Enhancement profiles of malignant lesion subgroups in MR-mammography: A computer assisted evaluation considering pharmacokinetic parameters

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Purpose

Dynamic contrast enhanced MR-mammography (MRM) has the highest sensitivity for detection of breast cancer. In order to differentiate benign from malignant lesions, morphologic and dynamic criteria are used. Computer Assisted Diagnosis (CAD) systems (or more general speaking: software analysis tools for dynamic enhancement pattern analysis) are increasingly used to assess dynamic enhancement features. Features of these systems include voxel by voxel calculation of parametric maps, colour-coding early and delayed enhancement characteristics. Lesions not passing a user-defined threshold for early enhancement are not colour-coded, a fact which can be used for differential diagnosis as malignant lesions are thought to enhance faster and stronger compared to benign lesions. Furthermore, the most suspect enhancing part of a lesion can be identified semiautomatically, avoiding multiple manual Region-of-Interest (ROI) measurements. However, although these features simplify enhancement pattern analysis, they do not provide information which isn’t available by means of manual or visual image interpretation. A feature unique to CAD systems is quantitative enhancement profile assessment. That means that all single curve types in an enhancing, threshold passing lesion can be analyzed at one step, providing volumetric data including subvolumes. Although this feature has been described in a general way, there is little data on enhancement patterns of different histological subgroups. This prospective investigation on previous acquired examinations was performed to investigate enhancement patterns of malignant subgroups in MRM.

Methods and Materials

279 consecutive malignant lesions from a time period of 22 months undergoing surgery after MR-mammography at our institution were enrolled in this study. Examinations after preoperative (neoadjuvant) chemotherapy were excluded from this work. All surgery specimen underwent histopathological workup by a board certified pathologist.

Imaging was performed on 1.5T clinical whole body scanners (Magnetom Symphony and Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany) using dedicated bilateral phased array breast coils. Dynamic scanning in 33 transverse sections using a spoiled Gradient Echo technique (FLASH 2D, GRAPPA factor 2, TR 113 ms, TE 5 ms, flip angle 90°, spatial resolution 1.1 x 0.9 x 3 mm) was performed once before and 7 times after contrast agent (CA) injection (automated injector, flow 3 ml/s, 0.1 mmol Gd-DTPA/kg bodyweight). Time of acquisition was 1 minute per measurement. Unenhanced
images were subtracted from enhanced dynamic images for lesion detection. No motion correction algorithms were used.

For dynamic data analysis including pharmacokinetic mapping, a commercial available CAD system (iCAD, former CADSciences) was used. In all cases, a threshold of 33% for initial enhancement was applied. The second postcontrast measurement was defined as cut-off between early and delayed enhancement. Investigated dynamic enhancement parameters were: Initial enhancement (IN) 2 min. after CA injection and Washout rate (WR, defined as subtraction of relative enhancement at 7 min. from relative enhancement at 2 min.) of the most suspect curve (system defined as worst washin/washout combination), percentage of whole lesion Washout (Wash%), Plateau (Plat%) and Persistent (Pers%) voxels (in percentages) as well as the pharmacokinetic parameters median lesion Permeability (Perm) and median lesion Extracellular Volume Fraction (EVF). All data analysis was performed by two trained observers blinded to histopathology on a consensus basis using the automatic 3D ROI method, activating analysis of all curve types (Washout, Plateau, Persistent). When this procedure was not possible due to strong background enhancement, the lesion was manually encircled on each slice in order to analyze a 3D volume.

CAD analysis is shown in figure 1 and figure 2.

Besides descriptive statistics (mean, median, standard deviation -SD), one-way analysis of variance (ANOVA) was performed for subgroups comparisons. All statistics in this study have exploratory character. A significance level of #=5% was applied.

Images for this section:

Fig. 1: 54 y old patient with invasive ductal cancer G3, A: Contrast enhanced subtraction image, first minute after contrast agent injection showing lobulated mass lesion with ill
defined borders and rim enhancement (arrow). B: Delayed contrast enhanced subtraction image 7 minutes after contrast agent injection. Peripheral washout and central persistent enhancement can be depicted. C: Colour-coded map showing initial enhancement as colour brightness (faster enhancement is coded brighter) and delayed enhancement curve type as colour type (red: Washout, green: Plateau, blue: persistent signal increase). In this case medium Washout is the most suspect curve type (brighter red voxels).

![Image]

**Fig. 2:** CAD analysis example, same patient as shown in figure n. A: 3D ROI marking the complete lesion (here, only one slice is shown), automatically identifying lesion diameters. B: pie diagram showing curve type distribution. More than 75% of the lesion show Washout (red) or Plateau (green) enhancement, indicative of a malignant lesion. D demonstrates Signal intensity time curves. Turquoise corresponds to the most suspect washin to washout combination (the curve referred to in this work). C, E: Distribution histograms of pharmacokinetic parameters Permeability (C) and Extracellular Volume Fraction (EVF), demonstrating enhancement heterogeneity.
Results

Histopathology revealed: invasive ductal cancer (IDC, n=219), invasive lobular cancer (ILC, n=23), DCIS (n=16), other malignancy (OM, n=21). Initial enhancement differed significantly between malignant subgroups with fastest enhancement in IDC/ILC and slowest enhancement in DCIS ($P=0.021$). Highest Washout rate was observed in IDC, whereas DCIS and OM showed lesser Washout ($P=0.018$). Washout voxel percentage ($\text{Wash}_\%$) was clearly highest in IDC and lowest in DCIS cases ($P<0.001$). Similar, but lesser differences were detected in Permeability ($P=0.018$), whereas Persistent voxel percentage distribution was reverse to Washout voxel percentage ($P=0.003$). EVF was equally high in all invasive cancers and low in DCIS ($P<0.001$). Plateau voxel percentage showed no significant differences between malignant subgroups ($P=0.909$).

For exact results c.f. table 1 (fig. 1) and figures 2-8.

Images for this section:

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Washout</th>
<th>Wash (%)</th>
<th>Plat (%)</th>
<th>Pers (%)</th>
<th>Perm</th>
<th>EVF</th>
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<td></td>
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<td></td>
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<tr>
<td>Mean</td>
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<td>52.5</td>
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<td>30.1</td>
<td>30.8</td>
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<tr>
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<tr>
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**Fig. 1:** Table 1: Enhancement profiles of malignant subgroups
**Fig. 2:** Boxplots of initial enhancement in malignant subgroups.
Fig. 3: Boxplots of Washourate in malignant subgroups.
**Fig. 4:** Boxplots of persistent voxel percentage in malignant subgroups.
Fig. 5: Boxplots of Plateau voxel percentage in malignant subgroups.
Fig. 6: Boxplots of Washout voxel percentage in malignant subgroups.
**Fig. 7:** Boxplots of median Permeability in malignant subgroups.
Fig. 8: Boxplots of median Extracellular Volume Fraction in malignant subgroups.
Conclusion

Enhancement profiles of malignant lesions differ significantly between histopathologic subgroups. The most obvious finding is a less aggressive enhancement pattern in DCIS lesions, which are thought to show lesser neoangiogenesis and thus lesser hypervascularisation compared to invasive cancers. IDC shows the most aggressive enhancement pattern with highest permeability and Washout rate. Taking these observations into account might improve differential diagnosis in MRM explaining known overlaps of enhancement features especially of non-classical IDC cases with benign lesions. The reported results also suggest further criteria to identify and differentiate early stages of breast disease like DCIS.

References


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