

DIVA+QUADRANT: novel visualisation software for DCE-MRI to aid breast cancer diagnosis and neoadjuvant chemotherapy monitoring

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Introduction: The clinical utility of dynamic contrast-enhanced MRI (DCE-MRI) is well established, but the analysis of data by radiologists can be time-consuming. Novel visualisation software, called DIVA+QUADRANT, has been developed which quickly and clearly indicates those regions within a tumour which display the highest contrast agent enhancement (uptake) rate and the greatest degree of contrast agent wash out (signal decay); both well-established indicators of malignancy following the BIRADS-MRI lexicon [1, 2]. The software can also be used to monitor response to chemotherapy as it can map out areas where enhancement and washout rates have decreased, i.e. areas where vasculature shutdown is occurring.

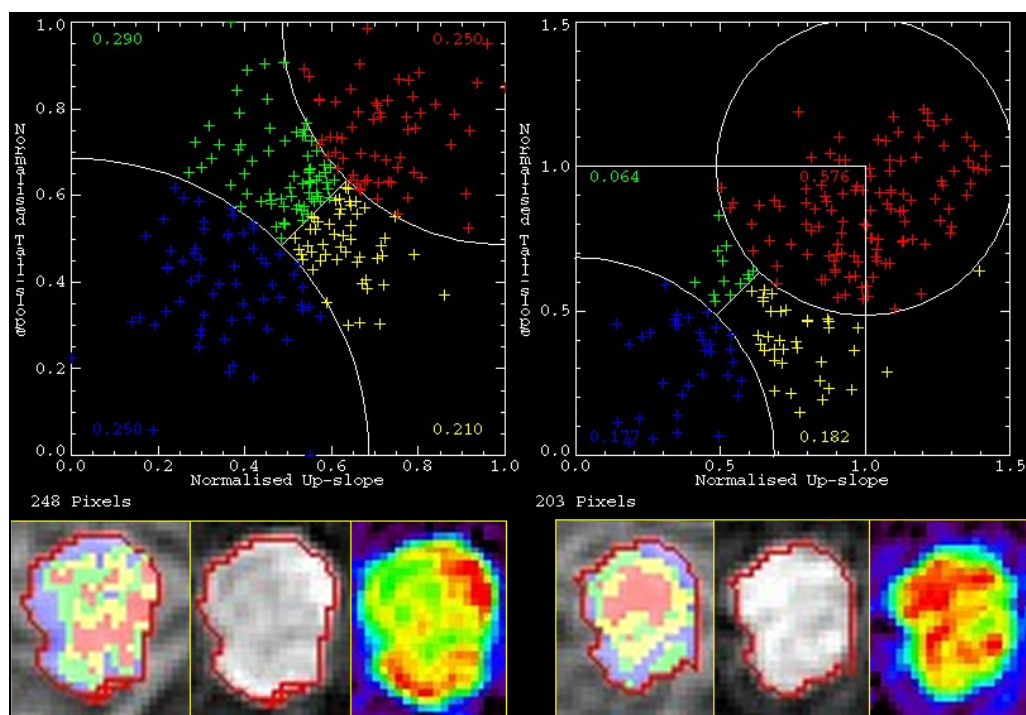
Methods: The QUADRANT image analysis algorithm works by measuring the contrast agent uptake rate (or up-slope, US) and wash-out rate (tail-slope, TS) for all pixels within a given tumour region of interest (ROI) using linear regression over two and four points respectively. The maximum and minimum uptake rates within the ROI are then used to normalise all of the uptake and wash-out rates to values lying between 0 and 1 using the following equations: Normalised uptake rate = $US' = [US - US(\min)] / [US(\max) - US(\min)]$; Normalised wash-out rate = $TS' = [TS - TS(\max)] / [TS(\min) - TS(\max)]$. When US equals US(min), US' equals 0; and when US equals US(max), US' equals 1. Also when TS equals TS(max), its most positive, TS' equals 0; and when TS equals TS(min), its most negative, TS' equals 1. Radii from (0,0) and (1,1) are then chosen which define quadrants (hence the algorithm's name) which encompass 25% of pixels each; pixels which are coded blue (most benign) and red (most malignant) respectively. The remaining 50% of pixels are separated using the line of identity ($y=x$) with those below and above the line being coded as yellow (more suspicious) and lime green (less suspicious) respectively.

The software was developed using IDL (ittvis.com) and tested using benign and malignant breast tumours imaged at 3.0 and 1.5 T using GE Signas (GE Medical Systems). One illustrative case of a locally advanced breast cancer imaged at 3.0 T prior to chemotherapy and shortly after the first course of chemotherapy using a sagittal, 3D, fast gradient-echo sequence (VIBRANT), is presented here. Twelve time-points from 144, two-mm thick slices were acquired on both occasions with a (delay) time between successive data points of 32.94 s. Field-of-view, matrix, TR and TE were 22 cm, 220x160, 4.06 ms and 1.60 ms fractional. The tumour was also imaged at 1.5 T after the eighth and final course in order to determine its final size before surgery.

Results: The graphic shows data from before and after course one on the left and right respectively. The QUADRANT grids are shown (top) where data have been normalised using the maximum and minimum slopes within the pre-treatment ROI. QUADRANT colour overlays are shown (bottom left) with parametric maps of the integral under the enhancement curve for comparison (greyscale bottom middle, colour bottom right). Both types of map display lesion heterogeneity, but with distinct patterns.

The pre-treatment ROI contains 248 pixels (1.83 cm²) of which 62 (25%) are red and it has a maximum diameter of 19 mm. The post-treatment ROI contains 203 pixels (1.50 cm²) and has a maximum diameter of 15 mm. The diameter has, therefore, reduced to 79% which would give an approximate volume ratio of 49% (79% cubed). The ROI area has reduced to 82% and it now contains 117 (58%) red pixels which represents a sharp increase in red pixel area to 189%.

The tumour went on to respond well to treatment, and had a maximum diameter of only 7 mm after the final



(fourth) course of chemotherapy. This represents a reduction in diameter to only 37% with an approximate volume ratio of only 5% (37% cubed); both indicative of "partial response" using the RECIST criteria [3]. That an ultimately partially responding tumour should enhance and wash out more rapidly (being indicative of increased vascularity) after one course of chemotherapy is counter-intuitive, but such an observation has been published before [4].

Conclusion: An algorithm (QUADRANT) has been developed which can accurately guide the radiologist to the regions within a tumour which demonstrate the most rapid contrast agent uptake and wash out, i.e. those regions which exhibit the most malignant-like characteristics, as defined by the BIRADS-MRI lexicon; something which should save time. The algorithm may also be useful in monitoring response to chemotherapy where a decreased red pixel volume could be used as a surrogate for vascular response. The algorithm will continue to be improved in a number of ways including multi-slice analysis and semi-automated maximum diameter determination. It is also intended to apply the algorithm to a retrospective data-set of chemotherapy cases imaged at 1.5 T in order to compare the predictive power of QUADRANT data, in terms of separating cases into those which will respond well and those which will not, to that of traditional pharmacokinetic and empirical (non-parametric, or model-free) variables [5].

References: [1] BI-RADS®-MRI, First Edition, American College of Radiology (ACR), Reston, VA, USA, 2003. [2] B. Erguvan-Dovan, *et al. AJR* 187, W152-W160 2006. [3] Therasse P, *et al. J. Nat. Cancer Inst.* 92: 205-216 2000. [4] M.D. Pickles, Doctoral Thesis, The University of Hull, UK, 2006. [5] M.D. Pickles, *et al. Breast Cancer Research and Treatment* 91(1) 1-10 2005.