

More efficient and accurate methods for measuring human cardiac PCr /ATP ratios: benefits of chemical exchange.

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Introduction

For a correct determination of the PCr/ATP ratio at practical repetition times (T_R) knowledge of the effective saturation of the PCr and ATP signals is required. Determination of the saturation factors is complicated by chemical exchange between γ -ATP and phosphocreatine (PCr). This exchange will shorten the apparent T_1 of PCr and increase the apparent T_1 of γ -ATP. Saturation correction using these apparent T_1 's in a model that neglects the exchange will lead to errors. Even at half the exchange rate found for human hearts [1] these errors will be considerable [2], and greatest at short repetition rates (see figure 1).

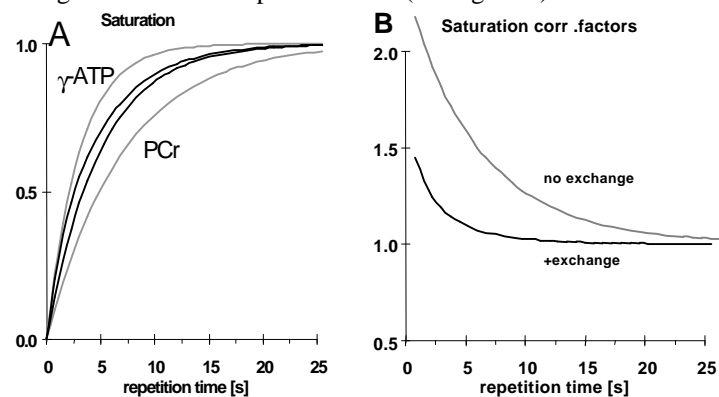


Figure 1 A: Simulated saturation factors (M/M_{eq}) of PCr ($T_1=7$ [s, top lines]) and γ -ATP ($T_1=3$ [s]bottom lines). The middle two lines are the curves with exchange B: the saturation correction factor for the ratio PCr/ γ -ATP ($=1.5$ at equilibrium) with (bottom line) and without PCr - ATP exchange at a rate of 0.25 [s^{-1}](top line).

Therefore effective saturation of PCr, γ -ATP, and β -ATP were measured at various repetition times. With the results efficiency of the measurement of human cardiac PCr/ATP ratios can be optimised for minimal influence of saturation correction, optimum signal to noise and minimal blood correction.

Methods

Localised cardiac ³¹P MR spectra were recorded on at 1.5 T with ECG gated 3D ISIS [3] at nominal repetition time (T_R) of 3[s] and 25 [s] on 12 subjects. On each of these subjects a third spectrum was recorded with $T_R=6$ ($n=4$), 10 ($n=4$) or 15 [s] ($n=4$). Signal intensities were fitted with VARPRO, adjusted for the number of averages and normalised to intensities derived at $T_R=25$ [s] for calculation of saturation factors.

Ratios and saturation factors

The measured metabolite ratios and the saturation correction factors are shown in Table 1. As predicted by simulations [2] the differences in PCr/ γ -ATP ratios at repetition times above 6 [s] are small.

The measured apparent longitudinal relaxation time constants (T_1^*) for PCr and γ -ATP depend on the repetition rates chosen for the progressive saturation measurement [2]. The pooled and normalised signals were fitted with a single exponential function. The apparent T_1 values were PCr: 6.04 ± 0.35 [s], γ -ATP: 4.20 ± 0.55 [s] and β -ATP: 2.46 ± 0.33 [s]. Of these values only the β -ATP is comparable to literature values because the values of other two depend on the choice of repetition times.

Table 1 PCr/ γ -ATP ratios and saturation correction factors

T_R	n	ratio	correction factor
3.425	12	1.25 ± 0.41	1.16 ± 0.39
6.425	4	1.39 ± 0.24	1.04 ± 0.28
10.425	4	1.35 ± 0.43	1.07 ± 0.38
15.425	4	1.36 ± 0.20	1.07 ± 0.26
25.425	12	1.45 ± 0.31	1.00 ± 0.31

averages \pm SD, n = number of volunteers.

The important and useful effect of chemical exchange is that the correction factors for the PCr/ γ -ATP can be small at repetition times above 6 [s].

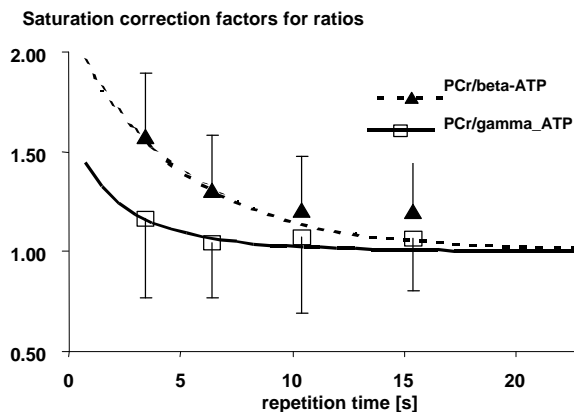


Figure 2 Saturation correction factors for the ratios PCr/ β -ATP (broken line, triangles) and PCr/ γ -ATP (solid line, open squares). Lines are to guide the eye, calculated as in figure 1, β -ATP calculated without exchange.

Blood correction and signal to noise

The blood correction (expressed as % of the γ -ATP signal) is expected to be lower at long repetition times because in contrast to the cardiac tissue the blood signal is not saturated at short repetition times. Blood correction was $23 \pm 11\%$ at $T_R=3$ [s] and $12 \pm 11\%$ at $T_R=25$ [s] (significantly smaller $p < 0.01$, $n=12$).

Theoretically, the optimum repetition rate for the best signal to noise per unit time (efficiency) is at 1.25 times the T_1 . Consequently the optimum repetition rate to measure γ -ATP and PCr would be around 5-8 seconds. In practice the total signal to noise power ratio, estimated by VARPRO and adjusted for total scan times did not significantly diminish up to repetition times of 10 [s] (10.6 ± 3.7 at 10[s] vs. 12.9 ± 4.6 at 3[s]) in spite of the faster relaxation of some of the spectral components.

Conclusions

Cardiac PCr/ATP ratios in humans are best measured using the signal of the γ -ATP phosphate at longer repetition times. For measurements at 1.5T, and 90° flip angles, repetition times between 6-10 seconds are recommended. The efficiency of the experiment is then near optimal for measuring PCr and γ -ATP signals. At these repetition rates the signal corrections for saturation and blood contamination will be smaller and the error introduced by uncertainties about the proper corrections are reduced.

References

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