Magnetic resonance metabolic profiling of breast cancer tissue obtained with core needle biopsy for predicting pathologic response to neoadjuvant chemotherapy

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Purpose

Neoadjuvant chemotherapy (NAC) is well established as a standard treatment for locally advanced breast cancer. The heterogeneous character of breast cancer, however, results in varied responses to NAC. Pretreatment prediction of pathologic response to NAC could enable development of personalized treatment protocols, reducing unnecessary exposure of patients to chemotherapy toxicity and improving long-term patient outcome. The purpose of our study was to determine whether metabolic profiling of core needle biopsy (CNB) samples using high resolution magic angle spinning magnetic resonance spectroscopy (HR-MAS MRS) could be used for predicting pathologic response to NAC in patients with locally advanced breast cancer.

Methods

After institutional review board approval and informed consent were obtained, CNB tissue samples were collected from 37 malignant lesions in 37 patients before NAC treatment. The metabolic profiling of CNB samples were performed by HR-MAS MRS (11.7 T). Metabolic profiles were compared according to pathologic response to NAC using the Mann-Whitney test. For multivariate analysis, orthogonal projections to latent structure-discriminant analysis (OPLS-DA) were performed to distinguish patient groups by pathologic response to NAC with HR-MAS MR spectral data of CNB samples obtained before NAC.

Results

Various metabolites including choline-containing compounds were identified and quantified by HR-MAS MRS in all 37 breast cancer tissue samples obtained by CNB. In univariate analysis, the metabolite concentrations and metabolic ratios of CNB samples obtained with HR-MAS MRS were not significantly different between different pathologic response groups. However, there was a trend of lower levels of phosphocholine/creatine ratio and choline-containing metabolite concentrations in the (pathologic complete response) pCR group compared to the non-pCR group. In multivariate analysis, the OPLS-DA models built with HR-MAS MR metabolic profiles showed visible discrimination between the pathologic response groups (Figure 1). Our OPLS-DA prediction model exhibited high sensitivities with range 84.6%–100% for differentiation pCR from other groups (Table 1).

Figure 1. (A) OPLS-DA score and loading S-plot of the HR-MAS MR spectra from pCR and non-pCR (PR and SD) groups.

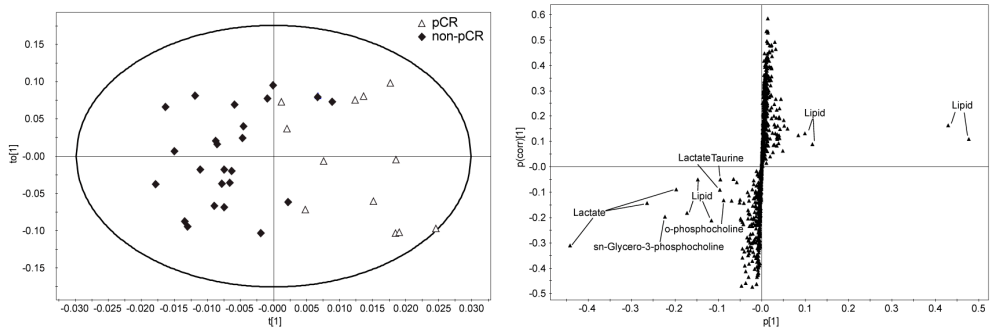

Table 1. Diagnostic performance of OPLS-DA for predicting pCR after neoadjuvamt chemotherapy.

	pCR vs. PR	pCR vs. SD	PR vs. SD*	pCR vs. non-pCR
Sensitivity	92.3 %	84.6 %	85.7 %	100 %
Specificity	100.0 %	90.0 %	90.0 %	87.5%

pCR: pathologic complete response; PR: partial response; SD: stable disease; non-pCR: PR and SD
*diagnostic performance for predicting PR

Discussion

Many previous studies using HR-MAS MRS have used surgically obtained tissue samples.[1,2,] Therefore, the metabolic profiles could not be used to directly influence the pretreatment planning of therapeutic strategies. We conducted HR-MAS MRS using 14-gauge CNB samples and performed metabolic profiling of breast cancer without any problem. US-guided CNB is the most frequently used method for diagnosis of suspicious breast lesions and for IHC analysis for lesion characterization. Accordingly, metabolic profiles of CNB samples can be clinically applicable for pretreatment prediction of NAC response or prognosis. Moreover, HR-MAS MRS using high magnetic field strength (11.7 T) could also be used to analyze individual choline-containing compounds, other metabolic markers such as taurine and glycine, and metabolic ratios, which showed significant associations with prognostic factors of breast cancer in previous studies.[3] Although we did not find statistical significance in this study, our HR-MAS MRS results also showed the differences in the levels of the aforementioned potential biomarkers according to its pathologic response to NAC. Considering previous studies with our own results, HR-MAS MRS using breast tissue acquired with minimally invasive CNB may be a clinically useful method to predict NAC response and to develop more personalized treatment protocols for locally advanced breast cancer patients, with respect to invasiveness and data quality.

Conclusion

This study showed that OPLS-DA multivariate analysis using choline-containing metabolites of pretreatment CNB samples assessed by HR-MAS MRS may be used to predict pathologic response before NAC treatment, although we did not identify the metabolite showing statistical significance in univariate analysis. Therefore, our preliminary results raise the necessity of further studies of HR-MAS MR metabolic profiling of CNB samples for a large number of cancers. In addition, we expect that HR-MAS MR metabolic profiling of pretreatment CNB samples may be helpful to develop more personalized treatment protocols for patients with locally advanced breast cancers.

Reference

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