The effects of iodinated CT contrast agent on phosphorus MRS

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Synopsis

Contrast-enhanced CT examination can influence ^{1}H-MRI measurements performed within 24h after the CT scan, due to a reduction in water T_1 and T_2 caused by the iodinated contrast agents used in CT. We have investigated whether contrast from a previous CT examination would also influence metabolic measurements made using ^{31}P-MRS, by measuring the T_1 of ^{1}H and ^{31}P signals in human blood. We find that iodinated CT contrast agent has no effect on phosphorus T_1s. Therefore, ^{31}P-MRS examinations will not be influenced by prior CT (unlike ^{1}H-MRI scans).

Introduction:

Cardiac MRI is a routine non-invasive imaging modality used to diagnose heart disease. It can quantify cardiac anatomy, function, perfusion and cardiac tissue energy metabolism. The latter is mainly probed by in vivo phosphorus MR spectroscopy (^{31}P-MRS), which allows measurement of high-energy metabolites, e.g. adenosine triphosphate (ATP) and phosphocreatine (PCr). The PCr/ATP concentration ratio has been shown to change in most major cardiac disease states[1,2]. However, owing in part to long scan times and comparatively limited spatial resolution, it is common to combine MRI with other imaging modalities for a more complete characterisation of cardiac disease. In particular, contrast-enhanced computed tomography (CT) is frequently used. As it is beneficial to schedule the CT and MR examinations in close succession, it is important to identify any potential interference between the two examinations. CT contrast agents contain iodine and act to shorten the T_1 and T_2 relaxation times of water signals in proton (^{1}H) MRI for up to 24 hours after the CT scan[3,4]. However, any potential confounding effects on ^{31}P-MRS remain unknown.

Therefore, our aim was to determine whether an iodinated contrast agent affects the longitudinal (T_1) relaxation time of ^{31}P metabolites, and thus whether an earlier contrast enhanced CT scan would potentially influence the quantification of the cardiac PCr/ATP ratio.

Materials and Methods:

All measurements were performed using a vertical bore 11.7T MRI system (Bruker Avance) equipped with a dual-tuned ^{1}H/^{31}P RF 20mm diameter birdcage coil (Rapid Biomedical).

Fresh human blood (4 × 4mL vials) was obtained from healthy volunteers via antecubital fossa venepuncture and stored in EDTA buffer (Vacutainer, BD Healthcare). T_1 relaxation times were measured on both channels (^{1}H and ^{31}P) in one vial sequentially after sampling using a non-localized pulse-acquire progressive saturation sequence with 6 TRs (1s, 3s, 6s, 10s, 15s and 30s), hard pulse excitation (150ms duration, $\theta \approx 60°$ nominal flip angle), 32 averages, sw=30kHz. The T_1 measurement was performed before and repeated after the addition of a clinically indicated dose of iodinated contrast agent, Iopamidol (1.5mL/kg, i.e. 80mL/vial), and the whole experiment was finished within 2 hours after blood sampling. Water signal from the ^{1}H spectra and 2,3-diphosphoglycerate (2,3-DPG) signal from the ^{31}P spectra were fitted as Lorentzians using a Matlab (Mathworks) implementation of AMARES[5], and used for determining mono-exponential T_1 relaxation curves in Matlab. The two peaks of 2,3-DPG were summed together for the mono-exponential fitting of T_1s.

The remaining three vials were then used to acquire high SNR, partially saturated ^{31}P spectra (TR=1s, $\theta \approx 60°$, 512 averages) before and after the addition of Iopamidol. The same fitting routine was used to fit the signals of 2,3-DPG, phosphodiesters (PDE), γ-ATP and α-ATP. A paired unequal variance t-test was used to compare the fitted signals with and without contrast agent, with $p<0.05$ considered statistically significant.

Results and Discussion:

