HR MAS MRS: a tool for breast cancer grading?

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Introduction:

Biochemical properties as described by MR spectroscopy characterise breast tumours (1, 2). Histopathological (tumour size, grade and number of axillary lymph node involved) and immunohistochemical (steroid hormone receptors, c-erbB2) evaluation of breast cancer specimens is the basis for the patient treatment plan. Additional methods for grading using tissue samples may be important for better treatment strategies.

Experimental:

Breast cancer and non-involved adjacent tissue were excised from patients with palpable breast cancer (diagnosed as invasive ductal carcinoma (IDC) grade I, II and III). 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 at 4 °C. Proton MR spin echo spectra were acquired with a total echo time of 285 ms and presaturation of the water peak. The samples were spun at 5000 Hz. After HR MAS MRS analysis, a pathologist scored the relative areas of normal and neoplastic epithelial elements visually. Tumour-content less than 5% in the analysed sample and pre-treatment before operation were exclusion criteria. This resulted in a final database consisting of 115 samples (48 non-involved tissue, 4 IDC I, 33 IDC II, and 30 IDC III). Principal component analysis (PCA) of selected spectral region (2.9-4.7 ppm) was performed to describe the sample variation and to achieve variable reduction. The 25 first principal component (PC) scores from PCA of the IDC samples only were used as input for classification by a probabilistic neural network (PNN) strategy (3). Both PCA and PNN were performed with full cross-validation.

Results:

The selected region of a HR MAS MR spectrum with assignments is shown in Figure 1. The 2D score plot of PC1 and PC2 is given in Figure 2. All samples from non-involved tissue are clearly separated from the rest. Table 1 shows the results from the PNN classification of the PCA scores from the IDC I-III samples. The sensitivity and specificity of classifications exceeds 80% for all groups.

Discussion and conclusion:

PCA led to a complete separation of the non-involved and cancerous samples, which confirms a basic difference in metabolite content. Within the group of cancerous samples, the IDCs intersperse with no possibility to differentiate among the three types of grading. The complexity of the samples makes it necessary to utilise more sophisticated non-linear methods in order to achieve complete classification, in which PNN proves to be a useful tool. Preliminary results from variable selection shows that all variables in the selected region are equally important to the classification achieved. Additional classification strategies are under investigation.

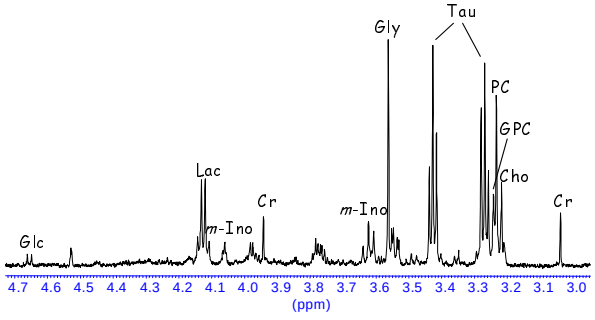
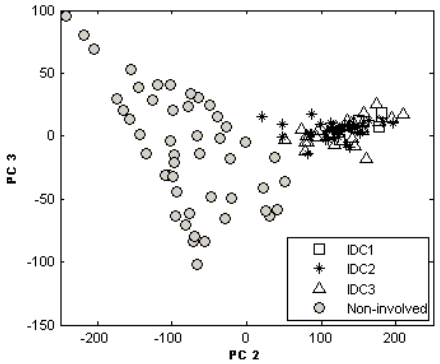


Figure 1: HR MAS MR spectrum of breast cancer from a patient diagnosed with IDC II.



Figur 2: Score plot from PCA of all samples.
Non-involved tissue is clearly different from malignant samples.

	Actual "IDC I"	Actual "IDC II"	Actual "IDC III"	Total
Classified as "I"	4	0	0	4
Classified as "II"	0	27	6	33
Classified as "III"	0	5	25	30
Total	4	32	31	67
Sensitivity	100.0%	84.4%	80.7%	
Specificity	100.0%	82.9%	86.1%	

Table 1: Results from PNN.

References:

1. Gribbestad et.al. NMR Biomed 1994;7: 181
2. Sitter et.al. NMR Biomed 2002;15: 327
3. Specht. Neural Networks 1990;3: