31P Magnetic Resonance Spectroscopic Imaging of the breast; influence of the menstrual cycle

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Introduction Breast cancer is the most common malignancy in women world wide. Radiological imaging is essential to establish a diagnosis and treatment plan for breast cancer patients. Contrast-enhanced MRI has an important role in breast cancer imaging, with a sensitivity of over 90%. However, with a specificity of approximately 70%, other techniques are investigated for an improved lesion characterization. One of the techniques that shows great potential is MR Spectroscopy (MRS). With MRS metabolic changes can be measured non-invasively, even before structural changes are visible. Recent studies have shown that 31P MRS at 7.0 Tesla (7T) is feasible for *in vivo* detection and quantification of phosphor metabolites[1] particularly when using multi echo acquisitions[2]. However, there is only little data on normal values and the variation between women or during the menstrual cycle. In addition, no information is available on T2 relaxation differences that may affect the detected signals. Here we investigated the phosphomonoester (PME) / phosphodiester (PDE) ratio in healthy females and if there are changes throughout the menstrual cycle. Furthermore, we determined apparent T2 relaxation times for multiple phosphor metabolites.

Materials & Methods Premenopausal women (n=5, age range 26-30 years old) with regular menstrual cycles, who did not use any hormonal contraceptives, underwent four 7T MRS exams: one every week during one menstrual cycle. Postmenopausal women (n=5, age range 51-60 years old) underwent one exam. The exams were performed on a 7T whole-body scanner (Philips Healthcare, Cleveland, OH, USA) using a two-channel double-tuned unilateral RF breast coil. The scan protocol included a 3D T1w sequence [TR/TE 4.0/2.0ms, binominal FA 5°, FOV 160x160x160 mm³, acquired resolution 1x1x2 mm³] and a 3D 31P multi-echo (1 FID and 5 echoes) MRS sequence [TR/TE 6000/45 ms, adiabatic FA 90°, FOV 320x160x320 mm³, acquired resolution 40x20x40 mm³]. The spectroscopy data was analysed using IDL and JMRUI software, using only the free-induction decay (FID) to calculate the signal of phosphoethanolamine (PE), phosphocholine (PC), glycerol phosphoethanolamine (GPE), and glycerol phosphocholine (GPC), which is unaffected by potential T2 variability. In the analysis the voxel with the highest PME signal was chosen, i.e. containing the most glandular tissue, while voxel bleeding of phosphocreatine (PCr) signal from the pectoral muscles was minimal. PE and PC signals (PMEs) were summed and divided by the GPE plus GPC signals (PDEs) for each exam. The estimated apparent T2 relaxation for the four metabolites was calculated using the FID and echo data.

