# New synthetic reference signal injection method for absolute quantitation of metabolite concentration

**D. Lee[1], E. G. Shankland[1], M. Mathis[1], K. I. Marro[1], C. E. Amara[1], C. E. Hayes[1], and M. J. Kushmerick[1]**

[1]Department of Radiology, University of Washington, Seattle, WA, United States

*Introduction*

The ability to quantify metabolites in vivo would improve the diagnosis of human diseases and lead to better understanding of basic physiologic processes. Noninvasive metabolite quantification can be achieved with MR spectroscopy using the synthetic signal injection method, which was previously reported by another research group[1]. The previously reported method originally claimed its feasibility for *in vivo* applications, but has not been successful to widely apply for *in vivo* measurements mainly due to significant radiofrequency (RF) radiation effects. In practice, this method is limited to in vitro applications or to small in vivo subject under an RF screening condition.

We have developed novel hardware and methodology to inject a synthetic reference signal inductively using a small "tickler coil" that was specially designed and constructed to minimize RF radiation effects. We have tested our approach both *in vitro* and in human muscle and our results confirm the accuracy and reliability of the method. The technique is relatively straightforward and can be implemented in any MR system.

*Methods*

Figure 1a shows a block diagram of the synthetic reference signal method as implemented on our 4.7 T system (Bruker magnet, Varian console running VNMR v6.1). An elliptic surface coil (lengths of major and minor axes of the ellipse are 4.5 cm and 3 cm, respectively; C1 in Figure 1b), tunable to the $^{1}$H and $^{31}$P resonance frequencies, was used to quantify human muscle metabolites in localized voxels using the ISIS pulse sequence. A 1 mm diameter tickler coil was used to inductively inject a synthetic reference signal, which was detected along with the in vivo metabolite signal.

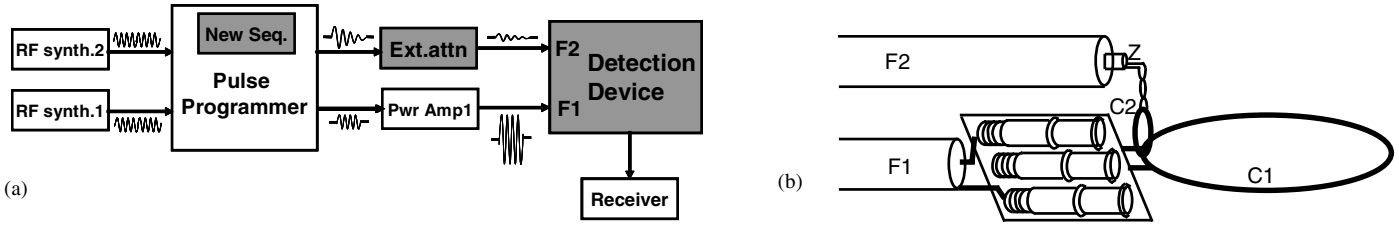


Figure 1. (a) Block diagram of the method with our modifications shown in shaded blocks for the pulse sequence (New Seq.), external attenuator (Ext. attn) and detection device. (b) The detection device for in vivo measurements.

*Results*

Peak areas were measured at different voxel locations to calibrate the synthetic signal as shown in Fig.2. Figure 3 displays a $^{31}$P spectrum acquired from a 1 x 2 x 1.5 cm$^3$ voxel in a human soleus *in vivo*. The concentrations of Pi, PCr, and γ-ATP were calculated to be $2.7 \pm 0.3$, $19.5 \pm 0.1$ and $3.4 \pm 0.3$ mM, respectively. These values are in excellent agreement with previously reported results acquired by the extensive MR quantification procedure using the external reference method.

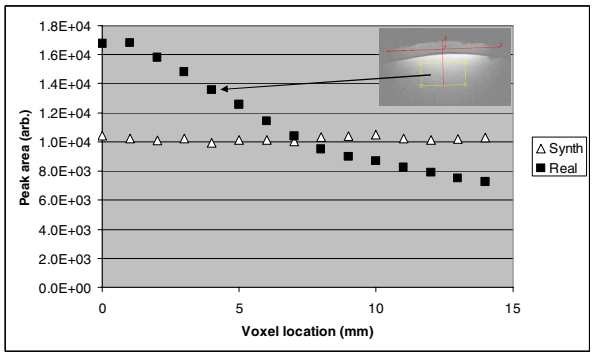


Figure 2. Calibration data for a phantom solution containing 30 mM inorganic phosphate in a 1 liter plastic bag. Real and synthetic signals were acquired for different voxel locations. The image shows the voxel location used for the *in vivo* acquisition shown in Fig.3.

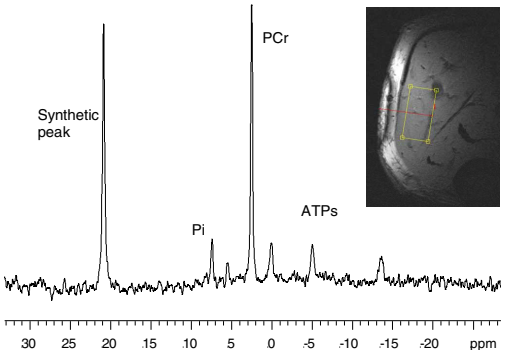


Figure 3. A localized $^{31}$P *in vivo* spectrum obtained from human soleus *in vivo* along with the synthetically injected signal that had been previously calibrated against an inorganic phosphate solution (30 mM). The image in the corner shows the voxel location.

*Discussion*

We have developed a novel reference signal method that eliminates errors due to radiation effects by using a small tickler coil that inductively couples to the main RF coil used to acquire the signal. The tickler coil remains in a fixed location adjacent and orthogonal to the acquisition coil and acts as a constant current source. This design minimizes RF radiation effects and undesirable coupling between the tickler coil and the sample. In this particular implementation the acquisition coil is a dual-tuned surface coil but the concepts and techniques we describe are broadly applicable to any MR-visible nucleus and can be used for both spectroscopy and imaging.

*References*

1. L. Barantin, A. Le Pape, and S. Akoka, A new method for absolute quantitation of MRS metabolites. Magn Reson in Med 38 (1997) 179-82