Detection of breast micro-calcifications at high-field MRI.

Bertine L. Stehouwer[1], Hendrik de Leeuw[2], Peter R. Seevinck[2], Fredy Visser[1,3], Peter R. Luijten[1], Dennis W.J. Klomp[1], Paul J. van Diest[4], Chris J.G. Bakker[2], and Wouter B. Veldhuis[1]

[1]Radiology, University Medical Center, Utrecht, Utrecht, Netherlands, [2]Image Sciences Institute, University Medical Center, Utrecht, Netherlands, [3]Philips Healthcare, Best, Netherlands, [4]Pathology, University Medical Center, Utrecht, Utrecht, Netherlands

Introduction: Ductal carcinoma in situ (DCIS) is considered a potential precursor to invasive ductal carcinoma [1]. It is therefore treated as such, with surgery, often followed by radiotherapy. Approximately 62-98% of DCIS presents with micro-calcifications on mammography [2-4]. MRI has been shown to be able to aid in the diagnosis of DCIS [5].Unfortunately, up to today clinical MR imaging protocols are not able to detect micro-calcifications. However, the concurrent MRI detection of micro-calcifications with enhancing breast masses and non-mass lesions may aid in discriminating likely higher-grade from likely lower-grade DCIS lesions and may improve the detection rate of small high-grade invasive lesions associated with micro-calcifications. Herein the feasibility of the detection of micro-calcifications with high-field MRI by exploiting the effect of the difference in susceptibility of calcifications and glandular tissue on the signal phase is investigated. First, the potential of the method is tested in a phantom setup containing various particles of calcium hydroxyapatite [4]. Second, the method is demonstrated in ex-vivo breast tissue containing micro-calcifications confirmed on mammography.

Materials and Methods: The phantom experiment was performed on a phantom consisting of an agarose gel (2%) doped with 20 mg/L $MnCl_2$ to adapt the T_1-relaxation time. In the gel small particles of calcium hydroxyapatite were scattered to simulate micro-calcifications [4]. It was scanned on a whole-body 7T MRI system using a homebuilt two-channel unilateral RF breast coil [6]. Scan protocol included a multi-echo (15 echoes) fast field gradient echo sequence (FOV 128^3 mm^3, 0.5mm isotropic resolution, flip angle 10°, TR 72ms, first echo 3ms and echo spacing 2ms, read-out bandwidth 1.kHz/pixel) with a scan duration of 32:47min. An ex-vivo breast specimen was obtained after skin-sparing mastectomy surgery. It was imaged on a 3T whole-body MR system, using a 16-channel bird-cage coil, after placing it in a plastic container filled with fomblin. Scan protocol included a multi echo (12 echoes) fast field echo sequence (FOV 200x160x80 mm^3, res. 1mm isotropic, flip angle 20°, TR 47ms, first echo and echo spacing 2.3 ms, read-out bw 1.25kHz/pixel) with a scan duration of 10:05min. The calcifications in the MR images of both the phantom and breast tissue specimen were traced by calculating the phase derivative [7]. To remove the influence of B_1 inhomogeneities, the derivative of the 1st echo was subtracted from the phase derivative images at the odd echoes. Results were compared to CT (thickness 0.67mm, increment 0.33mm, voltage 140kV and current 250mA, scan duration of 4.13s) in the phantom setup and to mammography for the mastectomy specimen.

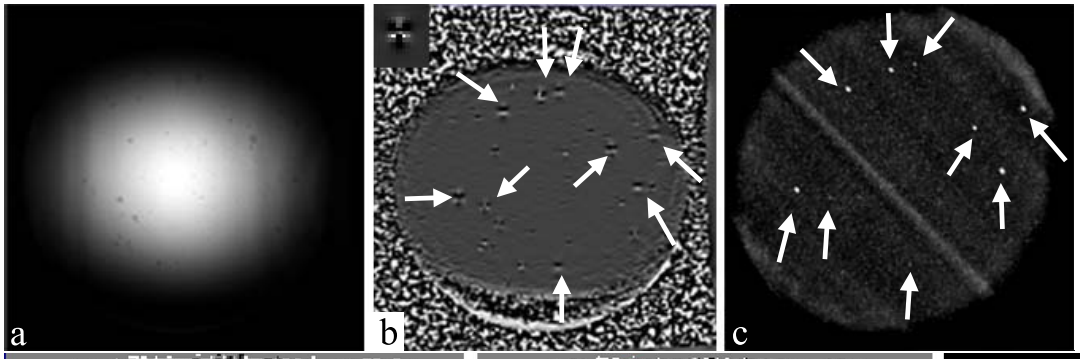

Figure 1: *A and b show intensity projections of the magnitude and phase derivative image at TE=25ms, respectively. Shown are projections over a number of slices that contain calcifications. Figure c shows the maximum intensity projection of the CT image over the same slices. Calcifications are indicated by arrows. The insert in Figure b displays the characteristic six-lobed pattern for a diamagnetic disturbance.*

