Peak alignment of MR spectra

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Introduction

Correction of misaligned peaks is an important part of multivariate preprocessing of MR spectra. Alignment of spectra is a relatively new procedure, and several alignment algorithms exist. Correlation optimized warping[1] (COW) and peak alignment by genetic algorithm[2] (PAGA) apply shifts to segments, while parametric time warping[3] (PTW) finds a continuous alignment function. In this study, three different peak alignment algorithms were tested on high resolution magic angle spinning (HR MAS) MR spectra from breast cancer tissue. Estrogen receptor (ER) status is an important prognostic factor in breast cancer, and has been shown to be related to metabolic profile[4]. Classification of spectra by partial least squares discriminant analysis (PLS-DA) based on ER status was performed in order to examine the different alignment algorithms.

Methods

Tumor samples from breast cancer patients diagnosed with invasive ductal carcinoma were analyzed by HR MAS MRS on a Bruker Avance DRX600 spectrometer. None of the patients had received neoadjuvant treatment before surgery. The relative areas of normal and neoplastic epithelial tissue were scored, and spectra from samples containing < 5% cancer cells were excluded. This resulted in a dataset of 202 spectra. A region of interest containing the spectral intensities 1.45-4.84 ppm was selected, and the spectra were baseline corrected, peak aligned and normalized to equal integral. Training and test sets were chosen by Kennard-Stone sample selection[5]. PLS-DA was performed using cross-validation, and blind samples (n=50) were predicted for verification.

Results and discussion

The spectral region 3.2-3.3 ppm of unaligned and aligned spectra is shown in Fig. 1. By visual inspection, COW and PTW seem to give the best alignment of this particular region. The results from PLS-DA of ER status using datasets from unaligned spectra and different alignment algorithms are shown in table 1. Datasets from COW and PAGA alignment gave the best prediction results by PLS-DA, and improved the sensitivity and specificity compared to unaligned data. The PTW aligned data did not improve the prediction error compared to unaligned data, but resulted in a better balanced rate of sensitivity and specificity.

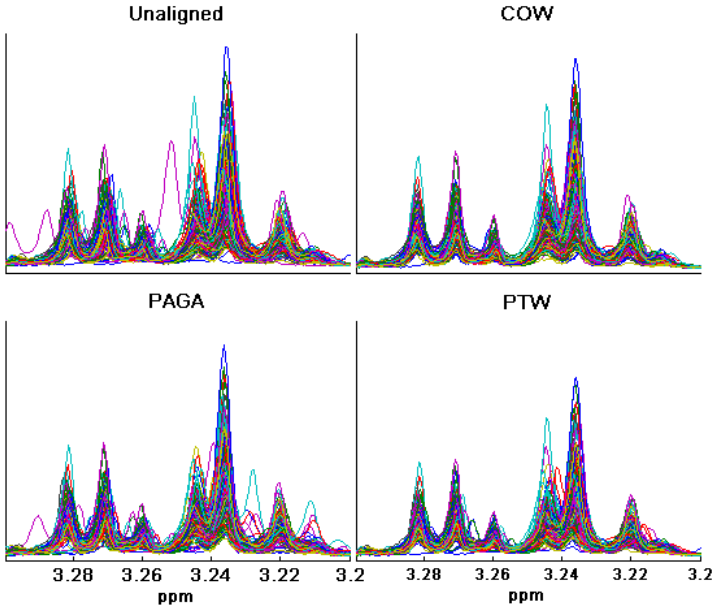

Table 1: Blind sample predictition of ER status for unaligned spectra and spectra aligned by COW, PAGA and PTW.

Method	Prediction error	Sensitivity	Specificity
Unaligned	28.4 %	90.0 %	30.0 %
COW	15.8 %	81.0 %	87.5 %
PAGA	14.2 %	89.7 %	81.8 %
PTW	27.5 %	85.0 %	60.0 %

Fig. 1: The spectral region 3.2-3.3 ppm of the unaligned spectra and spectra aligned by COW, PAGA and PTW.

Conclusion

COW and PAGA gave the lowest prediction error, and showed that ER status can be predicted from MR spectra with high sensitivity and specificity. PTW did not improve the prediction error of this dataset compared to unaligned data, indicating that PTW may not be as suitable for metabolomic MR data. COW and PAGA greatly improved the prediction ability compared to the unaligned dataset, demonstrating the importance of proper peak alignment of MR data.

References: (1) Tomasi et al. J Chemometrics 2004; 18:231 (2) Forshed et al. Anal Chim Acta 2003; 487:189 (3) Eilers. Anal Chem 2004; 76: 404 (4) Bathen et al. Breast Cancer Res Treat 2007; 104:181 (5) Kennard and Stone. Technometrics 1969; 11:137.