

Water fat separated MRI during cooling-reheating for the estimation of brown fat amount and activity

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Target audience: Researchers interested in quantification of brown adipose tissue, in obesity and type 2 diabetes.

Introduction: MRI based quantification of brown adipose tissue (BAT) amount and activity in humans is subject of ongoing research but to date no standardized method has been generally accepted. One of the promising techniques is water-fat MRI¹⁻³ where assumptions of higher water content in BAT than in white adipose tissue (WAT) and differences in R_2^* between the tissues (due to mitochondrial density, blood volume and oxygenation) are made. Multi-echo acquisition enables quantitative and simultaneous estimations of fat fraction (FF) and R_2^* for adipose tissue characterization⁴. Studies performed using FDG-PET/CT have shown intersubject and intrasubject (following 3h cold exposure) increase in CT Hounsfield units (HU) with BAT activation⁵⁻⁷. These results indicate decreased fat content in BAT after cold exposure, possibly as a result of intracellular lipid consumption. Yet, a corresponding decrease in BAT-FF, estimated by MRI, has not been presented. Neither has the possible contribution of blood volume, following altered perfusion, to the decreased fat content been assessed. A previous PET/CT study shows evidence of increased perfusion in supraclavicular BAT after cold exposure⁸ indicating the importance of considering perfusion in the interpretation of fat fraction measurements. By reheating a subject after cold exposure the possibly increased perfusion might return to baseline state and hence the two effects could be separated. **Purpose:** To evaluate: 1) the effect of mild 3h cooling on cervical-supraclavicular adipose tissue (hereafter denoted "BAT") FF and R_2^* 2) the potential of a cooling-reheating water-fat MRI protocol for assessing BAT amount and activity by targeting changes in FF and R_2^* between warm and cold conditions

Methods: Healthy volunteers (4 males, 5 females, age 30±5 [22-37] years, BMI 23.2±2.5, fasted for 4h) were imaged on a 1.5T clinical MR system (Philips Achieva, Philips Healthcare, Best, Netherlands) in the cervical-supraclavicular region using a spoiled 3D multi gradient echo sequence, a 16 channel neurovascular receive coil and a 4 min 40 s scan in free breathing. Scan parameters were: TR/TE1/ΔTE = 32.7/1.68/2.87 ms, 6 unipolar echoes, flip angle 6. The imaging protocol and the water-fat reconstruction has previously been presented⁹. Subjects were scanned at three timepoints; baseline, after mild cold exposure (18.7°C, 3h, standardized clothing) and after short reheating (blankets and a bottle of warm water, approx 20 min). Manual identification of a crude "BAT" VOI (including all slices) was performed with subsequent addition of range limits on FF (>40 %) and R_2^* (<50 s⁻¹) to exclude non-fatty tissues. Partial volume effects from neighbouring tissues were further reduced by morphological erosion. Delineation was made in the FF images, considering also the water signal and R_2^* data. Subcutaneous adipose tissue (SAT) was delineated by an automated method using a series of morphological operations to segment the posterior SAT volume. The same criteria for minimizing partial volume effects as in "BAT" were applied.

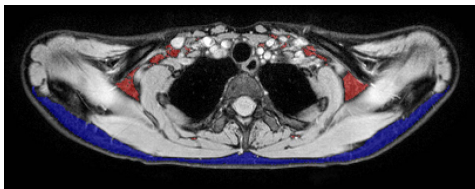


Figure 1: Representative example of "BAT" VOI (red) and SAT VOI (blue).

Timepoint	"BAT"-FF[%]	SAT-FF[%]	"BAT"- R_2^* [s ⁻¹]	SAT- R_2^* [s ⁻¹]
Baseline	82.8 ± 5.0	86.2 ± 4.6	21.0 ± 1.8	19.5 ± 2.7
After cold exposure	80.9 ± 6.4	86.4 ± 4.4	21.6 ± 2.1	20.0 ± 2.7
After reheating	80.9 ± 6.6	85.5 ± 4.6	21.1 ± 2.1	20.1 ± 3.1

