Increase in SNR of 370 % for 31P MR spectroscopy by adiabatic multi-echo polarization transfer and adiabatic multi-echo direct detection in one repetition time

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Introduction

Phosphomonoesters (PME) and phosphodiesters (PDE) have shown clinical potential to be used as a biomarkers in oncological and degenerative diseases. Direct ^{31}P measurement of these metabolites *in vivo* is hampered by an intrinsic low sensitivity. SNR enhancement for PME and PDE can be obtained by polarization transfer techniques, for instance by an adiabatic RINEPT i.e. a BINEPT. We have shown before that direct detection of ^{31}P can be combined with polarization transfer in the same scan time without compromising the polarization transfer signal, since a different pool of spins is observed[1]. However, the direct detection signal is hampered by the polarization transfer sequence because it contains a 180 pulse on the ^{31}P channel that inverts the z-magnetization of the ^{31}P spins, i.e. it makes the direct detection part an inversion recovery sequence. However, this effect can be minimized by doing multi-echo polarization transfer with an even number of 180 pulses on the ^{31}P channel as we will show here. Moreover, recently we demonstrated that adiabatic multi-echo spectroscopic imaging (AMESING[2]) can boost SNR even further, particularly in tissues with short T_2* like in the breast. In this work we acquire practically all signals possible, coming from both ^{1}H and ^{31}P pools in the detection of phospholipid metabolites: we capture the signal of the BINEPT, as well as adding an even number of refocusing pulses to capture signal with long T_2's, without distorting the ^{31}P pool. In addition, within the same T_R we detect the direct ^{31}P pool including multiple refocusing, all at the optimal T_R of 1.2 times the T_1 of the ^{31}P spins. The combined sequence that we propose (BINEPT-ME-AMESING) is depicted in Fig. 1. Using phantom measurements we demonstrate that multi-echo direct ^{31}P detection can be merged into a BINEPT multi-echo sequence without adversely affecting the SNR of polarization transfer or direct detection. In addition, we demonstrate its application in the detection of very low concentrations of PME in the healthy human breast.

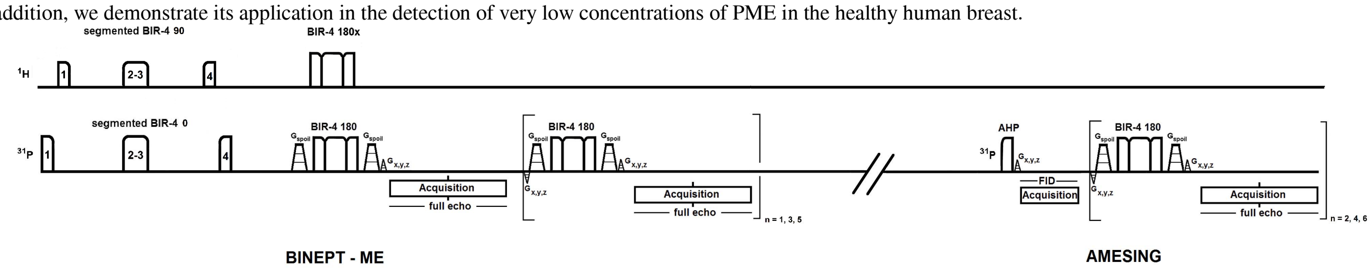

Fig.1. BINEPT multi-echo combined with a direct excitation adiabatic multi-echo sequence (BINEPT-ME-AMESING) for ^{31}P spectroscopic imaging in one TR. The sequence can be run within SAR limits in vivo with a TR of 6 seconds acquiring a BINEPT with 3 additional full echoes and a direct excitation FID with 4 full echoes. Duration of a full BIR-4 pulse is 4 ms, with 96 μT power on the ^{31}P channel and 38 μT on the ^{1}H channel.

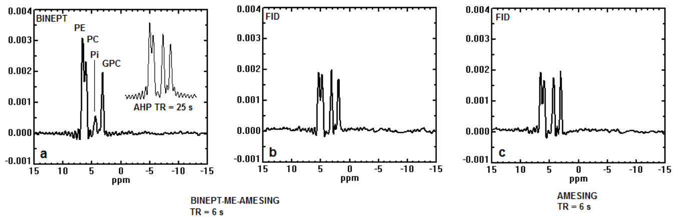

***Fig. 2.** ^{31}P Spectra obtained in a 20x20x20 mm3 voxel of a spherical phantom containing PE, PC, Pi and GPC with the proposed BINEPT-ME-AMESING sequence (**a** BINEPT and inlay figure a fully T_1 relaxed direct detection spectrum; **b** ^{31}P direct detection of FID) and for comparison with the AMESING (**c** direct detection of FID) sequence. The multi-echo spectra are, for brevity, not shown here.*

