Pharmacokinetic evaluation of DCIS

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Purpose

In contrast enhanced breast MRI both the morphology and the enhancement dynamics of a lesion are important parameters that can be used to classify the lesion as either benign or malignant. For the evaluation of lesion morphology high spatial resolution fat saturated T1 weighted images or subtraction images are mandatory. These high resolution images are often repeated several times in order to evaluate the enhancement dynamics. The enhancement dynamics are often evaluated in a manually selected region of interest (ROI) within the lesion. Another approach to evaluating contrast dynamics is by color coding the different enhancement patterns. This way the radiologist can analyze the enhancement pattern without selecting a ROI or evaluating enhancement curves.

Currently available workstations for the evaluation of contrast enhanced breast MRI can provide the radiologist with a color coded image based on either relative enhancement curve shape or pharmakokinetic parameters. It has been described that the use of color coding of pharmakokinetic parameters derived from three time point (3TP) can increase the diagnostic accuracy of inexperienced readers. Pharmakokinetic parameters of contrast enhancement can also be assessed with the evaluation of early enhancement using fast dynamic imaging. The value of high temporal resolution imaging has been confirmed by several authors and has proven to contribute to a better specificity.

Ductal carcinoma in situ (DCIS) is however still a challenge on MRI. In recent literature the sensitivity for DCIS has been reported as high as 92%. However, many other studies have reported significant lower sensitivity for the detection of DCIS. Because of the low relative enhancement values found in DCIS and because wash out is less common in DCIS compared to invasive carcinoma's, color coding in DCIS can easily be misinterpreted which might result in a false negative evaluation. In this study we compared the values of several pharmacokinetical parameters derived from the initial enhancement of pure DCIS to a group of invasive ductal carcinoma's and a group of benign breast lesions.

Methods and Materials
We included 79 patients in this study; 14 cases of pure DCIS were compared to a group of 42 cases of IDC, a group of 11 fibroadenomas and a group of 12 non-mass-like enhancing benign lesions (NML-B). The NML-B group consisted of 4 cases of fibrosis, 3 cases of adenosis, 2 cases of inflammation, 1 radial scar, 1 case of hyperplasia and 1 case of enhancing scar tissue.

All patients were examined using a 1.5-Tesla MRI scanner (Sonata or Symphony, Siemens, Erlangen, Germany) in combination with a double breast coil. After localizer images were obtained in three directions, low spatial resolution proton-density-weighted images were acquired in the transverse plane covering both breasts completely (TE 1.56, TR 800, FA 8, FOV 320, slices 24, TA 50 s, image resolution 3.9 x 1.3 x 4.0 mm). Subsequently, a coronally orientated high-resolution three-dimensional fast low-angle shot series (FLASH 3D) was acquired (TE 4, TR 7.5, FA 8, FOV 320, slices 120, TA 86 s, image resolution 1.3 x 1.3 x 1.3 mm). Thereafter, high temporal resolution T1-weighted images (turboFLASH) were recorded 22 times with identical spatial resolution and orientation as the proton-density-weighted images (TE 1.56, TR 66, FA 20, FOV 320, slices 24, TA 22 x 4.1 s) during an intravenous bolus injection of a paramagnetic gadolinium chelate-0.2 mmol of gadoterate meglumine (Dotarem; Guerbet, The Netherlands) per kilogram of body weight—which was administered with a power injector (Spectris; Medrad, Pittsburg, USA) at 2.5 ml/s and followed by a 15-ml saline flush. Following these series, the FLASH 3D series was repeated four times. Total scan time for this protocol was 9 min 42 s, including the time needed to record localizer images.

Figure 1: Combined dynamic scanning protocol. The slow-dynamic sequences have a high spatial resolution (slow/high) and provide high quality subtraction images that allow morphological evaluation and information about wash-out (not used in this poster). The fast dynamic sequences have a relatively low spatial resolution (fast / low). These sequences provide information about the initial enhancement of the lesion and are used in this poster to calculate the pharmacokinetic parameters.