Table 1: FF and R_2^* (n=9, mean ± std) of "BAT" and SAT

Results: On group level the FF tended to be lower in "BAT" compared to SAT, (p=0.066), whereas the R_2^* tended to be higher (p=0.139) in "BAT" than SAT (Table 1, Figure 2a). The "BAT"-FF decreased by 2% (P=0.015) on average following 3h cold exposure and remained decreased after reheating (P=0.008, compared to baseline). The "BAT"- R_2^* did not change significantly but tended to increase after cooling (P=0.066) and tended to normalize (P=0.722, compared to baseline) after reheating. Data from individual subjects are shown in Fig. 2. "BAT"-FF decreased in 78% of the subjects during cold exposure. However, after subsequent reheating both increasing and decreasing pattern in "BAT"-FF were observed. The "BAT"- R_2^* showed no general trend following cold exposure and subsequent reheating.

Discussion: The trends of lower FF and higher R_2^* in "BAT" compared to SAT is in line with previous studies using water-fat MRI, despite the use of a large VOI and without knowledge of actual BAT presence in present study. The decrease in "BAT"-FF after cold exposure in the majority of subjects supports results from previous studies showing increased CT Hounsfield units and may reflect both intracellular lipid consumption and increased perfusion. The intersubject variation in "BAT"-FF and "BAT"- R_2^* , after cold exposure and subsequent reheating, suggests individual relative amounts of BAT and WAT in the cervical-supraclavicular depot which possibly could be used for quantification of BAT in humans. The difference in FF and R_2^* between "BAT" and SAT could contribute to assessing the amount of BAT whereas the difference in "BAT" between baseline and reheating could help assessing BAT activity via quantification of consumed intracellular BAT lipids.

Conclusion: The general decrease in "BAT"-FF following 3h cold exposure confirms results from previous PET/CT-studies suggesting a decreased relative fat content after cooling. By adding a reheating timepoint to the cold exposure protocol, the BAT activity in terms of intracellular lipid consumption could potentially be separated from perfusion effects.

References: [1] Hu. AMJR 2013 Jan;200(1):177-83 [2] Chen. J Nucl Med. 2013 Sep;54(9):1584-7 [3] Rooijen. Invest Radiol. 2013 Oct;48(10):708-14 [4] Hu. JMRI 2010 31(5):1195-202 [5] Baba. J Nucl Med. 2010 Feb;51(2):246-50 [6] Hu HH, J Comput Assist Tomogr. 2011 Jan-Feb;35(1):65-71 [7] Ouellet. J Clin Invest. 2012 Feb 1;122(2):545-52 [8] Orava. Cell Metab. 2011 Aug 3;14(2):272-9 [9] Lundström. ISMRM 2013. 4050

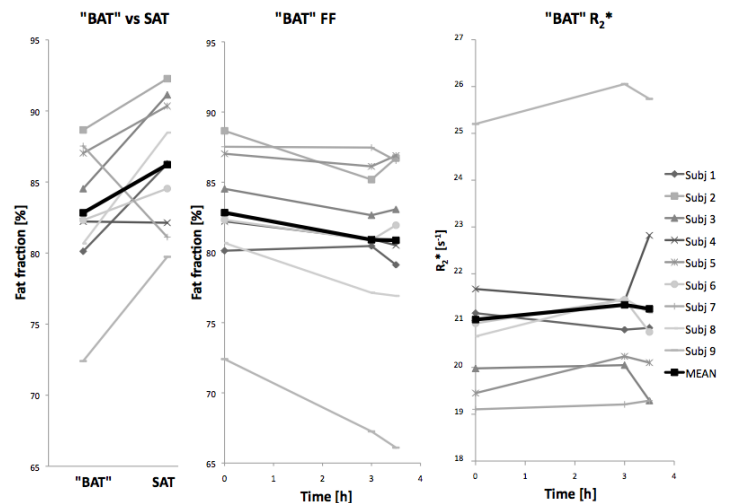


Figure 2: (a) FF of "BAT" and SAT. (b) FF and (c) R_2^* of "BAT" for each subject at baseline (t=0), after cold exposure (t=3h), after reheating (t=3.5h). Each FF and R_2^* value represents the mean VOI value.