

# Tumour necrosis assessed by magnetic resonance dynamic contrast-enhanced subtraction imaging is a predictor of chemoradiotherapy response in advanced cervical cancer

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## Introduction

Radiotherapy is effective in cervix cancer treatment. Imaging techniques that can predict treatment outcome would allow for further treatment individualisation. Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) has been shown to predict tumour response to treatment in cervical cancer [1]. However, generation of quantitative DCE parameters requires substantial post-processing using additional software. There have been various attempts to standardise the parameters used in DCE-MRI, but the current lack of standardised and independently validated analysis packages makes comparisons between different studies difficult. Instead, subtraction imaging is an easy tool that overcomes different centres variability in image protocols, and allows a feasible qualitative assessment of tumour necrosis defined as areas of non-enhancing tumour on subtracted images. It is also easy to perform and widely available in radiology departments. Subtraction imaging has been used for the diagnosis of malignant renal masses [2] and it improves confidence in breast lesions identification [3]. It is also useful in assessing tumour response to chemotherapy [4] and assessing the degree of enhancement in focal liver lesions [5]. The aim of this study was to prospectively evaluate DCE-MRI subtracted imaging as predictor of chemo-radiotherapy response in patients with advanced cervical cancer.

## Materials and Methods

Thirteen patients with advanced cervical cancer treated with chemo-radiotherapy underwent DCE-MRI at 3 time-points: before treatment, after 2 weeks and at the completion (5 weeks) of chemoradiotherapy but before the start of brachytherapy. The MRI protocol included T1W axial and T2W sagittal, axial and axial oblique images followed by a DCE-MRI sequence. This consisted of a 3D T1W fast spoiled gradient echo (TR/TE = 4.8/1.5 ms, flip angle = 18°) of 4 contiguous sagittal sections repeated every 3 seconds for a total of 180 seconds after contrast administration. Voxel-by-voxel subtraction imaging was performed at 18, 78 and 138 seconds after contrast medium injection using a workstation subtraction tool (Advantage Windows 4.2 GE Healthcare Buc, France). Two independent readers assessed the percentage of tumour necrosis, defined as areas of non-enhancing tumour on subtracted images, using a visual analogous scale (Fig 1). The percentage of tumour necrosis was correlated with radiological tumour response.

## Results

Thirteen patients had a total of 37 MRI examinations. There was an excellent inverse correlation between pre-treatment percentage tumour necrosis evaluated with arterial phase image subtraction and the percentage of tumour volume regression ( $r = -0.939$ ;  $p < 0.001$  and  $r = -0.906$ ;  $p < 0.001$  for reader 1 and 2 respectively) (Figure 2). A significant inverse correlation was seen between the percentage of tumour regression and pre-treatment percentage tumour necrosis evaluated with image subtraction at 78 seconds ( $r = -0.899$ ,  $p < 0.001$  and  $r = -0.674$ ;  $p < 0.001$  for reader 1 and 2 respectively) and 138 seconds ( $r = -0.846$ ,  $p < 0.001$  and  $r = -0.821$ ;  $p < 0.001$  for reader 1 and 2 respectively). However, there was no correlation between the percentage tumour necrosis evaluated with image subtraction (both arterial and later phases of enhancement) after 2 and 5 weeks of therapy and the percentage tumour regression.

## Conclusions

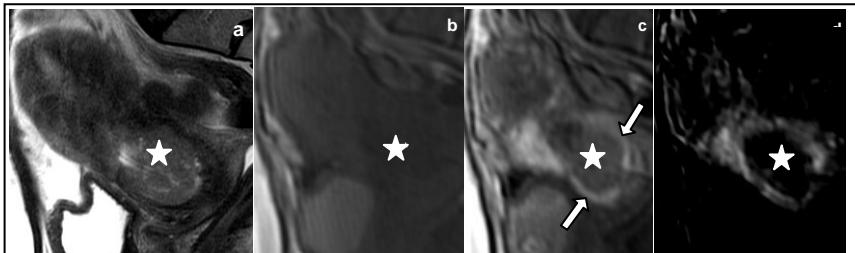
This study presents and assesses a new approach to use the DCE-MRI images in patients with advanced cervical cancer prior to start of treatment with chemo-radiotherapy. The method uses subtracted images obtained from the DCE-MRI images dataset in order to quickly provide information useful to the clinicians. Our results show that the percentage of necrosis evaluated with DCE-MRI subtracted imaging is an excellent predictor of radiation response in cervix cancer. This prognostic information reflecting the tumour perfusion characteristics could be used for treatment individualisation.

## References

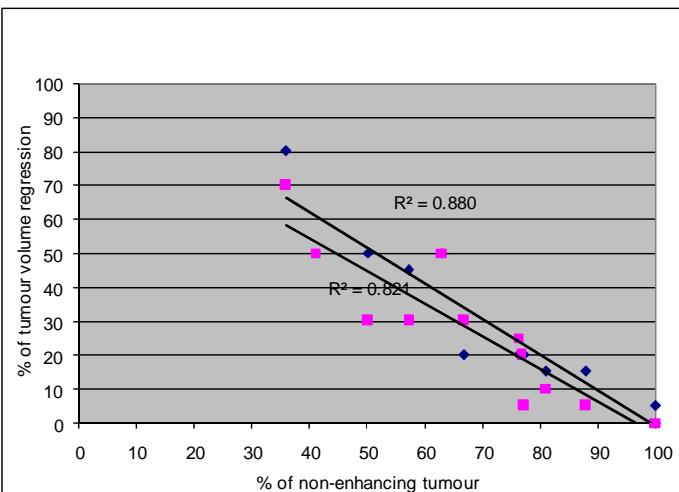
- [1] Mayr NA, et al. J Magn Reson Imaging, 2000, 12, 1027-1033.
- [2] Hecht EM, et al. Radiology, 2004, 232(2), 373-8.
- [3] Choi N, et al. J Comput Assist Tomogr, 2005, 29(6), 834-41.
- [4] Torricelli P, et al. Radiol Med (Torino), 2001, 101(3), 145-51.
- [5] Mainardi LT, et al. BMC Med Imaging, 2006, 7, 6:5.

## Acknowledgements

We are grateful to the MRIS radiographers. We also thank the ACT and the Royal College of Radiologists for funding the study.



**Figure 1:** Pre-treatment (a) sagittal T2W image shows an endocervical mass of intermediate signal intensity in keeping with known cervical carcinoma; (b) sagittal 3D T1W FSPGR pre-contrast image shows a low signal intensity endocervix; (c) 18 seconds post-contrast (arterial phase) image demonstrates little enhancement of the tumour (★) compared to avidly enhancing cervical stroma (arrows); (d) arterial subtracted image (image c less image b) shows areas of signal void visually assessed as 80% necrotic tumour). There was poor response to treatment with only 35% tumour volume regression.



**Figure 2:** Pre-treatment results using the arterial phase. This graph shows the correlations for reader 1 and reader 2 between the % of non enhancing tumour on the subtraction image vs. the % of tumour volume regression at the end of treatment.