Application of prospective cardio-respiratory gating for simultaneous quantitative DCE-MRI of multiple mammary tumours in the mouse.

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Target audience: Preclinical DCE-MRI users and developers.
Purpose: To assess the feasibility of quantitative DCE-MRI of abdominal and thoracic tumours that are subject to cardio-respiratory motions.
Methods: DCE-MRI was performed at 4.7T (Varian, VNMRS) using a RF and gradient-spoiled 3D gradient echo sequence (T_E = 0.6 ms, T_R = 1.15 ms, α = 5 nominal), in conjunction with a prospective cardio-respiratory gating (CR-gating) technique and automatic and immediate reacquisition of data corrupted by respiratory motion. Erratic cardiac and respiratory cycle times lead to erratic scan frame durations so timestamps were created at the time of application of the k=0 phase encode steps. B_1 homogeneity correction was applied using a respiratory-gated implementation of the Actual Flip angle Imaging technique[1] and T_1 was measured by repeating scans with an array of nominal flip angles applied at the same constant T_R as for the DCE scan.
Balb neuT mice bearing multiple spontaneous breast tumours were anaesthetised (1-3% isoflurane in room air), placed supine in the RF coil, and their temperature was maintained using an MR-compatible resistive heater control system. Subcutaneously implanted needles and a pressure balloon were used for detection of ECG and respiratory signal, respectively. These signals were analysed on-the-fly using a customised trigger control system (based upon the Biopac MP 150 and DTU 200 units). Gd contrast agent (gadodiamide, 0.5 M, 30 µl over 5 s) was automatically infused into the lateral tail vein triggered at the start of scan 11/50. The MRI protocol, including animal handling, took ca. 30 minutes to complete per mouse and enabled a throughput of ca. 16 mice/day.
Pharmacokinetic modelling of DCE-MRI data on a pixel-by-pixel basis using the standard Tofts model with population averaged AIF[2] was performed and parametric DCE-MRI maps were generated.
Results: CR-induced motion more than doubled the noise level across the time course when experiments were run in the absence of CR-gating. Although CR gating increased scan time by a factor of 2-3, images were quantitative for T_1 (and ΔT_1). Gating led to sample-dependent scan times resulting from erratic breathing rates. The mean scan time, for a group of 40 consecutively scanned mice and 50 images was 671 ± 75 s (range 586-830 s) and demonstrated the need for timestamping of gated dynamic acquisitions for temporal alignment in dynamic analysis. Crucially, this volumetric imaging technique allowed the simultaneous assessment of multiple breast tumours as shown in Figure 1. In this mouse 7 tumour lobes were found in the MRI scan. The position of these tumours was such that motion induced ghosting would occur if CR-gating was not applied. Parametric analysis of the DCE-MRI data allowed classification of these thoracic breast tumours based on their perfusion characteristics. Representative K_{ep} maps, superimposed on a coronal projection image of a Balb neuT mouse, are shown in Figure 1.

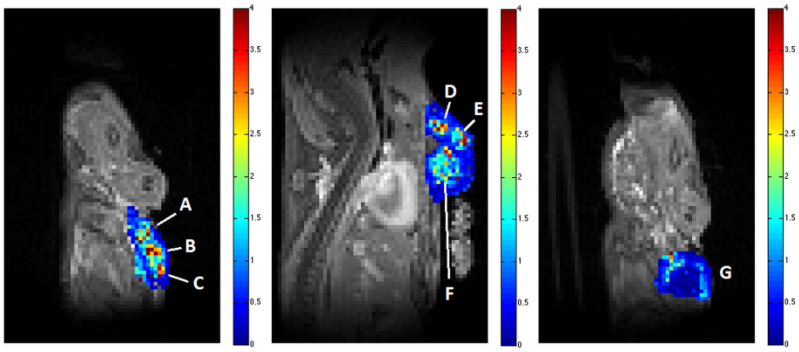

Figure 1: Coronal images of a representative Balb neuT mouse bearing multiple spontaneous breast tumours (A-G). K_{ep} maps of the tumours were superimposed onto the DCE-MRI image. Tumour 'G' showed significantly lower K_{ep} values as compared to the other tumours. The proximity of the tumours to heart and lung necessitated CR-gating and avoided motion induced ghosting.

Discussion: Volumetric and quantitative T_1 weighting was achieved through synchronisation with the CR cycles, maintenance of the steady state MR signal throughout the scan and calibration of the RF pulse transmission field. The timestamps allowed correct temporal sampling so that the unequal spacing of the images over time could be accounted for. Moreover, volume imaging permitted visualisation of multiple breast tumours in the chest during the same acquisition, avoiding operator dependent slice pre-selection errors and thus making full use of this non-invasive imaging method. Parametric DCE-MRI maps of each tumour could be generated allowing quantitative analysis of perfusion of tumours that are sensitive to motion artefacts.
Conclusion: Quantitative DCE-MRI of abdominal and thoracic tumours was made possible through the use of CR synchronisation techniques in conjunction with RF calibrations and accurate temporal sampling. As a result, multiple chest tumours which are highly susceptible to motion corruption during DCE-MRI protocols could be screened simultaneously and classified using quantitative DCE-MRI parameters in a manner that is compatible with high-throughput operation.

References:
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2. Heilmann M, Walczak C, Vautier J et al. Simultaneous dynamic T_1 and T_2* measurement for AIF assessment combined with DCE MRI in a mouse tumor model. MAGMA. 2007;20(4):193-203.