The Utility of 3D DCE-MRI for Assessing Treatment Response in Oesophageal Cancer

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Introduction

Oesophageal cancer is the eighth most common cancer and has a poor long term survival time. While surgery with or without chemotherapy, and concurrent chemo-radiotherapy (CRT) can cure a proportion of patients without distant spread, there is a need to develop methods that can assess treatment response and help individualise therapy. Monitoring treatment response in cancer has been achieved successfully using dynamic contrast-enhanced MRI (DCE-MRI) in various cancer types [1], but its use in oesophageal cancer is limited [2,3]. Imaging of the oesophagus is challenging due to its close proximity to the heart and major vessels and respiratory motion. We evaluate the utility of a 3D DCE-MRI technique, including measurement of baseline and time-varying T_1, an individually measured arterial input function and a commonly applied tracer kinetic model [4] to assess changes in physiological parameters, such as K^{trans}, due to chemo-radiotherapy. We assess the feasibility of using this 3D technique as a tool for assessing treatment response in oesophageal cancer.

Methods

Five patients with oesophageal cancer unsuitable for surgical resection were prospectively recruited in the study having obtained local research ethics permission. Each patient underwent two DCE-MRI scans, each separated by a course of radical CRT. Treatment normally comprised radiotherapy to a total dose of 50Gy in 25 fractions over 5 weeks with concurrent cisplatin and capecitabine chemotherapy. Imaging was performed at 1.5 T (Philips Achieva, Philips Healthcare, Best, The Netherlands). The DCE-MRI examination used a 3D Fast Field Echo (spoiled gradient echo) sequence in the axial plane with the following parameters: FOV = 375 mm x 375 mm; slice thickness = 3 mm; number of slices in volume = 33; matrix = 128 x 128; in-plane resolution = 2.92 mm x 2.92 mm; TR = 2.34 ms; TE = 0.70 ms. Baseline T_1 values were determined from three FFE acquisitions with different flip angles (2°, 10° and 20°) and with NSA = 4. The dynamic series used the same 3D acquisition sequence (TR, TE, geometry identical) with flip angle = 20°, NSA = 1. A total of 256 image volumes were acquired over a period of approximately 10 minutes, with a temporal resolution of 2.3 s. During the dynamic series acquisition, 0.1 mmol/kg of body weight of 0.5 mmol/ml gadoterate meglumine, Gd-DOTA, Dotarem (Geurbet, France) was administered at the 6th dynamic timepoint through a Spectris power injector (Medrad Inc., USA) at a rate of 3 ml/s followed by an equal volume of saline flush also at 3 ml/s.

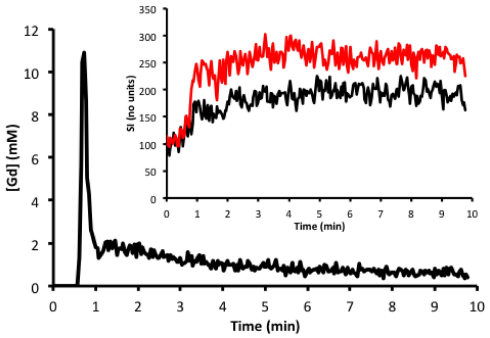

Figure 1: An example arterial input function measured from the descending aorta. Inset, tumour uptake curves from an example patient, pre- (black) and post-therapy (red).

Regions of interest (ROI) were defined for the whole tumour volume. The arterial input function (AIF) was determined for each patient and visit in the descending aorta using an automated technique [5]. Enhancing voxels were identified in the tumour ROI and the extended Kety tracer kinetic model [4] was applied to dynamic time series of these voxels to provide estimates of the fractional vascular plasma volume (v_p), contrast agent endothelial transfer coefficient (K^{trans}) (min^{-1}) and fractional extracellular extravascular volume (v_e). Voxel-wise measurements of the model-free parameter $IAUC_{60}$ were also measured. 3D maps of DCE-MRI parameters were generated and parameter medians were computed to summarize each individual. Two-tailed paired t-tests (p=0.05) were used to determine if there were significant changes pre- and post- therapy

Results

Individual AIFs were succesfully measured in all patients and were robust against inflow effects [6] and exhibited good first-pass peak characterisation (Fig,1). Whole tumour volume was reduced in 4 of the 5 patients post-therapy (ranging from +5% to -50% tumour volume change). Significant increases in $IAUC_{60}$ (p=0.006), K^{trans} (p=0.035) and v_e (p=0.015) were seen in all patients (Fig. 2). Changes in v_p following therapy were not significant (p=0.562). Parameter maps show estimation of K^{trans} across the whole tumour (Fig. 3).

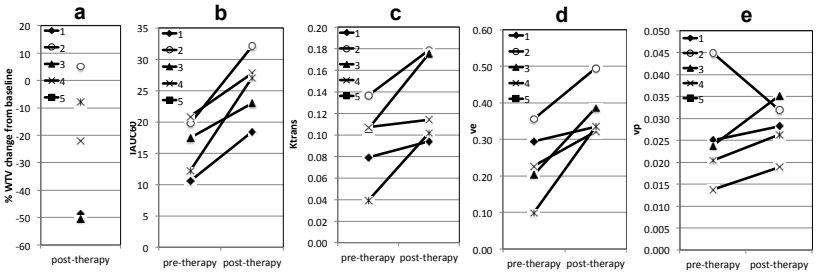

Figure 2: Pre- and post-therapy plots for whole tumour volume (a), estimated $IAUC_{60}$ (b), K^{trans} (c), v_e (d) and v_p (e). See text for pre- and post-therapy significance p-values.

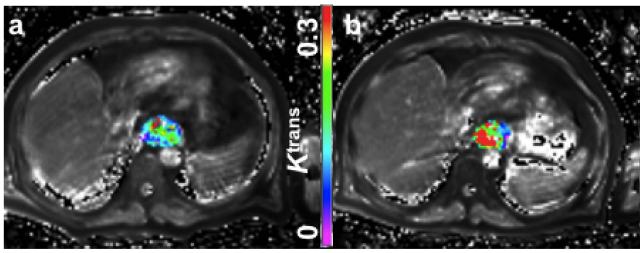

Figure 3: Tumour K^{trans} parameter maps for an example patient overlaid on a T_1 map. (a) Pre-therapy and (b) post-therapy.

Discsussion

Imaging in the oesophagus has known challenges and no studies to date have used 3D imaging together with quantitative modelling to assess its sensitivity to treatment response across the full tumour extent. All patients studied showed a response to treatment with a reduction in whole tumour volume. DCE-MRI pharmacokinetic parameters had similar and significant responses to therapy, which were contradictory to what has been previously reported [2]. The increases observed in K^{trans}, v_e and $IAUC_{60}$ suggest an acute response to radiation therapy that may be explained by the close timing of the post-treatment MR scan relative to treatment. We have successfully applied 3D DCE-MRI in oesophageal cancer and demonstrated its potential to assess treatment response. Further studies to determine its effectiveness in predicting treatment outcome and to personalise therapy is warranted.

References **1.** O'Connor J P et al. Br J Cancer 2007;96(2):189-195. **2.** Chang EY, et al. J Gastrointest Surg 2008;12(1):166-175. **3.** Oberholzer K, et al. J Magn Reson Imaging 2008;27(6):1296-1301. **4.** Tofts, P. J. Magn Reson Imaging 1997;7(1):91-101. **5.** Parker G.J. et al. Magn Reson Med 2006;56(5):993-1000. 6. Roberts et al. Magn Reson Med 2011;65(1):108-119.