

# Enhancing Fraction predicts Recurrence-free Survival in Patients with Carcinoma of the Cervix treated with Radiotherapy

S. B. Donaldson<sup>1,2</sup>, J. P. O'Connor<sup>2</sup>, C. M. West<sup>3</sup>, B. M. Carrington<sup>4</sup>, S. E. Davidson<sup>5</sup>, A. P. Jones<sup>1</sup>, and D. L. Buckley<sup>2</sup>

<sup>1</sup>North Western Medical Physics, Christie Hospital NHS Foundation Trust, Manchester, United Kingdom, <sup>2</sup>Imaging Science and Biomedical Engineering, University of Manchester, Manchester, United Kingdom, <sup>3</sup>Academic Department of Radiation Oncology, University of Manchester, Manchester, United Kingdom, <sup>4</sup>Department of Radiology, Christie Hospital NHS Foundation Trust, Manchester, United Kingdom, <sup>5</sup>Department of Clinical Oncology, Christie Hospital NHS Foundation Trust, Manchester, United Kingdom

## Purpose/Introduction

Patient survival in cervical cancer varies considerably. There is a need to predict, before or early in treatment, those patients unlikely to respond to conventional therapy so that additional treatments can be given. DCE-MRI parameters have shown varying degrees of success in predicting cervix cancer patient outcome<sup>1,2,3</sup>. Enhancing fraction ( $E_F$  = enhancing voxels / total tumour voxels) has been shown to predict clinical outcome following chemotherapy in patients with ovarian cancer<sup>4</sup>. The aim of this work is to analyse the prognostic value of  $E_F$  in cervix tumours prior to external-beam radiotherapy (EBRT) and to monitor changes in  $E_F$  following EBRT.

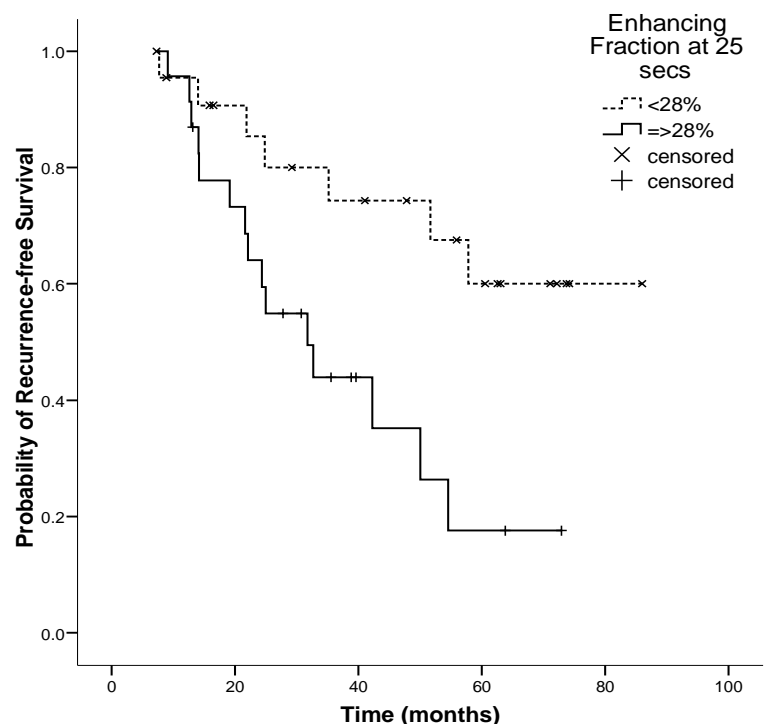
## Subjects and Methods

46 patients (stages II to IVA) underwent DCE-MRI scans prior to receiving EBRT. 10 of these patients also underwent DCE-MRI scans following 40-45 Gy EBRT. All MR scans were performed on a 1.0 T Siemens Magnetom Impact using a phased-array pelvic coil. The dynamic sequences consisted of 8 gradient echo T1-w sagittal scans through the tumour (TR / TE = 130 / 6.5 ms,  $\alpha = 70^\circ$ , FOV = 290 x 290 x 5 mm, matrix = 9 x 256 x 256). The time between successive dynamic scans was 25 seconds. Patients received an injection of 0.1 mmol/kg Gd-DTPA. 1 pre-contrast and 7 post-contrast scans were acquired. Whole tumour ROIs were outlined and  $E_F$  was calculated at 25, 50, 75 and 100 s post-contrast. Enhancing voxels were those which showed signal increases  $\geq 3$  times the standard deviation of the pre-contrast signal in the tumour. Patients were stratified by the median  $E_F$  obtained prior to treatment.  $E_F$  values obtained in 10 patients pre- and post-EBRT were compared using a paired t-test. A significance level of 0.05 was used throughout.

## Results

Significant relationships were seen between  $E_F$  and recurrence-free survival (RFS) at all time points (the data from the 25 s time point is shown in the figure). Patients whose tumours had high  $E_F$  had a significantly poorer RFS than tumours with low  $E_F$  ( $p=0.011$  at 25 s).

Average  $E_F$  measured in 10 patients pre- and post-EBRT increased at all time points although the increase only reached statistical significance at 100s post-contrast (79 to 97%,  $p = 0.05$ ).



## Discussion/Conclusion

The poor outcome of patients with high  $E_F$  may be indicative of more aggressive / angiogenic tumours, agreeing with previous reports in cervical<sup>3</sup> and ovarian<sup>4</sup> cancers.  $E_F$  is simple to calculate, even when the DCE-MRI data acquisition is sub-optimal. The increase in  $E_F$  following EBRT is consistent with an increase in blood flow and microvascular permeability.  $E_F$  reflects tumour heterogeneity which is known to be important in the success of treatment outcome<sup>5</sup>.  $E_F$  provides a simple radiological biomarker of prognosis in patients with cervix tumours.

## References

- <sup>1</sup> Lancaster JA, *et al.* (2002) *Int. J. Radiat. Oncol. Biol. Phys.* 54: 759-767;
- <sup>2</sup> Mayr NA, *et al.* (1998) *AJR* 170: 177-182;
- <sup>3</sup> Hawighorst H, *et al.* (1999) *Magn. Reson. Mater. Phys., Biol. Med.* 8: 55-62;
- <sup>4</sup> O'Connor JP, *et al.* (2007) *Clin. Cancer Res.* 13: 6,130-6,135;
- <sup>5</sup> Lyng H, *et al.* (2001) *Int. J. Cancer (Rad. Onc. Invest.)* 96: 182-190.