Markers of Metastatic Potential in Prostate Cancer using Magnetic Resonance Spectroscopy

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Introduction.

A major focus of translation research is to apply emerging technologies towards defining the malignant phenotype and to establish whether the malignant phenotype can differentiate normal from malignant. One such technique is magnetic resonance spectroscopy (MRS), a versatile non-invasive investigative technique based on the measurement of magnetic signals from nuclei responding to radiofrequency pulses. Initial clinical results of MRS studies of prostate cancer (PCa) have demonstrated a significant reduction of citrate and an elevation of choline containing compounds (Cho) in PCa compared with normal prostatic peripheral zone tissue and benign prostatic hypertrophy (Kurhanewicz et al. JMRI 2002; 16: 451-463). Studies of surgical prostate cancer specimens have demonstrated that compounds involved in phosphatidylcholine and phosphatidylethanolamine synthesis and hydrolysis contribute to the MR spectrum. Therefore, as in other human cancers, the elevation of the Cho peak is associated with changes in cell membrane synthesis and degradation that occur with the evolution of cancer. However the significance and specificity of these changes remains unclear. In this study intact prostatic cancer cell lines were profiled using ¹H magic angle spinning (MAS) MRS in order to establish whether MRS profiles could complement phenotypic characteristics of neoplastic cells.

Materials and Methods. The human prostate derived tumourogenic cell lines studied are summarised in the Table:

Cell line	Metastatic Potential	AR protein	Origin
DU145	High (>90%)	Negative	Brain metastasis
PC3	High (>90%)	Negative	Vertebral metastasis
LNCaP	Low (<10%)	Positive	Lymph node metastasis

All cell lines were grown in RPMI, supplemented with 10% fetal bovine serum (FBS). Cells were phenotyped immunocytochemically as previously described to ensure purity and obtain a partial fingerprint at the start of the studies (Mitchell et al. BJU Int 2000; 85: 932-944). Between 1×10^6 - 5×10^6 cells were placed in the 20_l sample holder for MAS. MAS MRS is a method where line broadening due to anisotropic interactions in solid materials is reduced by spinning the sample about its own axis at 4000Hz at a 54.7° angle to the static magnetic field (Weybright et al. MRM 1998; 39: 337-344). ¹H MAS MR spectra were acquired using a Doty CP/MAS probe interfaced with a JEOL Eclipse 500+ spectrometer (JEOL, UK) at a temperature of 25°C. Spectra were acquired with water pre-saturation using pulse-collect techniques and analysed using the fitting program AMARES.

Results Resonances assigned to choline-containing compounds (choline, phosphocholine, glycerophosphocholine and phosphatidylcholine) and to lipids (-CH₃ at 0.9ppm, -CH₂ at 1.3ppm and 2ppm) were observed in all spectra. The peak area ratio of (total Cho)/(total lipid) was significantly different between the cell lines (PC3: 0.206±0.008, DU145: 0.133±0.005; LNCaP: 0.100±0.002), p<0.001, ANOVA.

Conclusions. The MR spectral profile of human prostate derived tumourogenic cell lines is characteristic of the cell line phenotype, indicating that it may be possible to identify MR markers of metastatic potential in prostate cancer.