Hybrid Reference Tissue Calibrated Dual-Bolus 3D Quantitative Dynamic Contrast-Enhanced MRI in a Rabbit VX2 Tumor Model

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Introduction: Dynamic contrast-enhanced (DCE) MRI can be used to quantitatively measure pharmacokinetic parameters that indicate tumor angiogenesis and perfusion. The ability of quantitative DCE-MRI to generate physiological parameter maps has important implications in staging tumors and in evaluating the cancer therapeutic response. The purpose of this study was to develop an innovative hybrid reference tissue calibrated dual-bolus 3D quantitative DCE-MRI method.

Methods: In this study, we implanted six VX2 tumors total in the uteri of six rabbits [1]. 3 weeks after implantation, rabbits were imaged using a 1.5T clinical MRI scanner (Siemens Magnetom Sonata) with a dual-bolus DCE-MRI approach [2]. Before dynamic scan, an *in vivo* 3D B_1 map was generated using the double-angle method, and a baseline 3D R_{10} map was acquired using the variable flip-angle (FA) GRE method. We performed 3D dynamic GRE MRI to record the tissue enhancement over time after the first IV bolus injection of 0.04125 mmol/kg Gd-DTPA contrast agent. 10 minutes later, we used a 2D dynamic saturation recovery (SR) GRE sequence to characterize the shape of arterial input function (AIF) in the aorta after the second IV bolus injection of 0.005 mmol/kg Gd-DTPA, assuming a linear relationship between signal intensity and contrast agent concentration (Fig 1a). Imaging parameters included: 200 mm FOV; **3D GRE**: TR/TE = 6/1.66 ms, 128×72×8 matrix, baseline FA = 2°, 9°, 19°, 4 averages; dynamic FA = 9°, 1.6 sec sampling rate; **2D SR GRE**: TR/TE/TI = 3.2/1.2/47 ms, 128×64 matrix, FA = 15°, 0.4 sec sampling rate. With B_1 calibration and a baseline R_{10} map, 3D R_1 map time series and further contrast concentration map series were derived from the 3D DCE-MR image series [3]. The extended Tofts model was used for perfusion analysis, generating K^{trans} (volume transfer coefficient, min^{-1}), v_e (fractional volume occupied by extracellular extravascular space), and v_p (fractional volume of plasma space) parameter maps [4]. A lookup method was used to estimate the delay time during curve fitting (Fig 1b) [5]. Region of interest (ROI) analysis was used to compare the tumor hypervascular region, tumor core, and back muscle regions on the parameter maps for all six animals (Fig 2). Literature reference and measured v_e ratios from the back muscle were used to construct the final calibration for overall measurements [6].

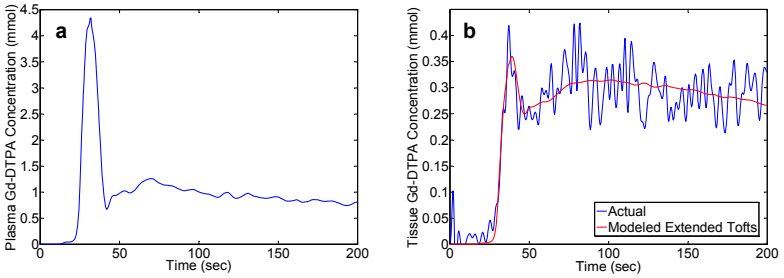


Fig 1. (a) Representative arterial input function. (b) Representative tissue concentration curves. Recorded signal in blue; extended Tofts model in red.

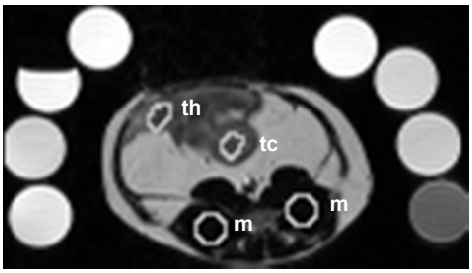
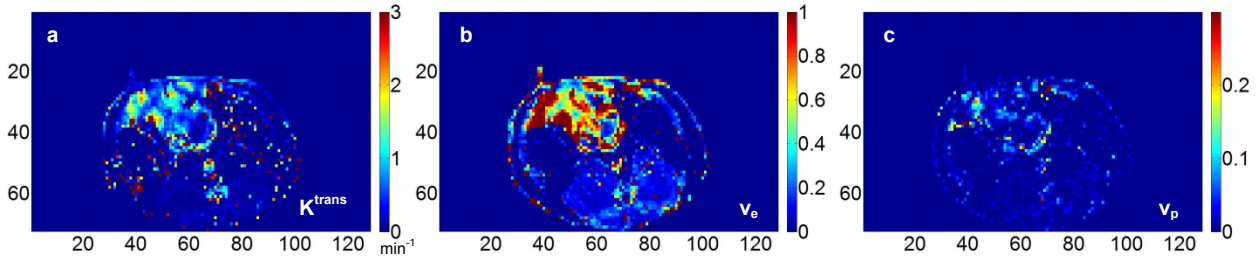


Fig 2. T2-weighted anatomical image with ROIs: th – tumor hypervascular region; tc – tumor core; m – back muscle.

Results: Parameter maps for K^{trans}, v_e, and v_p were generated using the extended Tofts model (Figs 3a to 3c). Significant differences were found between the tumor hypervascular region and the other two ROIs for K^{trans} ($p < 0.001$) 0.67±0.32 (mean ± std) to 0.066±0.043 and 0.070±0.027 and v_p ($p < 0.01$) 0.072±0.060 to 0.0049±0.0051 and 0.0079±0.0018. Significant differences in v_e values ($p < 0.001$) were found between the tumor hypervascular region 0.79±0.077, tumor core 0.33±0.18, and back muscle 0.10±0.042.



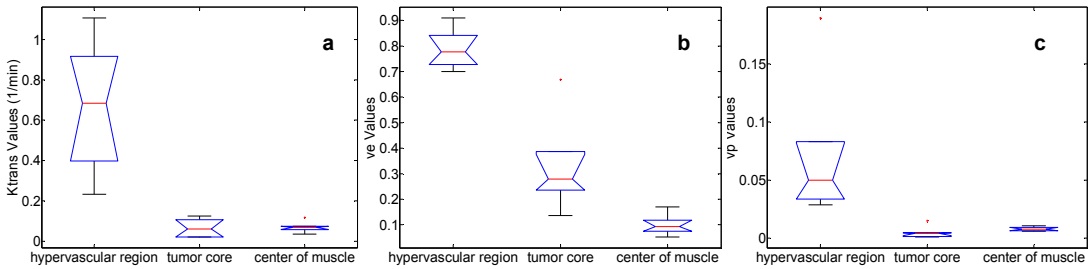


Fig 3 (top). Representative parameter maps: (a) K^{trans} map, (b) v_e map, and (c) v_p map.

Fig 4 (left). Box plots of (a) K^{trans} values, (b) v_e values, and (c) v_p values from ROIs.

Conclusions: A novel hybrid reference tissue calibrated dual-bolus 3D quantitative DCE-MRI technique was developed. Our results support the use of this quantitative DCE-MRI technique to differentiate hypervascular tumor tissue from the necrotic core, providing valuable diagnostic information about the stage and segmentation of a tumor.

References: [1] Rhee et al., JVIR 2007;18:411-418 [2] Christian, Radiology 2004;232:677-684 [3] Wang et al., MRM 2008;60:970–975 [4] Tofts et al., JMRI 1999;10:223-232 [5] Cheng, JMRI 2008;28:736-743 [6] Yankeelov et al., MRI 2005;23:519-529