MR determined metabolic phenotype - a possible tool for prediction of long term survival in breast cancer patients?

T. F. Bathen[1], B. Sitter[1], H. E. Fjösne[2], D. E. Axelson[3], S. Lundgren[4,5], and I. S. Gribbestad[6]

[1]Dept. of Circulation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway, [2]Dept. of Surgery, St. Olavs University Hospital, Trondheim, Norway, [3]MRi_Consulting, Kingston, Canada, [4]Dept. of Oncology, St.Olavs University Hospital, Trondheim, Norway, [5]Dept. of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway, [6]Dept. of Ciculation and Medical Imaging, Norwegian University of Science and Technology, Trondheim, Norway

Introduction:

Biochemical properties as described by MR spectroscopy characterise breast tumours (1, 2). The biochemical activity in cancer tissue is altered and high resolution magic angle spinning (HR MAS) spectral profiles of breast cancer tissue correlate to clinical parameters such as lymphatic spread and hormone status (3). The purpose of the current study was to investigate the feasibility of MR determined metabolic phenotype in prediction of long term breast cancer survival.

Experimental:

Breast cancer tissue was excised from patients with palpable breast cancer (diagnosed as invasive ductal carcinoma (IDC) grade I, II and III). None of the patients received neo-adjuvant treatment before the operation. Tissue specimens were analysed in D_2O-PBS in a 50 μL MAS rotor (4 mm o.d.). High resolution magic angle spinning (HR MAS) magnetic resonance (MR) spectra were recorded on a Bruker Avance DRX600 spectrometer. Proton MR spin echo spectra were acquired with a total echo time of 285 ms and presaturation of the water peak (4 °C, spin rate 5 kHz). After HR MAS MRS analysis, a pathologist scored the relative areas of normal and neoplastic epithelial elements visually. Spectra from biopsies with tumour-content less than 5% were excluded from further analysis. The survival status 4 years after surgery was known for all patients. This resulted in a dataset consisting of spectra from 40 patients, where 32 patients survived 4 years (represented by 38 spectra), and 8 patients (represented by 9 spectra) passed away before the 4 years limit. Partial least squares (PLS) regression was performed relating the selected spectral region (2.9-4.7 ppm) to survival 4 years after surgery. PLS was performed with mean-centering and full cross-validation. The number of PCs to retain in the model was determined by the PC were residual variance and root mean square error of prediction was minimised.

Results:

The selected spectral region used for PLS with assignments is shown in Figure 1A. The score plot of PC1 versus PC2 from PLS is given in Figure 1B. Three significant PCs were retained in the model, and the MR predicted versus the clinical known survival was significantly correlated, both for calibration ($r=0.77$, $p<0.01$) and validation ($r=0.48$, $p<0.01$).

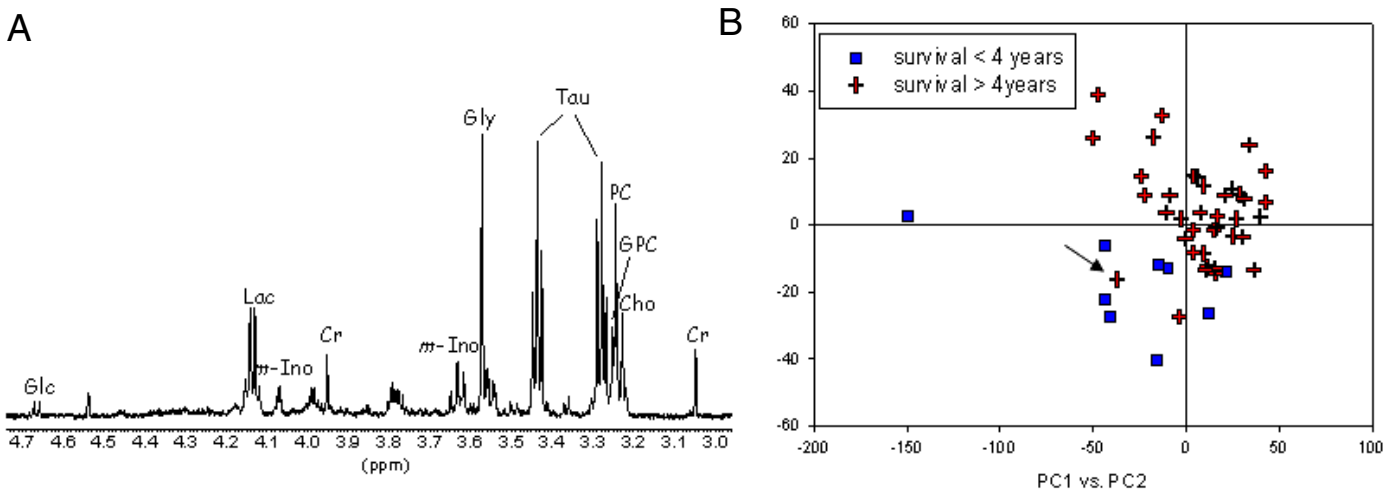

Figure 1: (A) HR MAS MR spectrum of breast cancer from a patient diagnosed with IDC II, showing signals from creatine (Cr), choline (Cho), phosphocholine (PC), glycerophosphocholine (GPC), taurine (Tau), myo-Inositol (m-Ino), lactate (Lac) and glucose (Glc). (B) Score plot of PC1 vs. PC2. The spectra are clearly clustered according to survival. The spectrum pointed towards by the arrow was obtained from a patient who was diagnosed with a recidive 4.5 years after the first surgery.

Discussion and conclusion:

This preliminary investigation suggests that MR determined metabolic phenotype may have a potential in prediction of long term breast cancer survival. Further validation, including more samples and blind testing will be necessary.

1. Gribbestad et.al. NMR Biomed 1994;7: 181
2. Sitter et.al. NMR Biomed 2002;15: 327
3. Bathen et. al. Breast Cancer Res Treat, DOI 10.1007/s10549-006-9400-z