The pharmacokinetic quantification was performed using an in house developed dynamic MRI software platform. In this evaluation, a region of interest (ROI) was selected within the enhancing lesion. The ROI's were sphere-shaped and placed in an area within the lesion where the parameter values of Ktrans, V and kep were highest, based on the color-overlays. The outer limit of the lesion was used as a boundary of the ROI to rule out partial volume effects.

Figure 2: ROI Selection. A sphere shaped ROI is placed within the enhancing lesion where the parameter values of Ktrans, V and Kep are highest based on the color overlays.
Images for this section:

Gd-injection

pre-contrast

slow/high fast/low fast/low

post-contrast

slow/high 4x slow/high

Fig. 1

Fig. 2
The mean parameter values for each of the subgroups are provided in table 1. The mean value for Ktrans and V was significantly lower for DCIS cases compared to the IDC cases (P < 0.01). The difference in Kep was not significant. Comparing DCIS to fibroadenomas or NML-B revealed no significant differences for any of the parameters (p>>0.05). The distribution of the pharmakokinetic parameter values is presented in figure 3.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Subgroup</th>
<th>N</th>
<th>Mean</th>
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</thead>
<tbody>
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<td>Ktrans</td>
<td>IDC</td>
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<td>2,5398</td>
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<tr>
<td></td>
<td>DCIS</td>
<td>14</td>
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<tr>
<td></td>
<td>Fibroadenoma</td>
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<tr>
<td></td>
<td>NML-B</td>
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<td>1,0342</td>
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<td>V</td>
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<td>DCIS</td>
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<td></td>
<td>NML-B</td>
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</tbody>
</table>

Table 1: Mean parameter values for each subgroup.

Figure 3: Box plot of Ktrans (a), V (b) and Kep (c). The Ktrans and V parameter values of IDC were significantly higher compared to the DCIS cases. There was no significant difference between the parameter values of DCIS when compared to the Fibroadenomas or NML-B lesions. An example of an IDC, Fibroadenoma and DCIS case is demonstrated in figure 4, 5 and 6.

Figure 4: Example of an IDC. Note that both the Ktrans (a) and V (b) parameter show high values.

Figure 5: Example of a Fibroadenoma. Note that both the Ktrans (a) and V (b) parameter show low values comparable to the DCIS (figure 6).
Figure 6: Example of a DCIS. Note that both the Ktrans (a) and V (b) parameter show low values comparable to the fibroadenoma (figure 5) and low compared to the IDC (figure 4).

Images for this section:

![Box plot of Ktr values for different lesions](image)

**Fig. 1: 3a**
Fig. 2: 3b
**Fig. 3: 3c**
Fig. 4: 4a
Fig. 5: 4b
Fig. 6: 5a
Fig. 7: 5b
Fig. 9: 6b
Conclusion

The pharmacokinetic parameters found in DCIS were significantly lower compared to the values found in the IDC cases. The parameter values observed in both benign groups were within the same range as the values found in the DCIS cases. Based on the values observed in this study it can be concluded that these early enhancement values cannot be used to differentiate between benign lesions in the breast and DCIS. Color coding of dynamic data based on these parameters can lead to serious misinterpretation of disease, with the risk that DCIS cases receive a false negative interpretation. Commercially available breast MRI workstations usually color code the dynamic data, this is either based on relative enhancement (Figure 7c) or based on pharmakokinetic modeling (figure 7d). Both the in figure 7 demonstrated workstations used for their color coding the relatively slow dynamic data, both workstations show in their results benign values for DCIS. This is similar to the results observed in our study based on the fast dynamic data.

Figure 7: Example of a DCIS. Figure 7a and 7b show a MIP and coronal subtraction image of a proven DCIS in the right breast. Figure 7c shows the color coding based on relative enhancement (Dynacad®). Figure 7d shows the color coding based on the 3TP pharmakokinetic modeling strategy. Note that both breast MRI workstations show benign values.

Because the dynamic aspects of DCIS found in this study and on the color coding provided by the commercially available breast MRI workstations can be misleading, it is important to carefully evaluate the morphology of low grade, slowly enhancing lesions on breast MRI in order to avoid the false negative evaluation of DCIS cases.

Images for this section:
Fig. 1: 7a
Fig. 2: 7b
References


Personal Information

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