Figure 1 depicts the T_1 fits of water and 2,3-DPG signals from ^{1}H and ^{31}P MRS acquisitions of blood, respectively. The water T_1 shortened after adding Iopamidol from 4.8±1.9s to 2.2±0.1s. This is in good agreement with previous observations of reduced proton T_1 in MRI after using iodinated contrast agents[3,4]. On the other hand, the T_1 of DPG remained unchanged after mixing with the contrast agent, 3.7±1.2s to 3.0±0.3s, respectively. This could be expected as the ^{31}P metabolites in blood are predominantly intracellular, and thus, there is no direct contact with the extracellular contrast agent that would influence the relaxation time, as is the case for the water signal. The effect on transverse relaxation (T_2) of water[4,6] was ignored in this study as ^{31}P metabolites have short T_2 times without contrast, and thus free induction decay signals are typically acquired in ^{31}P-MRS[7]. Figure 2 depicts representative high SNR spectra of the blood acquired before and after adding Iopamidol, not showing any visible difference. Similarly, Figure 3 shows a box-plot diagram of fitted metabolite signals showing no difference. Table 1 summarizes the fit details in all three vials with and without contrast, with no significant differences found. This supports our finding of no change in the longitudinal relaxation time after adding the contrast agent (Figure 1), suggesting that metabolic examination using ^{31}P-MRS after a contrast enhanced CT scan using the Iopamidol contrast agent would not be confounded.

Conclusion:

This study demonstrates that CT contrast agent Iopamidol, while having T_1 shortening effect on water signal, has no measurable effect on the ^{31}P-MRS signal. Therefore, we propose that ^{31}P-MRS datasets obtained in patients shortly after contrast-enhanced CT are directly quantifiable and comparable to those obtained without prior administration of CT contrast.

Acknowledgements

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Figures

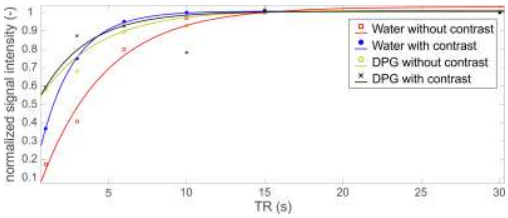

Figure 1: Mono-exponential T_1 fits of water and DPG signals of human blood pre- and post- addition of a clinical dose of CT contrast agent. The iodinated contrast agent shortens the T_1 of water substantially while having no observable effect on the relaxation of the DPG signal.

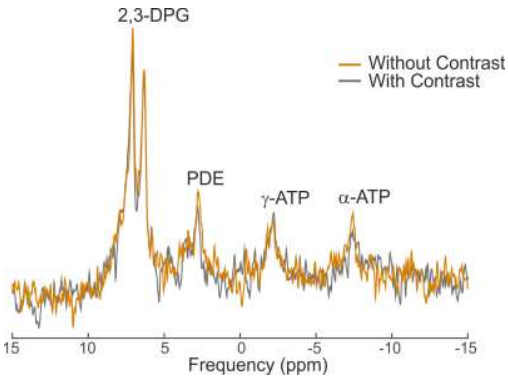

Figure 2: ^{31}P-MR spectra acquired from whole human blood before (brown) and after (grey) addition of Iopamidol. The magnitudes of 2,3-DPG, PDE, γ-ATP and α-ATP are all unaffected by the contrast agent.

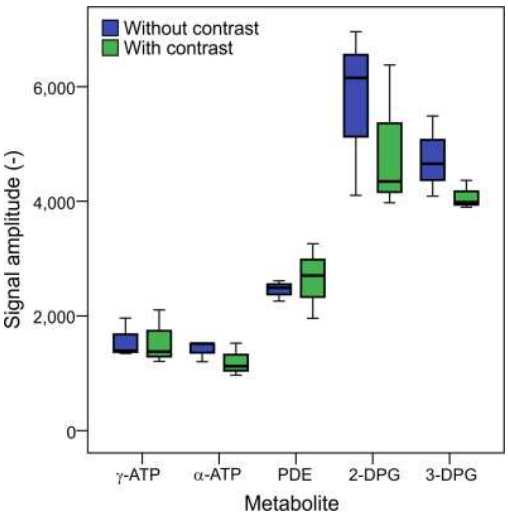

Figure 3: Iodinated contrast agent Iopamidol has no effect on the ^{31}P-MR signal of any of the observed metabolites, suggesting that a ^{31}P-MRS examination is feasible immediately after a contrast enhanced CT scan.

Metabolite	Contrast	Vial 1	Vial 2	Vial 3	p-value
	Pre	6153	6958	4103	

2-DPG	Post	4346	6377	3975	
3-DPG	Pre	4655	5488	4089	0.292
	Post	4364	3898	3984	
PDE	Pre	2613	2492	2259	0.611
	Post	2705	3261	1959	
γ-ATP	Pre	1395	1347	1963	0.968
	Post	1208	1379	2105	
α-ATP	Pre	1202	1517	1517	0.219
	Post	968	1526	1124	

Table 1: Metabolite signal measured in each blood vial before and after adding contrast agent. The last column provides the p-values of the paired t-test.