

The effects of iodinated CT contrast agent on phosphorus MRS

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Synopsis

Contrast-enhanced CT examination can influence ¹H-MRI measurements performed within 24h after the CT scan, due to a reduction in water T₁ and T₂ 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 ³¹P-MRS, by measuring the T₁ of ¹H and ³¹P signals in human blood. We find that iodinated CT contrast agent has no effect on phosphorus T₁s. Therefore, ³¹P-MRS examinations will not be influenced by prior CT (unlike ¹H-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 (³¹P-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 T₁ and T₂ relaxation times of water signals in proton (¹H) MRI for up to 24 hours after the CT scan^{3,4}. However, any potential confounding effects on ³¹P-MRS remain unknown.

Therefore, our aim was to determine whether an iodinated contrast agent affects the longitudinal (T₁) relaxation time of ³¹P 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 ¹H/³¹P 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). T₁ relaxation times were measured on both channels (¹H and ³¹P) 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, θ≈60° nominal flip angle), 32 averages, sw=30kHz. The T₁ measurement was performed before and repeated after the addition of a clinically indicated dose of iodinated contrast agent, lopamidol (1.5mL/kg, i.e. 80mL/vial), and the whole experiment was finished within 2 hours after blood sampling. Water signal from the ¹H spectra and 2,3-diphosphoglycerate (2,3-DPG) signal from the ³¹P spectra were fitted as Lorentzians using a Matlab (Mathworks) implementation of AMARES⁵, and used for determining mono-exponential T₁ relaxation curves in Matlab. The two peaks of 2,3-DPG were summed together for the mono-exponential fitting of T₁s.

The remaining three vials were then used to acquire high SNR, partially saturated ³¹P spectra (TR=1s, θ≈60°, 512 averages) before and after the addition of lopamidol. The same fitting routine was used to fit the signals of 2,3-DPG, phosphodiesteres (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 T₁ fits of water and 2,3-DPG signals from ¹H and ³¹P MRS acquisitions of blood, respectively. The water T₁ shortened after adding lopamidol from 4.8±1.9s to 2.2±0.1s. This is in good agreement with previous observations of reduced proton T₁ in MRI after using iodinated contrast agents^{3,4}. On the other hand, the T₁ 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 ³¹P 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 (T₂) of water^{4,6} was ignored in this study as ³¹P metabolites have short T₂ times without contrast, and thus free induction decay signals are typically acquired in ³¹P-MRS⁷. Figure 2 depicts representative high SNR spectra of the blood acquired before and after adding lopamidol, 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 ³¹P-MRS after a contrast enhanced CT scan using the lopamidol contrast agent would not be confounded.

Conclusion:

This study demonstrates that CT contrast agent lopamidol, while having T₁ shortening effect on water signal, has no measurable effect on the ³¹P-MRS signal. Therefore, we propose that ³¹P-MRS datasets obtained in patients shortly after contrast-enhanced CT are directly quantifiable and comparable to those obtained without prior administration of CT contrast.

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Figures

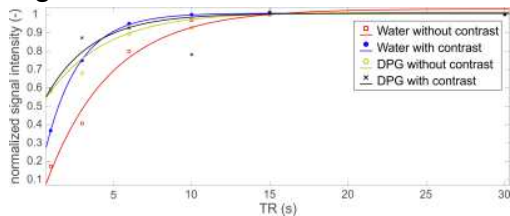


Figure 1: Mono-exponential T_1 fits of water and DPG signals of human blood pre- and post- addition of a clinical dose of CT contrast agent. The iodinated contrast agent shortens the T_1 of water substantially while having no observable effect on the relaxation of the DPG signal.

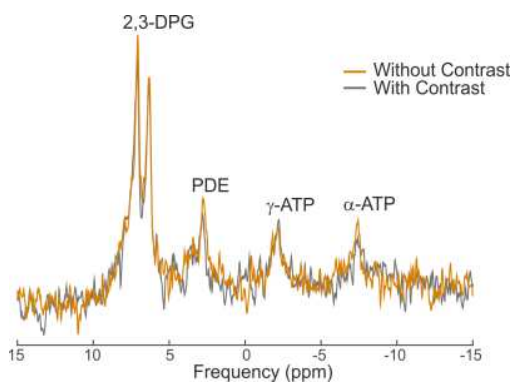


Figure 2: ^{31}P -MR spectra acquired from whole human blood before (brown) and after (grey) addition of lopamidol. The magnitudes of 2,3-DPG, PDE, γ -ATP and α -ATP are all unaffected by the contrast agent.

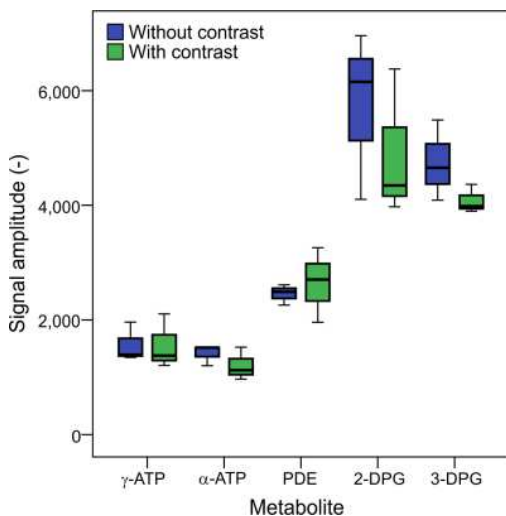


Figure 3: Iodinated contrast agent lopamidol has no effect on the ^{31}P -MR signal of any of the observed metabolites, suggesting that a ^{31}P -MRS examination is feasible immediately after a contrast enhanced CT scan.

Metabolite	Contrast	Vial 1	Vial 2	Vial 3	p-value
---	Pre	6153	6958	4100	---

2-DFP	Post	4346	6377	3975	0.292
	Pre	4655	5488	4089	
3-DPG	Post	4364	3396	3961	0.611
	Pre	2613	2492	2259	
FDE	Post	2705	3261	1959	0.968
	Pre	1395	1347	1963	
γ-ATP	Post	1208	1379	2105	0.219
	Pre	1282	1517	1517	
α-ATP	Post	968	1526	1124	
	Pre				

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.