Phospholipid contents measured in human breast cancer and in healthy glandular breast tissue in vivo at 7T

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Introduction

Individualization of chemotherapy requires accurate biomarkers that predict treatment efficacy. Studies in breast cancer cell lines and mouse models have shown that phospholipid metabolite concentrations correlate with efficacy of chemotherapy [1,2]. Unfortunately, non-invasive detection of these compounds using clinical breast MRI is restricted due to lack of sensitivity and chemical specificity [3]. In this feasibility study we demonstrate that use of dedicated focused field coils combined with the increased chemical shift dispersion at 7T-breast MRI for accurate non-invasive characterization of phospholipid metabolism in human breast tumors.

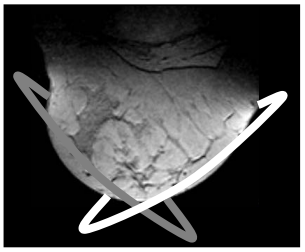

Figure 1. Schematic overview of the dual channel unilateral breast coil for detecting phosphorus and proton MR signals. The location of the two elements is illustrated by two ellipsoids on a transversal MRI of a human female breast obtained at 7T.

Methods

A two-channel unilateral RF coil was designed and built consisting of two circular loops oriented closely to the breast at + and - 45 degrees with respect to the prone position of the two women (one patient and one healhty volunteer) (fig 1). Each element was double tuned to 298MHz and 121MHz and interfaced via home-built (narrow band) transmit-receive switches and preamplifiers to a whole body 7T MR system (Philips, Cleveland, USA). Single voxel MR spectra of (2.0 cm)3 were obtained from a tumor in one breast cancer patient (histopathology proven T4 invasive breast cancer) and from glandular tissue in a healthy volunteer (semi LASER sequence, MEGA water and lipid suppression, TR = 4 s, 32 averages). Spectra were obtained at a TE of 56ms and 118ms to correct for T2 relaxation and water referencing was used for quantification. In addition, localized ^{31}P MR spectra were obtained using pulse acquired 3D CSI (with a TR of 1.5s and a flip angle of 39 degrees) B0 shimming was performed on the area depicted for the ^{1}H MRS measurements.

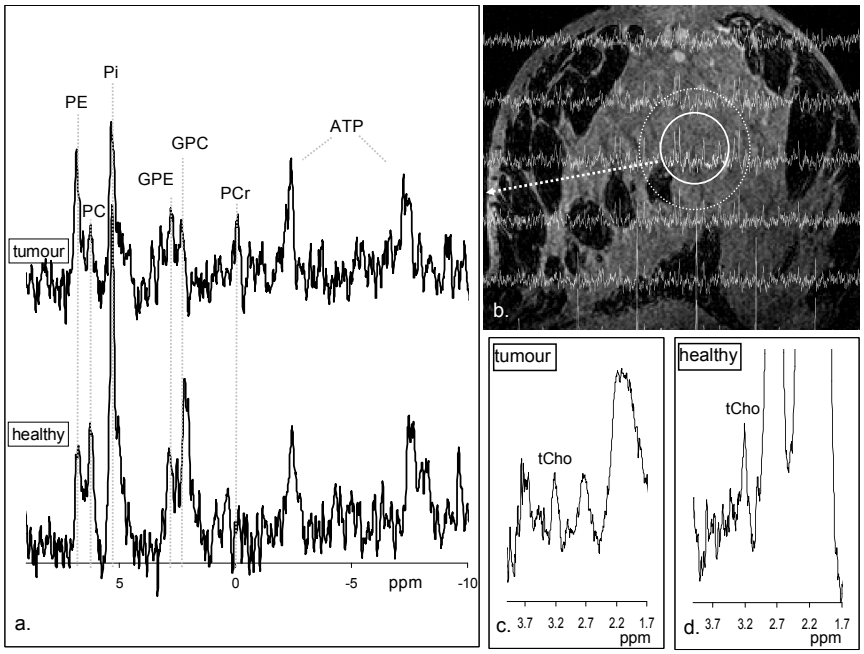

Figure 2. Localized phosphorus and proton MR spectra obtained from human breasts at 7T in vivo. One slice of phosphorus spectra is mapped onto a high resolution transversal MR image obtained from the patient with breast cancer (b). From the tumor area, indicated by the dotted circle, relatively higher levels of PE and PC with lower levels of GPE and GPC are detected in the phosphorus MR spectrum compared to a healthy control (a). In addition, levels of ATP and Pi could be detected (a). Proton MR spectra obtained from the breasts indicate a similar total choline level in the tumor (c) as in healthy glandular tissue (d).

Results

The total choline compound in the tumor was determined at 0.4 mM/kg water compared to 0.7 mM/kg water of the healthy volunteer with an accuracy of 0.1 mM based on the noise of the spectra (Cramer Rao Lower Bound). In the Phosphorus MR spectra, substantial changes in the ratio of PE + PC (Phospho-ethanolamine, -choline) to GPE + GPC (glycerol-PE and –PC) could be obtained when comparing the spectrum from tumor tissue with the spectrum of healthy subjects. In fact, due to the high spectral resolution, even distinct detection of PC, PE, GPC and GPE is feasible, as well as adenosine tri phosphate (ATP) and inorganic phosphate (Pi), which can be used to assess pH. Also due to the relatively high spatial resolution, signals from highly concentrated compounds in muscle do not contaminate the spectra from the selected voxels. Therefore even in healthy glandular tissue the presence of ATP levels .and an absence of phosphor creatine (PCr) could be observed .

Acquisition times for localized phosphorus MR spectroscopy of breast cancers remained within scan times of 20 minutes.

Conclusion and discussion

In this work we demonstrate the ability to detect multiple phospholipid metabolites in vivo in the human female breast. Signals can be detected locally with a spatial resolution of 10 ml, not only from cancerous tissue with high concentration of choline levels, but also from tissue at low levels of total choline (i.e. < 0.5 mM).

References

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