Results In 3/5 premenopausal and 3/5 postmenopausal women the MRS data analysis was successfully performed. In the other volunteers the signal to noise ratio was too low for assessment. **Figure 1** shows the MR spectra of one volunteer during four weeks of the menstrual cycle: the early follicular phase (EF), the late follicular phase (LF), the early luteal phase (EL), and the late luteal phase (LL), respectively. The PME/PDE ratio's of the three premenopausal women are shown in **Figure 2**. The postmenopausal results are shown in the figure as well (P). Note that for all measurements the PMEs are lower than the PDEs. Furthermore a variance of the ratio's during the menstrual cycle is seen, however no particular pattern is found. The apparent T2 relaxation times are shown in **Table 1**. Note the large variation in this small sample size, mostly for the PDEs.
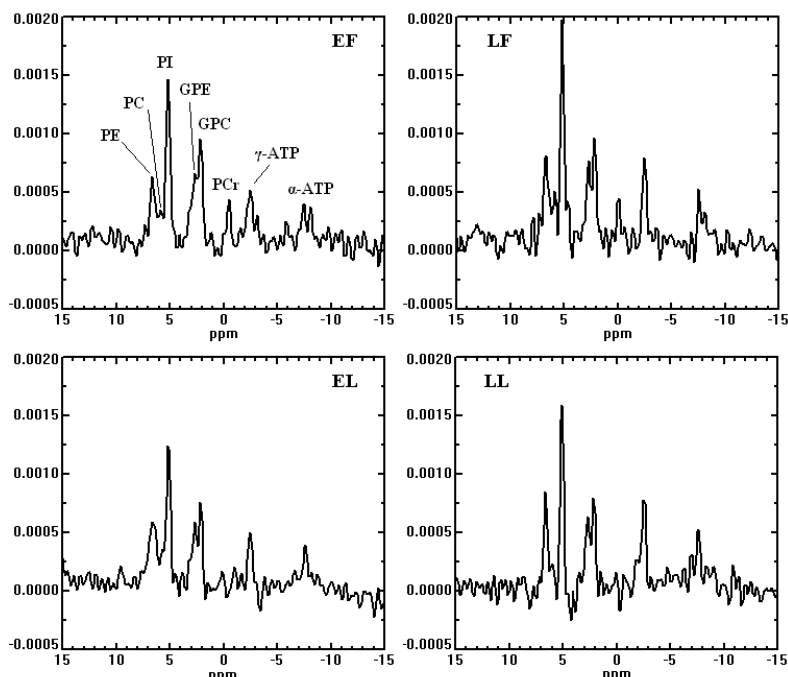
Figure 1: 31P spectra of one premenopausal woman throughout the menstrual cycle.
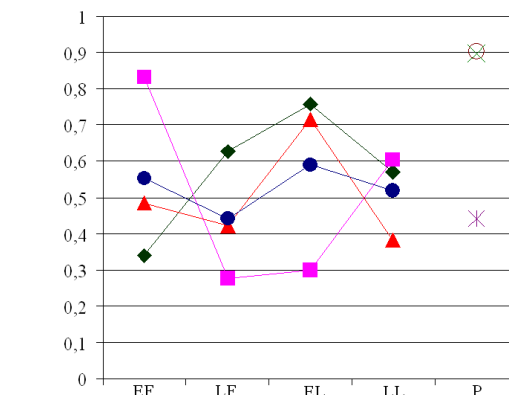
Figure 2: PME/PDE ratio's for 3 premenopausal women throughout the menstrual cycle (red triangles, pink squares and green diamonds; for the latter see the MR spectra in Figure 1), and the average ratio (blue circles). In column P the three postmenopausal women's ratio's are shown.

T2 (ms)

PE	PC	GPE	GPC
192 ± 46	201 ± 85	84 ± 82	102 ± 138

Table 1: estimated apparent T2 relaxation time of 31P spins of PE, PC, GPE and GPC.

Discussion We showed a variation in PME/PDE ratio's throughout the menstrual cycle, even though only 3 women were included in the data analysis. The ratio always remained below 1. In previous work a PME/PDE ratio of 0.3 was found combining data of 8 healthy postmenopausal women[3]. However, also ratio's higher than 1 during the menstrual cycle have been reported: 1.06, 1.75, 0.48 and 0.78 for EF, LF, EL and LL, respectively[4]. Note though that in contrast to those reports, we used accurate spatial localization with very low partial volume effects as illustrated by a small signal from PCr. Furthermore, the SNR in our study is higher. In addition, the apparent T2 relaxation times for phosphor metabolites in the breast are reported here for the first time showing a large variation, especially for PDEs. Consequently, care must be taken when using sensitivity enhancement techniques that include T2 effects. **In conclusion**, when using 31P MRS in a clinical setting results may differ between sequences and in different periods of the menstrual cycle as well as between women, which variance has to be taken into account during data analysis.

*References: **1**. Klomp DWJ, van de Bank BL, Raaijmakers A, et al. NMR Biomed 2011;24:1337-1343. **2**. van der Kemp WJM, Boer VO, Luijten PR, et al. ISMRM 2012; 4271. **3**. Twelves CJ, Porter DA, Lowry M, et al. Br. J. Cancer 1994;69:1151-1156. **4**. Payne GS, Dowsett M and Leach O. Hormone-dependent metabolic changes in the normal breast monitored non0invasively by 31P magnetic resonance (MR) spectroscopy. The Breast 1994;3:20-23.*