consecutively underwent both local staging breast MRI and surgery for pure DCIS at our Institution in 2013.

Breast MRI was carried out with a 1.5T magnet (GE Healthcare) and 8-channels coil and, for the purpose of the study, consisted of DWI followed by Dynamic Contrast-Enhanced MRI (DCE-MRI).

DWI was acquired by axial EPI sequence (b-value 0 and 900 s/mm²; slice thickness 4mm) while DCE-MRI by 3D T1w GRE sequence (slice thickness 2.6 mm; temporal resolution 90s). The 3D sequence was acquired before and 4 times continuously after iv administration of contrast agent (0.1mmol/kg of Gadobenate Dimeglumine-Bracco Imaging) at flow rate of 2ml/sec, followed by saline solution flush. A late acquisition was performed 2 minutes after the last sequence.

Full technical details of both DWI and DCE-MRI sequences are provided in Figure 1.

DWI and DCE-MRI images were qualitatively and independently reviewed by two readers (3 and 15 years of experience in breast imaging), blinded to mammography and clinical information of the patients. The only information provided to the readers was the site of the tumor (right vs left breast).

Lesion detection and descriptors were assessed at both DWI and DCE-MRI.

For DCE-MRI, morphologic descriptors were reported following the MR BIRADS Lexicon (shape, margins and internal characteristics for mass enhancing lesion; distribution, internal pattern and symmetry for non-mass enhancing areas). By adapting the lexicon, the same descriptors were used for areas of hyperintensity at DWI. List of descriptors is provided in Figure 2.

Inter-reader variability in lesion detection and diagnosis was evaluated.

The size of the lesions was assessed by electronic calipers at each MR technique. In the case of multifocal/multicentric disease, the lesion extent was defined by considering the largest measure between the most distant enhancing/hyperintense areas.

For both DCE-MRI and DWI, the measurements performed by the two readers were averaged and the results were then compared to pathology. A difference in size ±5mm between Imaging and pathology was considered as "discordant case".
Images for this section:

**Fig. 1:** DCE-MRI and DWI technical protocols
Fig. 2: Descriptors adopted for qualitative assessment of both DCE-MRI and DWI
Results

Pathology identified 3 multifocal Ductal Intraepithelial Neoplasia (DIN)1c, 8 DIN2 (of which 6 multifocal) and 8 DIN3 (of which 7 multifocal).

For both readers, the detection rate was 84% (16/19) and 100% (19/19) for DWI and DCE-MRI, respectively (Figg. 3-7). All the 3 false negative cases at DWI were multifocal DCIS (1 DIN1c and 2 DIN3) without cancerization of lobules and in which the pathologic size of the larger single focus was <3mm.

At DCE-MRI in 18/19 of the patients, DCIS presented as a non mass enhancing area asymmetric with respect to contralateral breast. Distribution was focal in 3 cases, segmental in 5 and linear in 10; 12 lesions showed clumped internal pattern, 5 heterogeneous and 1 homogenous. In the remaining subject, the disease appeared as mass lesion characterized by a round shape, irregular margins and heterogeneous internal characteristics.

In 15/16 cases detectable at DWI, DCIS appeared as non mass area of hyperintensity asymmetric with respect to the contralateral breast. Distribution was defined as focal in 2 cases, segmental in 5 and linear in 8. Internal pattern was assessed ad clumped in 10 cases, heterogeneous in 3 and homogenous in 2. In the remaining subject, the disease appeared as an area of hyperintensity characterized by a round shape, irregular margins and heterogeneous internal characteristics. In all the cases, both readers assigned the same descriptors for DCE-MRI and DWI (Figg. 3-5).

The averaged size of the 16 lesions detected by both MR techniques resulted 39mm ±19mm (range 8-70mm) for DCE-MRI and 23mm±14mm (range 16-70mm) for DWI. Concordance in lesion extent between MRI and DWI was observed in 13/16 (81%) of the cases.

With regards to correlation with pathology, the lesion extent was correctly assessed by DCE-MRI in 13/16 (81%) of the cases. In the remaining three cases, DCE-MRI overestimated the extent of unifocal DIN2 in 1 patient and multifocal DIN3 in 2 subjects. Overestimation did not resulted in unnecessary mastectomies. By considering DWI, it correctly assessed the lesion extent in 11/16 (68%) of the cases. In the remaining cases, DWI overestimated the extent of unifocal DIN2 in 1 patient and underestimated 3 multifocal DIN1c and 1 multifocal DIN2.

