AMESING and BINEPT 31P MRS at 7T distinguishes glycerophosphatidylcholine from glycerophosphocholine

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Introduction

Phosphocholine (PC) and glycerophosphocholine (GPC) are involved in cell membrane metabolism. Their concentration ratio has shown to be a marker in predicting cancer treatment response as shown in *ex vivo* NMR studies[1]. ^{31}P MRS can easily distinguish PC from GPC and these metabolites haves been used as biomarkers in many *in vivo* studies. However, in contrast to *ex vivo* methods that mostly reflect only aqueous pools due to extraction techniques, *in vivo* methods will also obtain signals from membrane phospholipids (MPL)[2]. Moreover, as these MPL have chemical shifts similar to GPC (glycerophosphatidylethanolamine (GPtE) has identical chemical shift as GPC, Fig. 1), *in vivo* distinction of these compounds is hampered. In this study we investigate the dominance of GPC and GPE over their membrane lipids in breast tissue as measured with ^{31}P MRS *in vivo*. Measurements were performed at 7T to distinguish GPE from GPC. Multi-echo acquisition (AMESING[3]) and ^{1}H to ^{31}P polarization transfer[4] were used to identify the mobility of the molecules as reflected in the T_2, which suggests a distinction between the aqueous GPE and GPC from the more restricted MPL (GPtE and GPtC). Data was obtained in breast glandular tissue and compared to GPC and GPE metabolites as measured in healthy liver tissue (all *in vivo*). It is known that healthy liver shows high signals of GPC and GPE in ^{31}P MRS *in vivo* and *ex vivo* extracts.

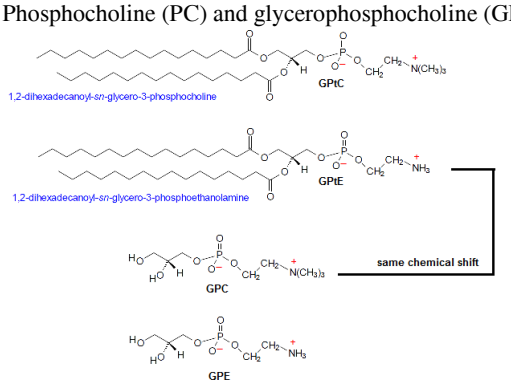

Fig. 1. Molecular structures of GPC, GPE and their membrane phospholipids (MPL) GPtC and GPtE.

Methods

^{31}P MRS measurements of glandular breast tissue and liver tissue were obtained from healthy volunteers using a dedicated breast coil (MR coils BV, Drunen, the Netherlands), or half volume coil for the liver, interfaced to a 7T MRI system (Philips, Cleveland, USA). Pulse acquire, multi-echo[2] and polarization transfer[3] acquisitions were obtained with adiabatic RF pulses, TR = 6s, 8x8x8 spherical acquired CSI, 2x4x4 cm^3 voxel sizes for the breast and 32x10 2D CSI voxel sizes 1x1 cm^3 for the liver.

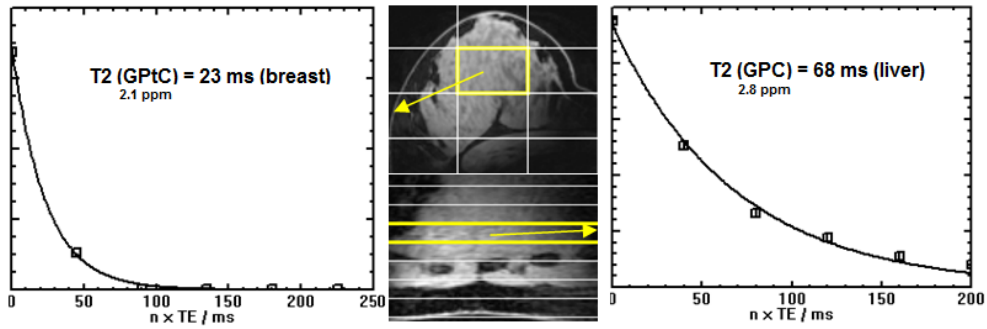

Fig. 3. Signal decay over echo time of the GPtC peak at 2.1 ppm obtained from the breast (left) and the true GPC peak from the liver (right) at 2.8 ppm. Note the three-fold reduced T_2 of the ^{31}P spins of GPtC in the breast as compared to GPC in the liver.

Results

While the efficiency in polarization transfer of PE and PC is similar to GPE and GPC, the spectra obtained from the breast, which are the average of three volunteers, only show enhancements in the phosphomonoesters PE and PC (Fig. 2b versus a/c). The chemical shifts of the GPC and GPE signals in liver (Fig 2d) do not correspond to the signals observed in the breast spectra, that are usually labelled GPC and GPE, but are actually GPtE+GPC and GPtC. Moreover, the T_2 of the ^{31}P spins at the chemical shift of GPtC(breast) differ by a factor 3 as compared to the ^{31}P spins of GPC in the liver (Fig. 3).

Conclusion and discussion

The phophomonoesters in breast glandular tissue clearly represent the metabolites PE and PC due to their correct chemical shift, their long T_2 and boosted SNR with polarization transfer. An *in vitro* extract study on breast tumors showed that GPE and GPC are hardly present in non-necrotic breast tumors and, at low field, diester signals observed *in vivo* are mainly from phospholipids[2]. Based on this and on altered chemical shifts[5] and low T_2 relaxation values as measured with both polarization transfer and multi-echo acquisition, the phosphodiester signals at 7T in healthy breast are identified as GPtC and the sum of GPtE and GPC. As PC over GPC is used as a biomarker, the in vivo obtained value will be contaminated with signal from GPtE, or the GPtC peak may be erroneously assigned as GPC.

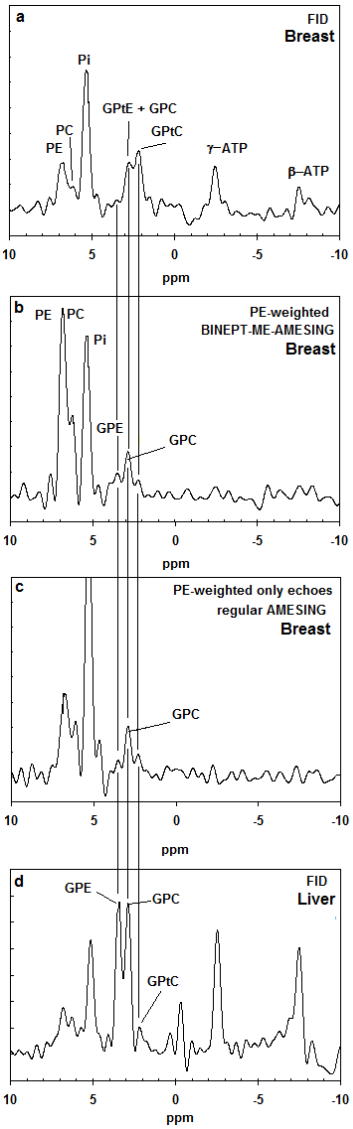

Fig. 2. (a) Pulse acquire, (b) polarization transfer (PT) and multi-echo summed (PE weighted), (c) multi-echo summed ^{31}P MR spectra from the breast and (d) liver. Note that only PE and PC are boosted by the PT and chemical shifts of liver GPE and GPC do not match the signals from the breast.

References

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