Changes in tCho/water ratio in the transition from pre-invasive to invasive cervical cancer using in vivo MR Spectroscopic Imaging

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Introduction: The development of invasive cervical cancer is preceded by a well-defined pre-invasive stage cervical intraepithelial neoplasia (CIN). Elevated levels of choline have previously been identified in a number of tumours including cervical cancer [1] but whether these metabolites are elevated in CIN tissue is still unclear. The aim of this study was to investigate the metabolic changes in the transition from pre-invasive to cervical cancer using *in vivo* ^{1}H magnetic resonance spectroscopic imaging (MRSI). To our knowledge, this study is the first to report on MRSI in the cervix using an endovaginal coil.

Methods: ***Patient criteria:*** Over a 6 month period, 20 women (10 women with moderate/severe CIN disease and 10 women with stage 1 cervical cancer confirmed histologically) were studied. Women with CIN disease were recruited following an abnormal smear test and prior to colposcopic treatment. All women underwent MR imaging and spectroscopy and were studied with their written informed consent and with the approval of the local ethics committee. An endovaginal coil of solenoid geometry ring design [2] was inserted endovaginally and positioned around the cervix. Air introduced into the vagina during coil placement was aspirated to reduce B_0 inhomogenities at the air/tissue interface.

In vivo MRS: MR spectroscopy was performed using a 1.5T scanner (Intera, Philips Medical System, Netherlands). The presence of tumour within the cervix was recorded on T_2-weighted images. A 7.5 cm^3 press box was placed over the tumour or centrally on the cervix on CIN patients. Acquisition of ^{1}H-MR spectra was performed using a PRESS-localised MRSI technique (TR 888 ms, TE 135 ms, SI scan resolution 16, 4 signal averages, 2 phase cycles, B_0 scan resolution 16, B_0 measurements 2, 17 mins). tCho peak was set as 3.2ppm and the peak area was measured using the AMARES algorithm included in the jMRUI software package [3]. Tissue water was used as an internal standard and the unsuppressed water signal from the corresponding voxel was used to calculate ratios. Statistical analysis was performed with SPSS for Windows and a p- value of less than 0.05 was chosen as the criterion for statistical significance.

Results:

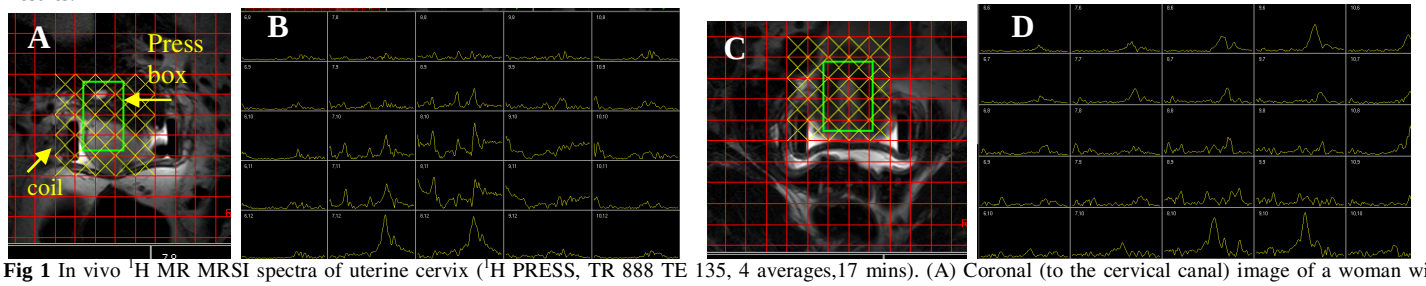

Fig 1 In vivo ^{1}H MR MRSI spectra of uterine cervix (^{1}H PRESS, TR 888 TE 135, 4 averages,17 mins). (A) Coronal (to the cervical canal) image of a woman with cervical cancer and (B) subsequent MRSI showing the selected region, (C). Coronal image of a woman with CIN disease and (D) subsequent MRSI showing the selected region.

	tCho/water x 10^{-4}	
	Voxel 1	Voxel 2
CIN (n=10)	7.25± 3.50	8.73± 4.94
Tumour (n=10)	15.2± 7.16	10.6± 5.35
p (*t*- test)	0.004	NS

Table 1 tCho/water ratio of voxels of interest. Voxel 1 represents tumour (in cancer patients) or CIN (in CIN patients). Voxel 2 represents normal cervix close to the area of abnormality. NS- not significant.

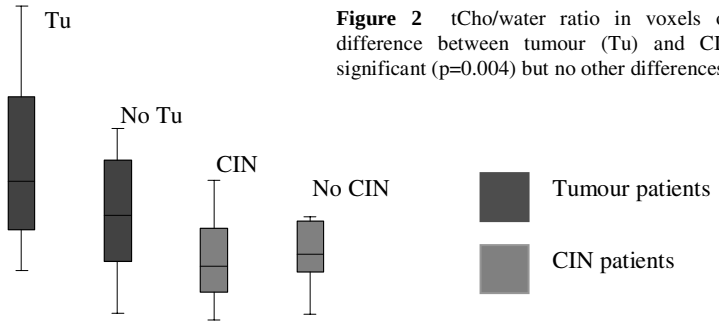

Figure 2 tCho/water ratio in voxels of interest. The difference between tumour (Tu) and CIN voxels were significant (p=0.004) but no other differences were observed.

Quantifiable metabolite spectra (fig 1) along with unsuppressed water spectra were obtained for all women. Visual analysis noted the presence of triglyceride peaks – CH_2 at 1.3 ppm, signal at 2 ppm and choline compounds at 3.2 ppm. For the purpose of this study only the tCho peak was investigated. In cancer patients, tumour voxels (where the tumour occupies >10% of the voxel) and a no-tumour voxel adjacent to the area of malignancy were analysed. In CIN patients, voxels representing CIN tissue where the endocervix (squamous epithelium) occupied >10% of the voxel and a voxel adjacent to the area of abnormality (no-CIN voxel) were chosen. Direct comparison between tumour voxels and CIN voxels showed that tCho/water ratio doubles in tumour (table 1). Also, the tCho/water ratio in voxels next to a malignancy (voxel 2 in tumour patients) was higher than in CIN patients (fig 2) although the small patient numbers and high standard deviation meant results were not statistically significant. CIN and no-CIN voxels had similar tCho/water ratios. No other comparisons were significant.

Discussion and Conclusion The tCho/ water ratio increases significantly between tumour and CIN voxels. tCho/water ratio in voxels adjacent to a tumour appeared increased in comparison to CIN voxels or no-CIN voxels although this did not reach significance because of small sample numbers and high standard deviation.. A larger study is being undertaken to establish whether tissue adjacent to a malignancy is metabolically abnormal.

References [1] deSouza, NM *et al*. NMR in Biomedicine, 2004;17:144-153. [2] deSouza, NM et al. Br. J. Obstet. Gynaecol. 1998;105:500-507.[3] L Vanhamme JMR **129**:35(1997).

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