Assumed AIFs in DCE-MRI: Which performs best for assessing breast cancer response?

David K Woolf[1], N. Jane Taylor[2], Nina Tunariu[3], Andreas Makris[1], Sonia P Li[1], Mei-Lin W Ah-See[1], Mark J Beresford[4], J. James Stirling[2], James A d'Arcy[3], David J Collins[3], and Anwar R Padhani[2]

[1]Academic Department of Oncology, Mount Vernon Hospital, Northwood, Middlesex, United Kingdom, [2]Paul Strickland Scanner Centre, Mount Vernon Hospital, Northwood, Middlesex, United Kingdom, [3]CR-UK-EPSRC Cancer Imaging Centre, Institute of Cancer Research & Royal Marsden Hospital, Sutton, Surrey, United Kingdom, [4]Royal United Hospital Bath, Bath, United Kingdom

Introduction: Dynamic Contrast-Enhanced MRI (DCE-MRI) has an established role for predicting response after 1-2 cycles of neoadjuvant chemotherapy (NAC) given for locally advanced breast cancer. Quantitative changes in transfer constant (K^{trans}) predict clinical and pathological response as well as disease-free and overall survival. To use quantitative DCE-MRI, the arterial input function (AIF) needs to be defined. There are different methods to define the AIF including invasive direct arterial sampling, measuring the AIF within vessels near tumours, normal tissue sampling combined with knowledge of leakage space to back-calculate the AIF[5]. The simplest, most popular method uses population based AIFs. There are a number of population AIFs in current use including data reported by Weinmann[1] (W), Fritz-Hansen et al[2] (FH), a Modified Fritz-Hansen[3] (MFH), Parker[4] (P), Cosine-Plasma[5] (CP) and Femoral Artery[6] (FA). However, there is little comparative data regarding the ability of these AIFs to produce physiological meaningful results, for model fitting to patient data, and their ability to yield clinically meaningful data in terms of test performance. We aimed to compare these six AIFs to see which performed best in the setting of NAC for breast cancer.

Materials and Methods: MRI was performed with a 1.5T Siemens Symphony scanner (Erlangen, Germany) using a bilateral breast coil. Sagittal proton density-weighted (PDw) GRE images were acquired followed by 40 matched sets of dynamic T1-weighted (T1w) images, 1 set every 12 seconds for a total imaging time of 8 minutes. 0.1mmol/kg Gd-DTPA (Magnevist: Bayer-Schering, Newbury, UK) was injected intravenously using a power injector. The PDw and T1w dynamic series of images were analyzed using MR Imaging Workbench software (v4.3; Institute of Cancer Research, London, UK). Quantitative DCE-MRI analysis was performed using the standard Tofts' model employing the AIFs above. Quantitative parameters including median transfer constant (K^{trans}, min^{-1}) values were calculated for each voxel within tumour ROIs.

Voxels which failed to fit were counted and classified, and removed from further analysis. Causes for fit failures were noted (including v_e value of ≥90% (not physiologically realistic) and non-enhancing voxels). Changes (%) in median values were calculated after two cycles of NAC. Pathological complete response (pCR) rates at the end of chemotherapy formed the standard of reference.

The reproducibility of the technique was calculated (n=12). The number of pCR and non-responders (NR) correctly assigned using r% were calculated and receiver operating characteristic (ROC) curves was used to assess test performance of each AIF with respect to predict pCR.

Results: The table shows reproducibility (wCV, r%), mean K^{trans} values and fit fails before and after 2 cycles of NAC, and ROC determined test performance for predicting eventual pCR for each AIF evaluated.

AIF	K^{trans} baseline	K^{trans} post chemo	% change in K^{trans} mean	pre NAC fit fails %	post fit fails %	wCV (%)	r (% mean)	Pathological CR correctly predicted	Non responder correctly predicted	ROC area	Sensitivity (%)	Specificity (%)
W	1.068	0.342	-54.6	8.1	18	28	-49.7	6/8	7/19	0.70	75	37
P	0.130	0.070	-41.6	5.8	25.7	12	-33.0	7/8	8/19	0.73	87.5	42
MFH	0.241	0.117	-45.0	3.6	18.8	14	-39.2	7/8	9/19	0.74	87.5	47
FH	0.333	0.175	-42.1	12.2	26.7	16	-33.6	7/8	9/19	0.73	87.5	47
FA	0.170	0.095	-40.7	19.4	43.3	18	-37.3	6/8	8/19	0.69	75	42
CP	0.115	0.066	-38.5	9.4	29.5	12	-27.8	7/8	8/19	0.72	87.5	42

All models were more successful in fitting data pre-chemotherapy (lower % fit failures). Most fit failures were caused by v_e values >90%, with the majority of the rest attributable to failure of enhancement. The greatest absolute values and spread of K^{trans} are noted for the Weinmann AIF, which also showed the largest reductions after chemotherapy (-54.6%). The other AIFs show a broadly similar range of K^{trans} reductions (-38.5 to -45%). Reproducibility was worst for Weinmann AIF. Using the K^{trans} reproducibility data (r%) to assess the ability of different AIFs to predict pCR, showed that test performance was broadly similar, with the MFH AIF approaching statistical significance ($p = 0.056$) using ROC methodology.

Discussion

Our analysis addressed the question of the best performing AIF using three analysis approaches: the ability of the AIF model to minimize the number of 'fit fails', to produce physiologically plausible results and their ability to predict pathological response to chemotherapy in breast cancer patients. It is notable that all AIFs perform less well in model fitting after chemotherapy. The worst performing AIF was the Femoral Artery function. The ability to judge which AIFs produces the most physiologically valid data is impaired by the lack of a solid standard of reference. The modified Fritz-Hansen AIF seems to perform best for assessing response to NAC. However other AIFs also performed reasonably well but the Weinmann and Femoral artery AIFs performed less well. On the basis of these results, we recommend that the Modified Fritz-Hansen AIF be used for assessing response of breast cancer to NAC. Femoral Artery & Weinmann AIFs should not be used for breast examinations because of excessive fit failures and poorer reproducibility respectively. It is uncertain how these results would compare with patient-specific AIF derivations.

References

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