Images for this section:
Fig. 3: CASE 1. A 47 year old woman with familiarity for breast cancer, who underwent screening mammography. At Mammography (A, Cranio-Caudal view; B Medio-Lateral view), a cluster of suspicious microcalcifications was identified in the upper-external quadrant of the left breast (red arrows).
Fig. 4: Same case of Figure 3. Mammography magnification (C,D) better showed the indistinct morphology of the clustered microcalcifications (red arrow). Imaging guided biopsy identified a high grade Ductal Carcinoma In Situ (DCIS, B5a).
Fig. 5: Same case of Figures 3 and 4. In the site of the cancer, late subtracted MR images (E, top row) showed a non-mass enhancing area characterized by linear distribution, heterogeneous internal pattern and asymmetry with respect to the contralateral breast (yellow arrows). The extent of the lesion resulted larger at DCE-MRI than at mammography. DCIS was detectable at DWI (F, bottom row) as a non mass area of hyperintensity with similar descriptors with respect to DCE-MRI. In fact, the area of hyperintensity at DWI showed linear distribution, heterogeneous internal pattern and asymmetry with respect to the contralateral breast (green arrows). The lesion extent at DWI resulted similar to that at DCE-MRI. The patient underwent surgery and pathology confirmed the presence of multifocal DCIS with high nuclear grade (DIN3 sec. WHO) ER 72%; PgR 90%.
CASE 2

A 40 years old woman without familiarity for breast cancer, who underwent first mammography. The examination revealed a small cluster of suspicious microcalcifications in the lower inner quadrant of the left breast (not shown). The Patient underwent vacuum assisted biopsy. Specimens radiography (A) identified the cluster of microcalcifications in the biopsy specimen nr. 10 (B). For this reason, a clip marker was positioned in the biopsy site (Post biopsy mammograms: C, Cranio-Caudal view; D Lateral view). The histopathologic diagnosis was a low-intermediate grade DCIS.

Fig. 6: CASE 2. A 40 years old woman without familiarity for breast cancer, who underwent first mammography. The examination revealed a small cluster of suspicious microcalcifications in the lower inner quadrant of the left breast (not shown). The Patient underwent vacuum assisted biopsy. Specimens radiography (A) identified the cluster of microcalcifications in the biopsy specimen nr. 10 (B). For this reason, a clip marker was positioned in the biopsy site (Post biopsy mammograms: C, Cranio-Caudal view; D Lateral view). The histopathologic diagnosis was a low-intermediate grade DCIS.
**Fig. 7:** Same case of figure 6. At late subtracted MR images (E,F) a small signal void artifact was identifiable in the site of vacuum assisted biopsy. Within the medial margin of the site of the biopsy, a non mass enhancing area characterized by focal distribution and heterogeneous internal pattern was detectable (yellow arrows), suggesting residual disease. At DWI (G) the signal void due to the clip marker was identifiable. Within the lateral margin of the biopsy site, chemical shift artifacts were also recognizable (green arrows) while no abnormal areas of hyperintensity were reported within the medial margin of the biopsy site. The patient underwent surgery and pathology confirmed the presence of residual cribriform DCIS with low-intermediate nuclear grade (DIN 1C-DIN2 sec. WHO) ER 98%; PgR 99%.
Conclusion

The role of DWI in breast diseases is still under investigation. This technique has been evaluated in terms of characterization of breast lesions, showing potential in improving the diagnostic performance of DCE-MRI. More recently, a few studies evaluated its role in the identification of breast cancer, demonstrating a good cancer detection rate (up to 78%), especially for invasive disease.

Our series demonstrated that DWI is more than a promising technique in the identification of pure DCIS. In fact, its detection rate resulted equal to 84% (16/19). Our preliminary results suggest that false negative cases of DWI could be related to both suboptimal spatial resolution of the technique and pathological characteristics of the disease. Similar concerns could be considered for the assessment of the extent of pure DCIS. DWI was less accurate than DCE-MRI, underestimating the size of the disease in 3 cases of multifocal DIN1c.

In all the cases both readers assigned the same descriptors for DCE-MRI and DWI, showing that MR morphological descriptors adopted in clinical practice could be translated to DWI.

In conclusion, unenhanced MRI in screening breast cancer is under investigation. In this scenario, DWI may play a significant role even in detection and diagnosis of pure DCIS. Knowledge of both descriptors and limitations of DWI result critical for its clinical application. Further evaluation is required to validate our results in a larger series of cases.

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