THE RESPONSE TO CHEMOTHERAPY OF MESOTHELIOMA TUMOURS AS ASSESSED BY DYNAMIC CONTRAST-ENHANCED MRI: FIRST IMPRESSIONS

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Target audience

This abstract is aimed at physicists and clinicians researching DCE-MRI and pharmacokinetic modeling techniques especially those with a particular interest in mesothelioma and other lung tumours.

Purpose

This was a pilot project aiming to assess the role of DCE MRI in determining early treatment response in patients with mesothelioma in correlation with the current gold standard: modified RECIST CT criteria. This study used a compact bolus of contrast agent and the 'extended Tofts model'[1] for analysis (yielding K^{trans}, v_e and v_p), as opposed to the prolonged bolus and non-standard analysis technique of previously published papers describing DCE-MRI investigations of this cancer [2,3].

Methods

The study was approved by the local regional ethics committee. To date, 13 patients have been recruited each having given informed written consent. Where there was long enough survival, each subject received three MR examinations, one before treatment, and then following 3 and 6 cycles of pemetrexed based chemotherapy treatment. At each examination, a main bolus of 0.1 mmol/kg of 1M gadobutrol contrast agent (Gadovist, Bayer-Schering Pharma AG, Berlin, Germany) was administered by power injector (Spectris Solaris, Medrad, PA) at a rate of 3 ml/s.

The dynamic series (see Fig 1b) was acquired on a 1.5T system (Avanto, Siemens) using an axial 3D spoiled gradient echo (VIBE) sequence with the following parameters: TR/TE 3.63/1.57 ms; matrix 128 × 160 × 48; flip-angle 18°; bw 496 Hz/pixel; slice thickness 5mm; FOV 28 × 35 cm. The sequence had a temporal resolution of ~5.7 s and was continued for 120 measurements (~10 minutes in total). T_1 maps were derived using a multiple flip-angle method, from a similar sequence run with flip-angles [1°, 2°, 5°, 10°, 15°, 20°].

The AIF was measured by a pre-bolus method whereby a tenth dose (i.e. 0.01 mmol/kg) of gadobutrol was administered (before the main bolus) and a separate dynamic acquisition collected. This was a 3D spoiled gradient-echo sequence and was oriented sagittal-obliquely to capture the descending aorta in section (see Fig.1a). It had the following parameters: TR/TE 4.35/1.5 ms; matrix 192 × 115 × 10; flip-angle 20°; slice thickness 5 mm. The time resolution was ~1.7 s and the acquisition lasted ~4.5 min.

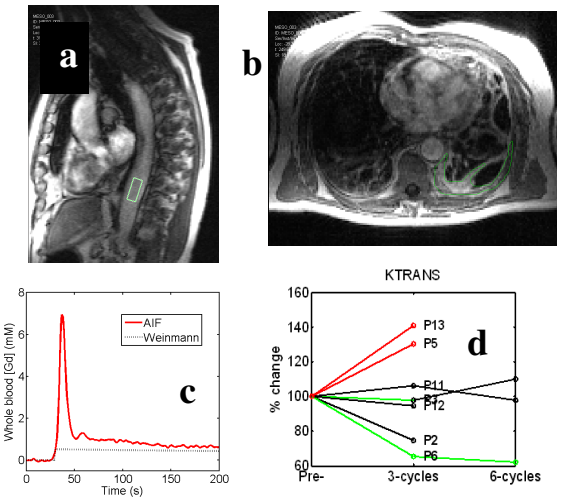

Fig. 1 (a) Example image through aorta for measurement of AIF from pre-bolus; (b) example image from dynamic series with ROI for extraction of tumour enhancement curves; (c) scaled sample-averaged AIF; (d) results for change in K^{trans} after treatment, shown schematically for each patient (red lines indicate that disease progressed, as assessed by lesion size RECIST criteria on control CT images; green lines indicate that disease responded to treatment when assessed by CT).

Areas of tumour were outlined in the posterior of the lung on the T_1 map of each slice by an experienced radiologist using custom software written in Matlab (Mathworks, Natick, MA). No image registration techniques were used, there being little physiological motion observed in the tumour tissue positioned in the posterior of the lung. Signal-to-[Gd] conversion was achieved using the method summarized by Schabel *et al* [4] and was performed on a pixel-by-pixel basis for the tumour regions of interest. The pre-bolus AIF was extracted from a ROI drawn in the distal descending aorta: scaling from pre-bolus to main bolus concentrations was achieved using the method of Kostler *et al* [5]. A sample-averaged AIF was constructed from the AIFs measured for each patient visit, and thereafter used in the model-fitting process. Using custom software written in Matlab, the extended Tofts model[1] was applied to the resulting voxel [Gd] uptake curves and the resulting maps for K^{trans} were subjected to histogram analysis. The outlined tumour median value was reported.

Results

The measured sample-averaged AIF is shown in Fig. 1c and corresponds well to a population-averaged AIF in the literature[6], though it should be noted that a different contrast agent was used. The 'wash-out' region of the AIF converges satisfactorily to the Weinmann curve[7]. The results for median tumour K^{trans} for each patient visit are shown in Fig. 1d and show a variety of changes post-treatment with chemotherapy. As an aid to interpretation, the response to treatment was also assessed using RECIST criteria on CT images taken on the same day as each MR examination. The MR results for those patients who responded to treatment as assessed by CT RECIST are shown in green in the figure; non-responders (progression of disease) are shown in red; where response or progression was unclear on CT, the lines are shown in black.

Discussion

It can be seen that the non-responders (P5 & P13) had an increase in K^{trans} after treatment and one responder (P6) had a decrease in K^{trans} after treatment. These results are consistent with a hypothesis of response to treatment being associated with an effective antiangiogenic effect of the drug administered (although pemetrexed is not specifically antiangiogenic in its immediate action). However, another responder (P3) showed little decrease in median K^{trans} and a patient (P2) with a non-clear outcome showed a large decrease in K^{trans}. The other pharmacokinetic model parameters derived (v_e and v_p) showed no clear trends with respect to treatment response. At present, the low number of recruits prohibits a quantitative statistical analysis.

Conclusion

Initial findings suggest that volumetric tumour perfusion measured by DCE MRI (with a standard pharmacokinetic model analysis) correlates well with the established imaging gold standand (CT), and that it may have a role in accurately determining treatment response.

References

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