Changes in Dynamic Contrast-Enhanced MRI Pharmacokinetic Parameters pre- and post-Radiotherapy in Cervical Carcinoma

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Introduction

Evidence suggests that the success of radiotherapy (RT) depends on the degree of tumour oxygenation[1]. Use of dynamic contrast-enhanced MRI (DCE-MRI) can reflect oxygenation levels in tumours non-invasively[1] and an appropriate pharmacokinetic model can be fitted to DCE-MRI data to obtain parameters such as the amplitude (A) and rate (k_{ep}) of contrast agent uptake. DCE-MRI was performed in 10 patients with carcinoma of the cervix pre- and post-external beam RT. Currently patients undergo a post-RT scan shortly after completion of external beam RT and patient management choices are often made on the results of this scan. Changes in pharmacokinetic parameters related to perfusion may influence tumour response[2] giving additional information which could improve patient management.

Method

DCE-MRI studies were performed as previously described[1,3] - 1.0 T Siemens Magnetom, T1-w gradient echo sequence (TR = 130ms; TE=6.5ms; flip angle = 70°), administration of 0.1mmol/kg Gd-DTPA as fast bolus injection and use of body and phased array pelvic coils. Studies were performed on 10 patients before RT and following 40-45 Gy of external beam RT given in 20 fractions over 28 days. The second MR scan was performed on average 4 days after completion of RT (range = 1 to 10 days). Regions of interest (ROI) containing the whole tumour were outlined and tumour volume was calculated. A simplified Brix model[4] was fitted to the contrast agent uptake curves and the parameters A and k_{ep} derived pixel-by-pixel. Median A and k_{ep} values were calculated along with the skewness and kurtosis of the distributions of A and k_{ep} over the whole tumour. Histogram plots showing the distribution of A and k_{ep} pre- and post-RT were produced. The percentage change in median values was calculated and correlated with clinical outcome.

Results

All tumour volumes decreased following RT from a mean of 68cm^3 to 14cm^3 (P=0.007) with no consistent change in median k_{ep}. There was an inverse correlation between the percentage decrease in tumour volume and the percentage change in median k_{ep} (r=-0.67, P=0.036). Patients were divided into 2 groups – recurrent (n=4) and non-recurrent (n=6) in a mean follow-up time of 33 months. Non-recurrent patients had a decrease in median k_{ep} (2.3 *vs* 2.1 min^{-1}) while recurrent patients had an increase in median k_{ep} (1.9 *vs* 2.9 min^{-1}). Similar results were obtained when analysing values of A.

Discussion

These findings suggest a large decrease in tumour volume following RT may be associated with a small change in k_{ep} and together a good long-term response to RT. Patients with smaller reductions in tumour volume had an increase in k_{ep} and a poor long-term prognosis. Fig. 1 shows the distribution of median k_{ep} values over the ROI for a patient in a) the non-recurrent and b) the recurrent patient groups. The histogram for a patient in the non-recurrent group shows little change in shape and is accompanied by a negligible change in median k_{ep} following RT. The histogram for a patient in the recurrent group shows a shift in k_{ep} values to the right and this is accompanied by a large increase in median k_{ep} following RT. Pre-RT values of skewness were approximately 50 for both patient groups, suggesting that the pre-RT distribution of k_{ep} values does not determine outcome. Post-RT this had dropped to 20 and 35 for recurrent and non-recurrent patients respectively. Kurtosis was approximately 4,000 pre-RT for both patient groups and had dropped to 600 and 2,000 for non-recurrent and recurrent patients respectively. The distribution of k_{ep} values has become less peaked for the recurrent group and there are more high values of k_{ep} in the tumour. Again this seems to suggest that overall exchange has increased and the associated prognosis is poor.

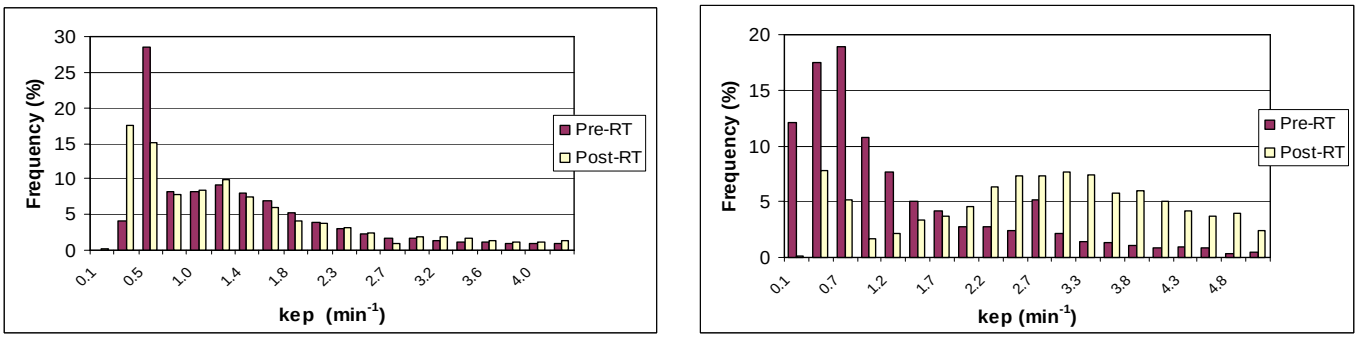

Fig 1: Histograms showing distribution of k_{ep} pre- and post-RT for 2 patients:

a) Patient with the largest tumour volume decrease (91%); median k_{ep} was 1.3 min^{-1} both pre- and post-RT. This patient had experienced no recurrence of the disease at the time of analysis (29 months).

b) Patient with the smallest volume decrease (45%); median k_{ep} was 1.3 min^{-1} pre-RT and 3.1 min^{-1} post-RT. This patient had local recurrence at 6 months post-RT.

Conclusions

Changes in k_{ep} values may have potential in determining the prognosis of patients undergoing RT. If post-RT scans are performed shortly after completion of RT individual treatment regimens could be altered depending on changes in pharmacokinetic parameters.

References

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