Comparison of MRI tumour diameter and volume changes with apparent diffusion coefficient (ADC) values in prediction of pathological response following neoadjuvant chemotherapy (NACT)

Sara Vigano[1,2], Andrew J. Patterson[3], Mary McLean[4], Elena Provenzano[5], Louise Hiller[6], Janet Dunn[6], Anne-Laure Vallier[7], Louise Grybowicz[7], Reem Bedair[8], Matthew G Wallis[9], Martin J Graves[10], Helena Earl[11], and Fiona J Gilbert[8]

[1]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [2]Universita' degli Studi di Milano, Milano, Italy, [3]Radiology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [4]CRUK Cambridge Institute, University of Cambridge, United Kingdom, [5]Department of Histopathology and Cambridge Breast Unit, Cambridge University Hospital NHS Foundation Trust and NIHR Cambridge Biomedical Research Centre, United Kingdom, [6]Warwick Clinical Trials Unit, University of Warwick, Coventry, United Kingdom, [7]Department of Oncology, Cambridge Cancer Trials Centre, Cambridge Breast Unit, Cambridge University Hospitals NHS Foundation Trust, United Kingdom, [8]Radiology, University of Cambridge, Cambridge, United Kingdom, [9]Cambridge Breast Unit and NIHR Biomedical Research centre, Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom, [10]Radiology, Cambridge University Hospital NHS Foundation Trust and NIHR Cambridge Biomedical Research Centre, United Kingdom, [11]Department of Oncology, NIHR Cambridge Biomedical Research Centre and Cambridge Breast Unit, University of Cambridge, Cambridge, United Kingdom

TARGET AUDIENCE: MRI Scientists and Clinicians with an interest in breast cancer and monitoring chemotherapy

PURPOSE: Neoadjuvant chemotherapy (NACT) allows for less extensive surgery in breast cancer patients. Non-invasive imaging techniques can be used to monitor and predict response to treatment. MRI is an established tool for assessing response [1] and functional parameters such as ADC have been suggested as a biomarker of response. [2,3] However, response is typically evaluated using the defined RECIST criteria by measuring changes in the maximum diameter of the tumour. The aim of this study is to prospectively assess whether MR derived volume and diameter assessment or quantitative ADC values can predict pathological response in breast cancer patients receiving NACT.

METHODS: The study was approved by an Ethics Committee and patients with breast cancer scheduled for NACT gave informed consent before recruitment. Dynamic contrast enhanced (DCE) images and diffusion-weighted echo-planar images (DWI) were acquired using a 1.5T whole body scanner (MR450, GE Healthcare, Waukesha, WI) using an 8 channel breast array. Patients were imaged pre-NACT, and after 3 and 6 cycles of treatment. Maximum tumour diameter, total tumour volume and ADC were measured blinded to the pathological outcome. The maximum diameter was measured in three orthogonal planes on DCE images and the longest dimension was used regardless of orientation. Tumour volume was measured on DCE images by manually defining regions of interest on each appropriate slice. ADC maps were calculated from diffusion-weighted echo-planar images (b= 0, 700 s/mm^2). Histology assessment with grading of response was performed following treatment by surgical excision of the tumour site. Specimens were characterised into group 1 (pathological complete response or minimal residual disease) or group 2 (partial response or no response). The interaction between pathological response (group 1 versus group 2) and change in each respective metric over time was modelled using a MANOVA test. The study tested two hypotheses: 1. whether the initial rate of change in each metric between baseline and mid-treatment varied between patients who went on to exhibit a complete pathological response and patients who didn't, 2. whether change between baseline and end-of-treatment varied using the same analysis.

RESULTS: Eighty-two patients were recruited and forty-five of those entered the analysis (mean age 47±9.8 years, range 26-71). Of these, 32 (71%) had an invasive ductal cancer (IDC), 8 (18%) an invasive lobular (ILC), 1 mixed IDC and ILC, and 4 others (1 papillary, 1 mucinous, 1 microinvasive and 1 metaplastic). At baseline 71% had unifocal disease and 29% had multifocal/multicentric disease. The grade of pathological response on the excision specimen were 6 complete response, 10 partial response with minimal residual disease, 28 partial response and 1 no response. At mid-treatment, a statistically significant difference was found between responders (Group 1) and non-responders (Group 2) in ADC ($p<0.001$). However, tumour volume and diameter changes were not significantly different between the two groups. There was a statistically significant difference between responders and non-responders in ADC ($p<0.001$) and gross tumour volume ($p=0.007$) by the end of the study; maximum tumour diameter was borderline significant ($p=0.05$). (Fig. 1)

DISCUSSION: As expected tumour volume and diameter changed over the course of treatment. ADC values also changed and the difference in the change in those patients who went on to have a good pathological response was statistically significant. All three parameters, particularly enhancing tumour volume and ADC, may represent good parameters to monitor NACT response, but only change in ADC was strongly predictive of pathological outcome by mid-treatment. Therefore, ADC values may represent a more sensitive method of predicting pathological outcome.

CONCLUSION: ADC and tumour volume changes can be used to monitor NACT response. ADC changes in combination with other multi-factorial information may have utility in determining the optimal treatment strategy.

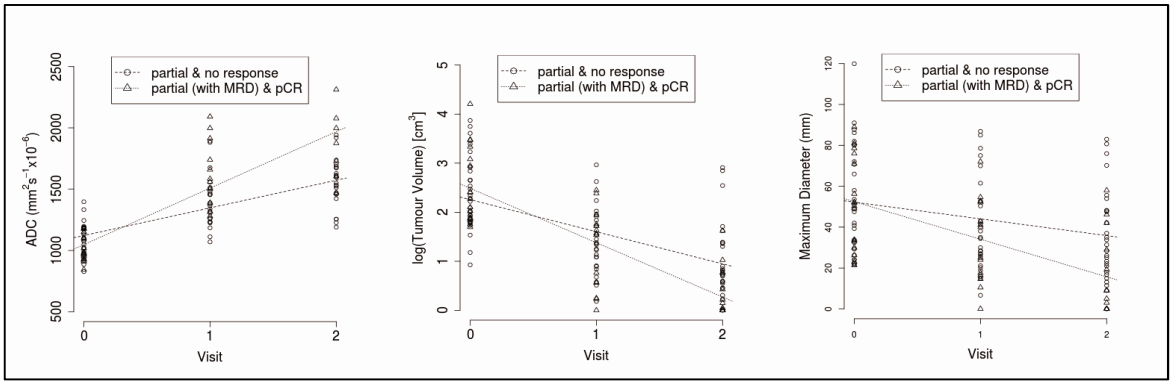

FIGURE 1: ADC (left), the log of tumour volume (middle) and maximal tumour diameter (right) at baseline and following 3 and 6 cycles of NACT. Fits are shown separately for responders (solid line) and non-responders (dotted line).

REFERENCES

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