

# Increase in SNR for $^{31}\text{P}$ MR spectroscopy by integrating polarization transfer and direct detection in one repetition time.

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**Introduction:** Phosphomonoesters and phosphodiesters are involved in phospholipid metabolism and have shown clinical potential to be used as a biomarker in oncological and degenerative diseases. However, direct  $^{31}\text{P}$  measurement in vivo is hampered by an intrinsic low sensitivity. SNR enhancement can be obtained by polarization transfer techniques, for instance by an RINEPT, (refocused insensitive nuclei enhanced polarization transfer) or its adiabatic variant (BINEPT). Due to interfering inter-proton coupling, the intrinsic signal intensity for an BINEPT and direct  $^{31}\text{P}$  detection are approximately equal. However, as the BINEPT is based on polarization of a complete different pool of spins ( $^1\text{H}$ ) compared to direct detection ( $^{31}\text{P}$ ), the SNR per unit of time will be more favorable (since  $T_1^{^{31}\text{P}} > 4T_1^{^1\text{H}}$ ).

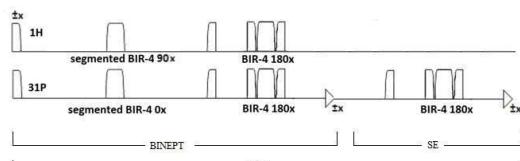


Fig.1. Integrated BINEPT-SE sequence used for  $^{31}\text{P}$  spectroscopy.

In fact, excitation of  $^{31}\text{P}$  spins has no effect on the polarization of  $^1\text{H}$  spins, even if these nuclei are J-coupled. Therefore, direct detection can be combined with polarization transferred detection within the same scan time, see Fig. 1, yielding independent signals without signal loss. Combining these signals will result in enhanced SNR for coupled spins, but also provides information of spins that are not detected by polarization transfer. Using phantom measurements we first demonstrate that direct  $^{31}\text{P}$  detection can be merged into a BINEPT sequence without affecting its SNR. In addition, we demonstrate the detection of very low concentrations of phospho-esters in the healthy human breast using an optimized BINEPT, while still detecting the non  $^1\text{H}$ -coupled signals of inorganic phosphate and ATP.

**Experimental:** As a proof of principle,  $^{31}\text{P}$  MRS measurements were obtained with an BINEPT sequence and a direct detection sequence (adiabatic SE, with the same TE<sub>31P</sub> of 34ms as used in the BINEPT) at various T<sub>R</sub> for each sequence separately, and integrated within the same T<sub>R</sub>. A spherical phantom filled with 12 mM phosphoethanolamine (PE) and 15 mM phosphocholine(PC) solution buffered to pH = 7.0 was used and submersed in a larger semi-sphere filled with NaCl solution for coil loading. Measurements were performed with a whole body 7 Tesla MR system (Philips, Cleveland, USA) using a home-build dual-tuned coil. The integrated BINEPT-SE sequence and the separate BINEPT and SE were also applied to the breast of a healthy female volunteer.

**Results and discussion:** The phantom measurements are shown for the integrated and the normal BINEPT and SE sequences in Fig. 2. For the integrated sequence, no impeding effect of the SE on the signal of the BINEPT is observed. The BINEPT, however, has an impeding effect on the SE intensity in the integrated sequence, which is due to the BIR-4 180 pulse of the BINEPT on the phosphor channel that leads to partial inversion of longitudinal magnetization. Moreover, there are additional T<sub>2</sub> losses in the segmented BIR4-0° pulse, and there is the off-resonance imperfection of this segmented pulse. Losses due to inversion could be overcome by adding an inversion pulse just before the SE.

