^{31}CSI and MRS at 7T detect an alkaline pH compartment in resting human soleus muscle

H. E. Kan[1], D. W. Klomp[2], A. G. Webb[1], P. R. Luijten[2], and J. A. Jeneson[3]

[1]Radiology, Leiden University Medical Center, Leiden, Netherlands, [2]High field MR laboratory, RNN, University Medical Center Utrecht, Utrecht, Netherlands, [3]3Biomedical NMR Laboratory, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands

Introduction. Non-invasive fiber-type profiling of human skeletal muscles has been a longtime objective in musculoskeletal MR research. Past MR investigations have typically looked for differential metabolic and pH changes ('split Pi peak') in contracting muscles (1,2). There is, however, some evidence that intracellular pH may also be a sensitive biomarker of muscle fiber type composition in resting muscle (1,3). Specifically, *in vivo* intracellular pH tended to be slightly more alkaline in muscle composed of oxidative fibers than in muscle composed of oxidative as well as glycolytic fibers (1,3). Here, this hypothesis was investigated in human skeletal muscle employing the superior spectral resolution at 7 Tesla.

Methods. The study was conducted in a healthy male subject and adhered to the institutional Medical Ethics Committee guidelines. Data were collected at 7 Tesla on a Philips whole-body scanner (Philips Medical Systems, Cleveland, OH) interfaced with a Varian Inova console. Proton images were acquired using a Nova Medical transmit and receive quadrature birdcage head coil, ^{31}P data were obtained using a home-built transmit and receive linear coil (diameter 5 cm) fitted with a positional MRI marker.

^{31}P MRS. ^{31}P MR spectra (10kHz, 4k datapoints; 64 averages) were acquired from resting soleus and gastrocnemius muscles, respectively, using simple pulse-acquire (200 µs rectangular RF pulse at 500W of RF peak power; TR 1 s) and surface coil localization (Fig 1). Coil placement was guided by manual palpation of the tibia bone and verified using gradient echo images.

^{31}P 3D-CSI. With the surface coil centered on the interface of the medial lobes of the gastrocnemius and soleus muscles, a 512 array of pulse-acquire shots was acquired using the same settings as above synchronised to a Philips 7T MR system that played out the 400 µs phase encode gradients for 3D CSI encoding (4 averages per phase encode step).

Data processing. Spectra were processed and analyzed in the frequency domain using jMRUI. IDL was used for reconstruction of the 3D-CSI data. Intracellular pH was calculated from the chemical shift difference between the P_i and PCr resonances (1).

Results. In the surface-coil localized ^{31}P MR spectrum of the resting soleus muscle, a resonance ~ 0.4 ppm upfield of the main Pi peak was clearly observed and attributed to a second Pi pool (Fig 1C). This resonance was absent in resting gastrocnemius muscle (fig 1D). The CSI data set confirmed this result (data not shown). The two distinct Pi signals in resting soleus report on two pH compartments in the muscle, one with pH = 7.0 (main peak) and one with pH = 7.4. The pH in gastrocnemius muscle was 7.0.

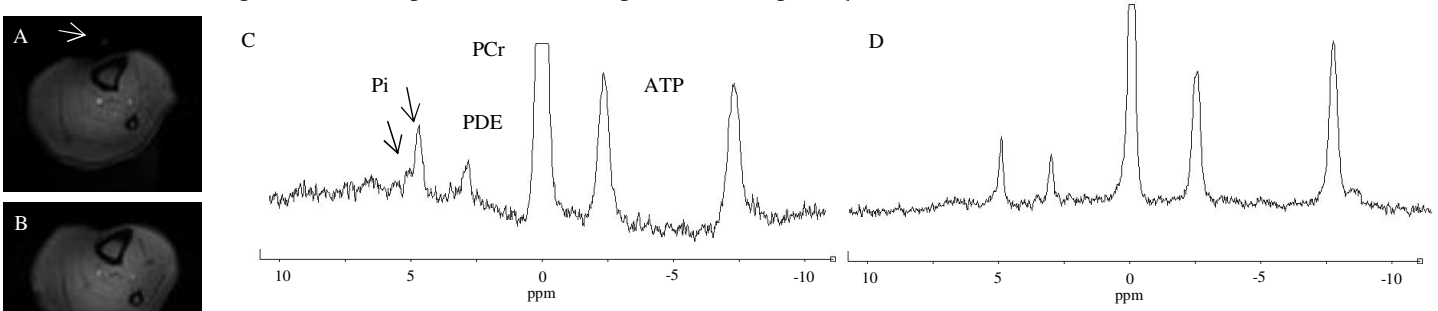

Fig 1. Gradient echo images showing the location of the coil (white arrows) on top of the soleus muscle (A) and the gastrocnemius muscle (B). Corresponding spectra are shown in C and D. The second Pi peak representative of intra mitochondrial Pi in the soleus muscle is visible as a clear shoulder of the main Pi peak in (C), while this is absent in (D).

Discussion. This is the first *in vivo* observation of a Pi resonance from an alkaline compartment in human muscle. The superior spectral resolution at 7T laid at the basis of its discovery. Interestingly, the very same ^{31}P spectrum that we obtained from resting soleus muscle was predicted by Bayesian spectral decomposition of CSI data from the human calf (3). On basis of various considerations including pH and T1 of Pi in the mitochondrial matrix (4), we hypothesize that the Pi resonance at 5.2 ppm originates from the mitochondrial matrix in type I myofibers. If so, ^{31}P MRS at 7T could provide much needed answers to a longstanding, question on the *in vivo* free Pi concentration in mitochondria benefiting computational modeling of cardiac and skeletal muscle (5).

References

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