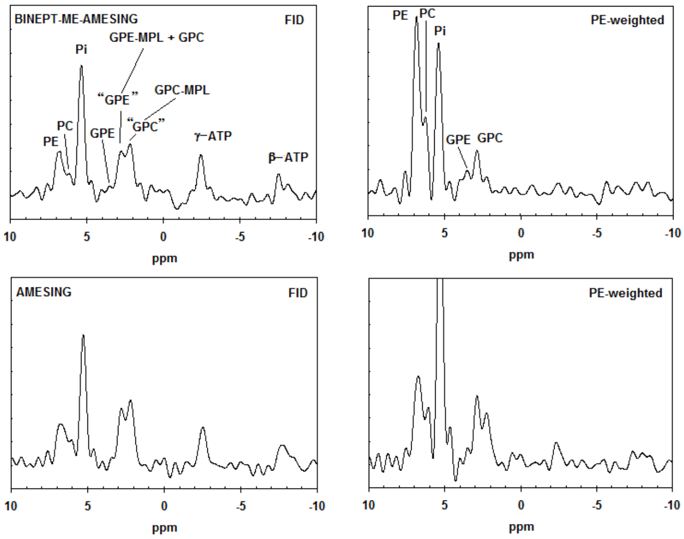

***Fig. 3.** Average of measured ^{31}P MR spectra in a voxel of 40x20x40 mm3 of the breast of three healthy volunteers; T_R = 6 s. Top row: FID and PE weighted spectra of the BINEPT-ME-AMESING sequence. Bottom row FID and PE weighted spectra obtained with the AMESING sequence, without polarization transfer.*

Experimental

The BINEPT-ME-AMESING sequence was tested on a spherical phantom containing aqueous phosphoethanolamine (PE) phosphocholine (PC), inorganic phosphate (Pi) and glycerophosphocholine (GPC). For comparison a fully T_1 relaxed ^{31}P MRS spectrum was measured and ^{31}P spectra using the AMESING sequence without the BINEPT-ME were acquired. The sequence was subsequently used for measuring ^{31}P spectra in the breast of three healthy female volunteers. All measurements were performed with a whole body 7 Tesla MR system (Philips, Cleveland, USA) using a home-build dual-tuned coil.

Results and discussion

The phantom measurements are shown in Fig. 2 for the BINEPT-ME-AMESING and the AMESING sequences. Note that the BINEPT spectrum of the J-coupled metabolites corresponds well to the fully T_1 relaxed direct detection inlay spectrum (AHP T_R = 25 s) shown in Fig. 2a. The small Pi peak is because of pulse imperfection of the segmented BIR-4 0 pulse on the ^{31}P channel and not using phase cycling. The subsequent direct detection FID spectrum Fig. 2b, that was measured after 3 s of the start of the BINEPT-ME, is only marginally lower in SNR than the spectrum shown in Fig 2c that is the FID of an AMESING acquisition without polarization transfer. Fig. 3 shows a comparison of the ^{31}P spectra acquired in a voxel of fibro-glandular tissue of three healthy female volunteers with the BINEPT-ME-AMESING sequence and the AMESING sequence. The spectra shown in Fig. 3 are the average over three volunteers. Note that the FID spectra are of similar signal intensity, implying very little signal loss by combining the BINEPT-ME with the AMESING in one T_R. The PE-weighted spectra reveal the increase in SNR that is obtained when a weighted average of FID and all echoes are calculated using the fitted T_2 = 165 ms for PE. The SNR gain for the phosphomonoesters acquired with the new sequence is 400 % when compared to the direct detection FID, or approximately 370 % when compared to a low flip Ernst angle excitation pulse acquire. The peaks usually assigned to GPC and GPE are mainly signals from a mobile fraction of membrane phospholipids (MPL), with short T_2 that show hardly any enhancement. Only GPC that is under the GPE-MPL peak surfaces after one echo time.

Conclusion

The SNR per time unit of the signals of heteronuclear J-coupled ^{31}P metabolites can be increased by using an adiabatic multi-echo polarization transfer technique with an even number of 180 refocusing pulses on the ^{31}P channel combined with an adiabatic multi-echo direct detection sequence in one T_R, without adversely affecting the polarization transfer or the direct detection signal. The *in vivo* increase in SNR for phosphomonoesters as compared to low flip Ernst angle excitation pulse acquire can be up to 370%.

References

1. van der Kemp WJM, Boer VO, Luijten PR, Wijnen JP, Klomp DWJ, Magn Reson Med. 2012 **68**: 353-7.
2. van der Kemp WJM, Boer VO, Luijten PR, Stehouwer BL, Veldhuis WB, Klomp DWJ. NMR Biomed. 2013 **26**: 1299-307.