Diffusion MRI predicts response in advance of tumour size changes in women receiving chemoradiation for cervical cancer

V. N. Harry[1], S. I. Semple[2], D. E. Parkin[1], and F. J. Gilbert[2]

[1]Gynaecological Oncology, Aberdeen Royal Infirmary, Aberdeen, Aberdeenshire, United Kingdom, [2]Radiology, University of Aberdeen, Aberdeen, United Kingdom

Introduction:

One of the greatest challenges in cancer management is the inability to rapidly or objectively predict the response of a tumour to a recommended therapy regimen. Traditionally, response to treatment has been assessed via changes in tumour size measurements despite recognised limitations of size change as a tumour response variable[1]. Alterations in size are often considered to be late events, usually preceded by functional changes in tumour biology. An early marker or predictor of response would have immense clinical value as persisting with ineffective treatment is associated with increased toxicity and morbidity as well as unnecessary expense. One of the most rapidly evolving imaging techniques in the MRI field is diffusion weighted MRI (DWI). This method exploits the random translational movement of water molecules and has the ability to characterise tissues based on their water diffusion properties. By observing the water mobility within tumours, DWI can act as a biomarker that highly correlates with cellularity. DWI allows for calculation of the apparent diffusion coefficient (ADC), a parameter reflective of the specific diffusion capacity of tissue, particularly sensitive to tissue necrosis. Although ADC has therefore proved to be of benefit in early detection of therapy response in various malignancies such as brain[2] and rectal [3] tumours, this has not been fully explored in cervical cancer.

We investigated the use of ADC as an early measure of treatment response in women receiving concurrent radiotherapy and chemotherapy (chemoradiation) for advanced cervical cancer and compared it with an assessment of early change of longest tumour diameter.[4]

Methods:

Fifteen women clinically assessed as FIGO stage 2B and above were included in a prospective cohort study. They received 5 weeks of external beam pelvic radiotherapy (45Gy/25 fractions) accompanied by a weekly 40mg/m² dose of cisplatin chemotherapy and this was followed by brachytherapy in the form of intracavitary caesium. DWI was carried out prior to treatment and then repeated after two weeks of therapy, using the phased array torso coil of a 1.5 T GE NVi/CVi scanner (Waukeshau, USA) using a diffusion weighted epi acquisition (b-value = 1000). Longest tumour diameter from radiological assessments and tumour ADC values were noted at these time points. Change in ADC between these two examinations was then tested for correlation with eventual tumour response or non-response as determined by a clinical examination under anaesthetic performed following therapy (the standard response assessment method for this patient group).

Results:

Table 1 demonstrates the ADC and longest tumour diameter for individual patients before and after 2 weeks of chemoradiation. Paired-sample *t* tests revealed that the difference between the longest tumour diameter measurements at these two time points was not significant (p=0.113). In contrast, significant differences were noted in the ADC values at these two intervals (p=0.001). In addition, the change in ADC after only 2 weeks of therapy was found to significantly correlate with eventual tumour response (Spearman's ρ=0.606, p=0.017) as shown in Figure 1. Sample ADC maps are presented in Figure 2, before and after two weeks of therapy.

Conclusions:

Our results indicate that DWI may provide a reliable biomarker capable of early prediction of response to therapy prior to size changes. ADC is particularly sensitive to apoptosis and ADC changes are therefore observed in these tumours before any clinical size reduction is evident. DWI may therefore have great potential in assessing early cervical cancer response to therapy, allowing customisation of patient-specific regimens.

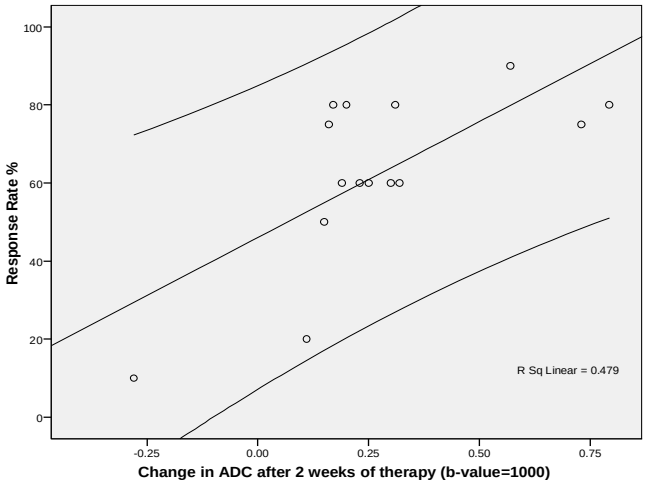
Table 1

ADC and longest tumour diameter for each patient

Patient	ADC ($\times 10^{-3}$ mm^2/s)		Longest tumour diameter	
	Pre-therapy	After 2 weeks	Pre-therapy	After 2 weeks
1	1.27	1.58	39.2	26.5
2	1.19	1.49	53.9	51.4
3	1.50	1.61	60.4	69.4
4	1.36	1.55	47.0	42.4
5	1.18	1.38	42.7	38.3
6	1.15	1.30	30.0	28.5
7	1.43	1.15	29.5	27.2
8	1.31	2.04	20.0	34.8
9	1.23	1.48	40.1	29.6
10	0.99	1.78	32.8	31.3
11	1.12	1.44	58.6	48.9
12	1.44	1.67	44.1	30.8
13	1.60	2.17	18.5	11.0
14	1.21	1.38	27.8	25.7
15	1.38	1.54	28.7	28.1

Figure 1

Correlation between ΔADC after 2 weeks and response rate



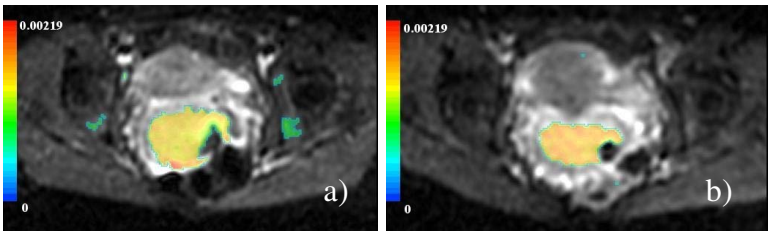


Figure 2: Sample ADC maps a) before, and b) after two weeks radiotherapy.

References

1. Padhani AR. Eur J Cancer 2002. 38 :2116-2127
2 Chenevert TL et al . J Natl Cancer Inst 2000. 92 :2029-2036
3. Dzik-Jurasz A et al. Lancet 2002. 360 :307-308
4. Therasse P et al. J NatlCancer Inst 2000.92 :205-216