

# A new FAST method for in-vivo measurement of chemical exchange rates

Ronald Ouwerkerk, Ray Lee, Robert G. Weiss & Paul Bottomley

Division of Magnetic Resonance Research, Department of Radiology, Johns Hopkins University, Baltimore, MD, USA

## Introduction

Compromised energy metabolism is central to many disease states including ischemia and heart failure (1). The measurement in humans of absolute metabolite concentrations, phosphocreatine (PCr) and ATP by in vivo  $^{31}\text{P}$  MRS and total creatine (CR) by  $^1\text{H}$  MRS offers a near-complete picture of the creatine kinase (CK) reaction in steady-state. The forward flux of PCr, creating ATP, is also accessible via saturation transfer  $^{31}\text{P}$  MRS (2). However, current techniques for quantifying chemical exchange require acquisition of about 10 data sets, many fully relaxed, making them untenable for patient studies.

We developed a new method for measuring chemical exchange rates, the **Four-Angle Saturation Transfer (FAST)** method, which cuts scan time by seven-fold or more relative to the conventional method. FAST is based on the Dual Angle method for measuring  $T_1$  (3). We validated the technique in localized and unlocalized measurements of the CK forward reaction rate constant,  $k$ , in the leg, and applied it to the human heart.

## Theory

The FAST method consists of two pairs of measurements:

- Measure the PCr signal at flip angles  $\alpha=15^\circ$  and  $\beta=60^\circ$  with saturation of  $\gamma\text{-ATP}$  as  $S^S(\alpha)$  and  $S^S(\beta)$ .
- Measure the PCr signal at flip angles  $\alpha$  and  $\beta$  in the control experiment as  $S^C(\alpha)$  and  $S^C(\beta)$ . The flux is:

$$k = \left(1 - \frac{M_0^S}{M_0^C}\right) \frac{1}{T_1^S} \quad [1]$$

with  $T_1^S$  defined as the  $T_1$  measured during saturation of  $\gamma\text{-ATP}$  calculated from (3). The equilibrium magnetization with saturation,  $M_0^S$ , and with off-resonance control saturation,  $M_0^C$ , are:

$$M_0 = \frac{S\alpha (\cos[\beta] - \cos[\alpha])}{\sin[\alpha] (\cos[\beta] - 1) - R \sin[\beta] (\cos[\alpha] - 1)} \quad [2]$$

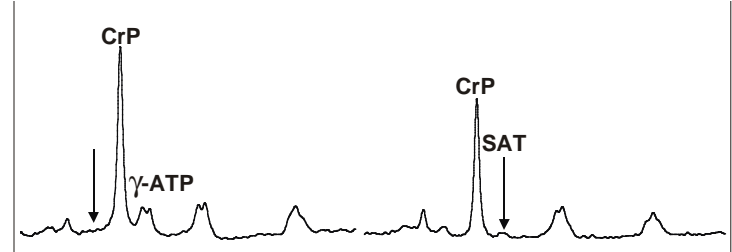
Equation [2] assumes that the longitudinal relaxation can be described by a single exponential, which is valid for the signals acquired with  $\gamma\text{-ATP}$  saturated. Analysis shows that putative errors (4) introduced by the approximations are negligible.

## Methods

$^{31}\text{P}$  MRS was performed on a 1.5 T GE Signa with a 6-cm surface coil. BIRP adiabatic excitation pulses (5) of 4 ms were used to provide exact flip-angles. Square pulses at 2% of the maximum MRS power level were used for selective saturation of  $\gamma\text{-ATP}$  at  $-2.7$  ppm and control irradiation at  $2.7$  ppm relative to PCr. Classic saturation-transfer measurements were first done with variable repetition times (TR = 0.5, 1, 2, 4, 6, 12 and 15 s) while irradiating at  $-2.7$  ppm to measure  $T_1^S$ . TR was set to 16 or 32 s for control measurements of  $M_0^C$  with irradiation at  $+2.7$  ppm  $k$  was then calculated for the classic method from Eq [1].

Next, FAST measurements were performed with TR = 1 s and a 0.8 s saturation pulse with  $15^\circ$  and  $60^\circ$  excitation pulses. After 16 dummy scans, 32 averages were recorded. Non-localized FAST measurements were performed on the calf muscles of 10 normal volunteers, and compared with the classic measurements.

Finally, localized measurements, using 1D phase-encoded MRS were performed on the calf muscle of 4 volunteers, and on the heart of three volunteers.



**Figure 1.**  $60^\circ$  flip angle spectra of human calf muscle with control irradiation (left) and saturation of  $\gamma\text{-ATP}$  (right). Selective RF frequencies indicated by arrows.

## Results and Discussion

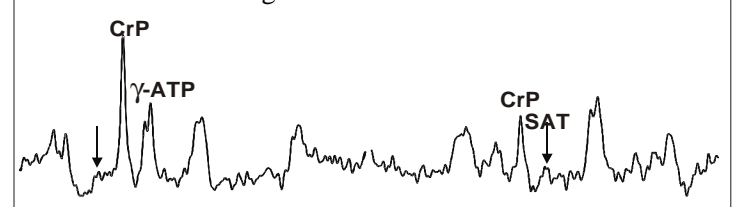
Results for localized and non-localized measurements of the CK forward reaction rate constant,  $k$  in human calf muscle are shown in Table 1.

**Table 1**

Method	Classic method	FAST unlocalized	FAST 1D localized
Mean $k$ ( $\text{s}^{-1}$ )	0.29	0.29	0.27
SD	0.06	0.06	0.09
n	10	10	16 slices, n = 4

In our experiments the unlocalized FAST measurements were acquired seven times faster than for the classic experiments (3 min vs. 21 min.) and delivered the same results and accuracy.

The speed of this new technique makes measurement of CK flux in the human heart at 1.5T feasible in patients. Results from the human heart obtained in 40 min acquisition times are shown in Fig. 2.



**Figure 2.** Spectra ( $60^\circ$  flip angle) of human heart with control RF (left) and saturation of  $\gamma\text{-ATP}$  (right).

## References

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