Meta-Population Breast Cancer Screening with the ΔKtrans DCE-MRI Parameter

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Introduction: The new DCE-MRI pharmacokinetic parameter (ΔKtrans) shows remarkable breast cancer screening effectiveness (1-3). It results from analyzing a DCE-MRI data set twice, once with the Standard Model (SM) and once with the Shutter-Speed Model (SSM). ΔKtrans is defined as [Ktrans(MSM) - Ktrans(SMM)], where Ktrans is a contrast reagent (CR) extravasation rate constant. Thus, it appraises precisely the only SM/SSM difference - their treatments of inter- compartmental water exchange kinetics. The SM assumes the exchange kinetics are always effectively infinitely fast; all exchange MR systems remain in their fast-exchange-limit [FXL] conditions. The SSM admits these systems can transiently depart their FXLs during bolus CR passage through the tissue ROI or voxel (1,2). Since ΔKtrans seems a very sensitive vascular compromise measure, we tested its consistency across three disparate patient sub-populations at three different institutions.

Methods: The first sub-population [U. at Stony Brook (USB)] comprises 6 mammography-positive (M+) women (1 lesion each): DCE-MRI details have been reported (1,2,4). The challenging second cohort [Mem. Sloan Kettering Can. Cen. (MSKCC)] consists of 92 mammography-negative (M-) women. Since they are in the high-risk category (family history and/or BRCA1/2 mutations), they were also screened by clinical MRI and received positive diagnoses (95 lesions): DCE-MRI details are each for the first 16 (1,2) and the first 92 (3) have been reported. The third sub-population [Or. Health & Science U. (OHSU)] comprises 31 M+ women (36 lesions). In all, the meta-population comprises 137 suspicious lesions in 129 patients [8 presented 2 tumors each]. They were radiologically rated as probably malignant by a radiologist (n = 130) and referred for biopsies as standard care. The research DCE-MRI data were acquired prior to biopsies, and were analyzed with the FXR-a [fast-exchange-regime-adjusted] SSM version (1,2). The USB, MSKCC, and OHSU DCE-MRI data were acquired with Philips/Marconi (Picker) 1.5T, GE 1.5T, and Siemens 3T instruments, respectively. Different 3D DCE-MRI acquisitions (with similar exchange-sensitivities) were employed: conventional sagittal unidirectional gradient echo (GRE)/USB/MSSC) and axial bilateral TWIST (OHSU) sequences. The latter is a new k-space undersampling and data sharing GRE method (5), delivering near isotropic 1 mm voxels at 18.6(±0.9) frame rate.

Results: Figure 1 is a scatter-plot of lesion ROI ΔKtrans value [ordinate] vs. population or pathology [abscissa]. The 6 M+ USB results occupy the 1st column [malignant; t, total]. The 95 M- (but MRI-visible) MSKCC cohort points comprise the 2nd and 3rd columns. The 36 M+ OHSU cohort pathology types are indicated in the right columns. The meta-population entailed 312 malignant (M+) lesions (IDCs), 3 IDC/ductal carcinomas (ICMs), and 105 benign [12 atypcial ductal hyperplasias (ADHs), 10 lobular carcinomas in situ (LCIs), 1 atypical lobular hyperplasia (ALH), 1 tubular adenoma (TA), 24 fibrocystic changes (FCs), 17 fibroadenomas (FA), 11 benign parenchymas (BPs), 5 papillaries (PLs), 8 stromal fibres (SFs), and 16 others] tumors. If excisional biopsies followed core needle biopsies (CNBs) as standard care, the former pathology results were used to correlate with the MRI results. The ROI drawing and SM and SSM analyses were accomplished by pathology-blind investigators: the vertical (MRI) and horizontal (pathology) axes are independent.

Remarkably, the “training” binary classifier value obtained from the 6 USB and first 16 MSKCC lesions [2], [ROI-averaged] ΔKtrans = 0.028 min⁻¹ (solid horizontal line), separates all but 1 of the 105 benign lesions from all but 3 of the 32 malignant tumors in the meta-population: 19 of the 20 malignancies missed by mammography (screening background, scanner, Ktrans(MSM) or 1.5T) would move up further than the benign points, leading to increased separation. All malignant breast tumor Ktrans(MSM) or Ktrans(SSM) maps so far reported (2,3,4) show distinct hot spots; as small as 1 mm in diameter. It appears that transient FXL-departures (i.e., increased ΔKtrans) are often focal, and that these can be very diagnostic for breast malignancy. In somes ways, ΔKtrans mapping behaves as a form of in vivo histological analysis of tissue microvasculature, with a larger FOV. Though the ΔKtrans map scale (mm) is not as fine as that of histology (μm), the removal of tissue from the body is not required.

The remarkable independence from cohort screening background, scanner vendor (platform/software), acquisition, CR, and magnetic field strength is gratifying, and suggests SSM robustness. It also argues that the ΔKtrans subtraction minimizes/eliminates many other systematic DCE-MRI quantification errors (e.g., from Arterial Input Function (AIF) uncertainty: the same AIF is used for both analyses). SSM DCE-MRI can potentially reduce unnecessary benign breast biopsies and spare many ABL patients from not only CNB procedures but also subsequent unnecessary surgeries. The latter are usually more invasive, deforming, and costly.