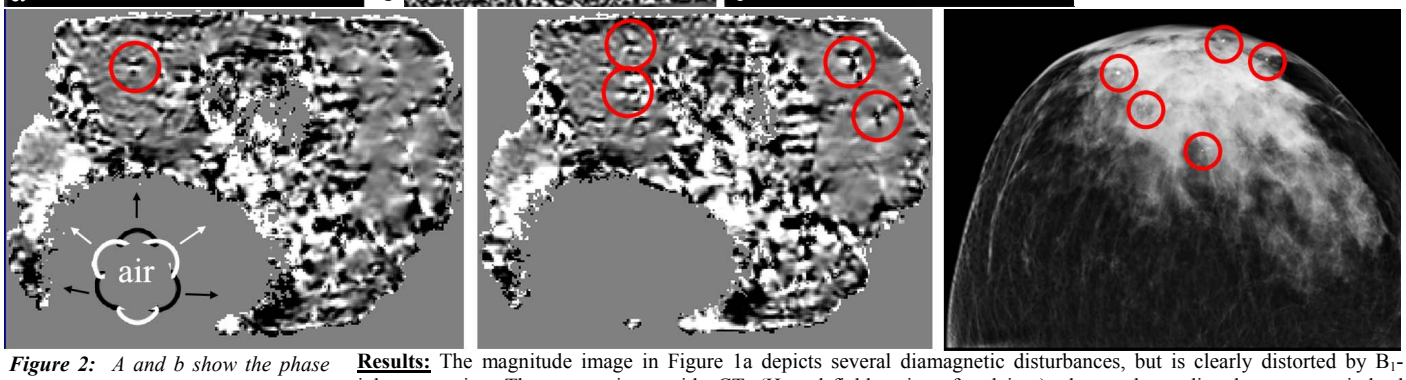

Figure 2: *A and b show the phase derivative at TE=27,6ms at two slices of the mastectomy specimen. Multiple calcifications are visualised (circles). The six-lobed pattern of the calcification is the same as in Figure 1b (insert), and negative of the pattern of air. The cranio-caudal mammogram (c) confirms the presence of calcifications (circles).*

Results: The magnitude image in Figure 1a depicts several diamagnetic disturbances, but is clearly distorted by B_1-inhomogeneity. The comparison with CT (Houndsfield units of calcium) shows these disturbances are indeed calcifications. The phase derivative image (Figure 1b) is not hampered by B_1-inhomogeneity and shows a high sensitivity for the calcifications. All calcifications, with particles down to a size of 3x1 voxels or smaller on CT, were detected. The calcifications exhibit the characteristic blooming pattern for a diamagnetic disturbance, which extends beyond the object-size [8]. The applicability of this technique ex-vivo is shown in Figure 2. The phase derivative image (Figure 2a, b) again shows characteristic blooming pattern calcifications (circles), the insert in Fig. 2a illustrates the six lobed pattern of a paramagnetic disturbance formed by the air balloon that is used to fixate the specimen. As for the phantom experiments, the mammogram of the breast (Figure 2c) clearly confirms the MR-detected calcifications (circles), with the smallest calcification measured to be of submillimeter size.

Discussion: Both the phantom and the ex-vivo experiment show the feasibility of detecting micro-calcifications on high-field MR. The magnitude images can be used to detect field disturbances, but cannot discriminate between calcium and, for example, a hemosiderin-rich blood clot. The magnitude images are furthermore severely hampered by B_1-inhomogeneities. The insensitivity to B_1-inhomogeneities of the phase derivative makes these images, together with the inherent high sensitivity for field disturbances, the method of choice especially at high magnetic field strengths. The phase derivative allowed characterization of the calcifications in the phantom and ex-vivo specimen. These successful attempts are a first step towards future in-vivo application. However, in-vivo measurements will be challenging because of field disturbances due to breathing and air in the lungs [9]. Before in-vivo application, such problems need to be addressed, for example by using the method of van Gelderen et al. and methods based here upon [10,11]. Both the phantom and ex-vivo experiment illustrate the very high sensitivity to small field disturbances, such as calcifications, at high field MRI. The increased SNR of 7T allows for ultra-high morphological imaging, which combined with contrast-enhancement and concurrent detection of micro-calcifications may improve the detection and evaluation of DCIS [6]. In conclusion, we have demonstrated the feasibility of detecting micro-calcifications with high-field MR, in a phantom and in an ex-vivo breast specimen.

References: [1] Leonard G.D. et al. J Natl Cancer Inst;96(12):906-920, 2004. [2] Allegra C.J. et al. J Natl Cancer Inst;102(3):161-169, 2010. [3] Holland R. et al. Semin Diagn Pathol;11(3):167-180, 1994. [4] Baker, R. et al. Brit J. Of Cancer;72(5):610-626, 2003. [5] Kuhl, C.K. et al. Lancet;370:485-492, 2007. [6] Korteweg, M.A. et al. Inv Rad 6:370-376, 2011. [7] Bakker C.J.G. et al. PMB; 53(18):N349–N358, 2008. [8] Reichenbach, J.R. et al. JMRI,7:266–279, 1997. [9] Peters, N.H.G.M. et al. JMRI; 29(3):731-735, 2009. [10] van Gelderen, P. et al. MRM;57(2): 362-368, 2007. [11] Boer, V.O. et al. MRM *in press*