Do DCE-MRI parameters obtained during neoadjuvant chemotherapy provide an insight into long term survival?

M. D. Pickles[1], D. J. Manton[1], M. Lowry[1], and L. W. Turnbull[1]
[1]Centre for Magnetic Resonance Investigations, University of Hull, Hull, East Yorkshire, United Kingdom

Introduction.

DCE-MRI parameters have been utilised by a number of groups in an attempt to predict an individual's response to radiotherapy and chemotherapy. In a number of cases these parameters have demonstrated differences between eventual responders and non-responders prior to and early during treatment. However, all of these results are concerned with short-term treatment response and not longer term survival. The same underlining pathophysiology that allows vascular kinetic data to differentiate eventual treatment response may provide an insight into disease free survival (DFS). The aim of this study was firstly to test the hypothesis that DCE-MRI data obtained prior to and early during initial neoadjuvant chemotherapy can predict DFS in breast cancer patients and secondly, to compare the results to traditional survival indicators obtained prior to and following treatment.

Methods.

Pharmacokinetic modelled and empirical DCE-MRI parameters were obtained in 68 patients prior to and early during (post 2^{nd} or 3^{rd} cycle) neoadjuvant chemotherapy. Pharmacokinetic parameters were derived from an open two compartment model resulting in 3 parameters, while empirical analysis provided 9 parameters In addition the difference, absolute (Δ) and relative (%), between the two time-points were also analysed. For all DCE-MRI parameters ≤median values were compared to >median for statistical analysis of survival. Pre treatment biopsy samples provided the following traditional survival indicators: oestrogen receptor (ER) status (negative or positive), progesterone (PR) status (negative or positive), tumour type (special type or no special type) and grade (I and II or III), while surgical specimens provided final grade (I and II or III), final type (special type or no special type) and nodal status (negative or positive). MRI data provided tumour size comparisons (≤median vs. >median). Kaplan-Meier survival plots were generated for each parameter, treatment failure (critical event) was defined as tumour remission and/or metastasis, whilst data from patients without treatment failure were treated as censored. Patient status, critical or censored, was determined by reviewing patient notes. Group comparisons were made utilising logrank tests, $p < 0.05$ was taken to represent significant differences in DFS intervals.

Results.

14 patients were lost to follow-up. 19 patients suffered a treatment failure and 35 patients were censored. The median follow-up time for patients with recurrence was 453 days, range 147 to 1414 days, while for censored patients median follow-up time was 1277 days, range 756 to 2014 days. Table I presents those parameters demonstrating a significant difference in DFS interval, note that no pharmacokinetic parameter reached a significant level. Kaplan-Meier survival plots for the most predictive DCE-MRI and traditional histology based parameters are illustrated in Figure I.

Parameter	Source	p-value
Pre volume	MRI	0.0023
$\Delta_{(pre\text{-}early)}$ volume	MRI	0.0211
Pre initial slope	Empirical	0.0088
Pre $EF_{(@30sec)}$	Empirical	0.0088
Pre AUC	Empirical	0.0097
$\Delta_{(pre\text{-}early)}$ $PC_{(@30sec)}$	Empirical	0.0379
Pre nMITR	Empirical	0.0432
$\%_{(pre\text{-}early)}$ $PC_{(@30sec)}$	Empirical	0.0449
PR	Biopsy	0.0207
Final grade	Surgical	0.0029
Nodes	Surgical	0.0229

Table I.

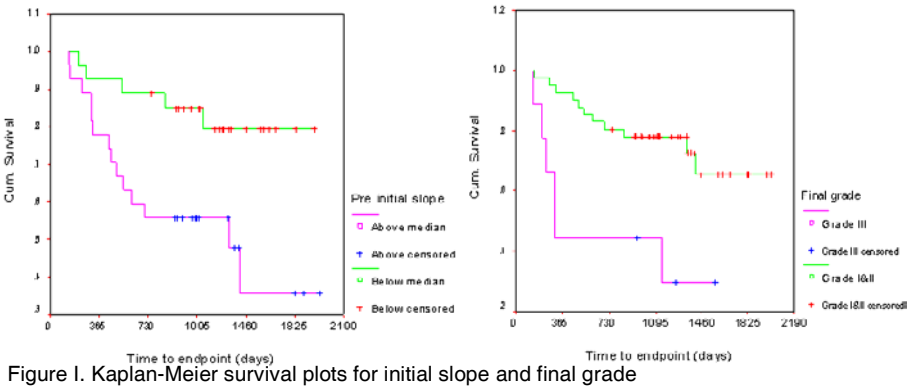

Figure I. Kaplan-Meier survival plots for initial slope and final grade

Conclusion.

These results indicate that while pharmacokinetic-modelled DCE-MRI parameters did not provide a significant insight into DFS, empirical analysis of DCE-MRI data did. Indeed empirical analysis out-preformed the more traditional survival indicators obtained from pre treatment biopsy samples. However, following treatment histological data from surgical specimens, final grade (I and II vs. III), provided a superior indication of DFS. Nevertheless the parameter that demonstrated the greatest difference in DFS interval was pre treatment MR derived tumour volume measurements (≤median vs. >median). In summary, while the underlining pathophysiology as described by empirical analysis of DCE-MRI data does contain some important DFS information both pre treatment tumour volume measurements and post treatment surgical histopathology provides a superior indication of DFS.