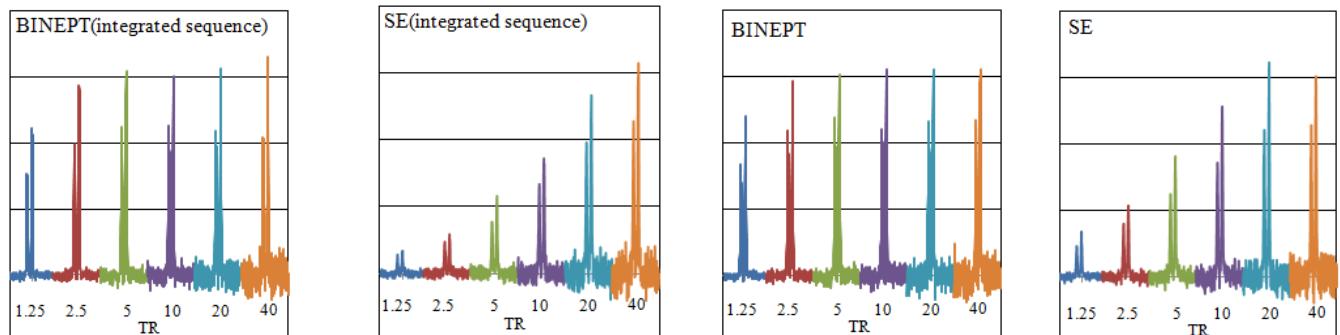


Fig. 2. Measured  $^{31}\text{P}$  spectra on a PC and PE phantom for an integrated BINEPT – SE sequence and for separate BINEPT and SE sequences at various T<sub>R</sub>, with fixed scan time of 80 s. Note that the BINEPT is hardly affected by the integration of an additional SE experiment.

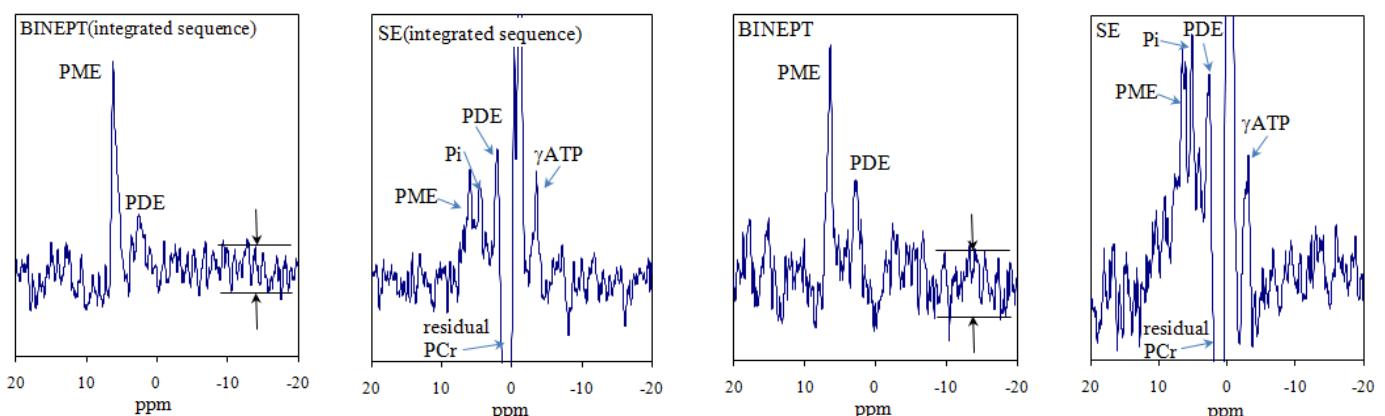


Fig. 3.  $^{31}\text{P}$  breast spectra of a healthy female volunteer. Integrated [BINEPT + SE]<sub>NSA=128</sub> sequence; and separate [BINEPT]<sub>NSA=64</sub> and [SE]<sub>NSA=64</sub> sequences. Scan time for each spectrum 320 s, T<sub>R</sub>=5 s. Note the noise reduction in the BINEPT(integrated sequence) spectrum as compared to the BINEPT spectrum.

The  $^{31}\text{P}$  breast spectra of a healthy female volunteer are shown in Fig. 3. Here we show the integrated [BINEPT + SE]<sub>NSA=128</sub> spectra and for comparison the [BINEPT]<sub>NSA=64</sub> and [SE]<sub>NSA=64</sub> spectra. The integrated BINEPT and SE spectra are, due to the factor 2 higher NSA, less noisy. Here we used the integrated sequence to obtain more SNR for the BINEPT per unit time. Alternatively, the integrated sequence can also be used to obtain an BINEPT at the same SNR in the same time that one would need to obtain a normal BINEPT spectrum, but now with all the additional information that direct detection provides.

**Conclusion:** The SNR per time unit of the signals of phosphoesters can be increased by using an integrated BINEPT - SE sequence. Or alternatively, the integrated sequence can be used to obtain an BINEPT at the same SNR, but with the additional information on metabolite content (PME, PDE, Pi, PCr, ATP) that direct detection offers.