There has been a long-standing interest in measuring ATP synthesis rates in vivo. Recent studies using 31P saturation transfer (ST) suggest that the inorganic phosphate (Pi) → ATP flux in skeletal muscle may differ with age and development of insulin resistance and type 2 diabetes. Although simple in principle, ST requires prolonged saturation of γ-ATP, typically 5 – 9 sec, which can at some fields be SAR limited. An alternative technique is inversion transfer (IT), but the conventional approach of selective inversion of γ-ATP is less efficient in reducing the Pi signal due to rapid leaking of magnetization to other spins in the exchange network, especially phosphocreatine (PCr).

PURPOSE: This study was designed to develop a magnetization transfer (MT) method that is sensitive to the γ-ATP ↔ Pi exchange pathway and that can be easily implemented on a human scanner for skeletal muscle studies.

METHODS: Wideband inversion was used to invert all major 31P spins upfield of Pi, including PCr (0 ppm), γ-, α- and β-ATP (-2.4, -7.4 and -16.0 ppm) followed by a variable post-inversion delay period (td) to allow for chemical and spin magnetization exchanges before a hard-pulse readout. A series of 31P spectra were acquired at 7T from human calf muscle of 4 healthy subjects at rest with varying td from 35 ms to 10 sec (12 data points) while keeping TR constant (20 sec). To correct for any partial inversion of Pi spins, 31P data were also acquired using an inversion pulse with the same bandwidth (2700 Hz) but applied on the opposite side of Pi. A partial volume 1H/31P coil (φ = 10 cm) was used for 31P detection. The protocol was approved by our local IRB.

RESULTS: 31P spectra acquired with wideband inversion (Fig 1a) clearly showed a reduction in the intensity of Pi due to chemical exchange (Fig1b). There was a 4.5-fold increase in MT effect at Pi when using wideband inversion as compared to frequency-selective inversion of only γ-ATP (18% vs 4%, measured from Pi Mz/Mzmax ~ td curves at the maximal Mz reduction points, Fig 1b inset). The first-order rate constant for ATP synthesis calculated from these data was 0.06 ± 0.02 s⁻¹ (n=4), in agreement with results by frequency-selective inversion (0.05 s⁻¹) and by ST (0.05 – 0.11 s⁻¹) in literatures.

DISCUSSION: With wideband inversion, both PCr and γ-ATP are inverted. This enables the replenishment of inverted γ-ATP by the long T1 of PCr (Fig 1c) via creatine kinase-mediated pathway, and consequently amplifying chemical exchange effects at Pi. In comparison, using frequency-selective inversion of only γ-ATP, the inverted γ-ATP is drained by un-inverted PCr thereby attenuating the exchange effects seen at Pi (Fig 1c). For studies of γ-ATP ↔ Pi exchange kinetics, it is advantageous to choose wideband over frequency-selective inversion at high fields due to the increased T1 value for PCr.

CONCLUSIONS: Wideband 31P inversion provides an alternative approach for monitoring ATP synthesis in skeletal muscle. The single 31P inversion pulse necessary for this measurement was easy to implement on the 7T scanner.

Fig.1 (a) 31P MR spectra after wideband inversion at different delay times (td). (b) Inversion recovery data showing replenishment of the inverted γ-ATP signal and the long-T1 PCr signal where Mzmax is the equilibrium Z-magnetization at TR 20 sec. Other NMR parameters: NSA = 4; excitation bandwidth 4 KHz; wideband/ selective inversion bandwidth 2700/250 Hz.