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Detection and quantification of fat in liver and brown adipose tissue in humans.

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The importance of fat fraction quantification in the human tissue is growing with the epidemic of obesity and increasing prevalence of diabetes mellitus type 2 and non alcoholic fatty liver disease. Magnetic resonance imaging approach employs different relaxation behavior and signal phase evolution of protons in water and fat molecules for the calculation of water/fat fraction maps of observed tissue. Our project consisted of two parts. The first one was focused on the verification of MR System manufacturer (Siemens Healthineers, Germany) proprietary Fat Fraction quantification tool from MRI (Magnetic Resonance Imaging) data and compare it with spectroscopic measurements especially in the dynamic range of low FF values characteristic for human liver; in the second part, we tried to find the best way for reliable detection and accurate quantification of BAT (Brown Adipose Tissue) in humans.

In the end of the year 2015 and during the whole year 2016 were realized four visits (Radim Kořínek, PhD) in Vienna (Universitätsklinik für Innere Medizin III, Klin.Abt. für Endokrinologie und Stoffwechsel), and two visits (Martin Krššak, PhD and Radka Tušková, PhD) in Brno (Brno University of Technology, Department of Theoretical and Experimental Electrical Engineering; Institute of Scientific Instruments of the CAS, v. v. i.). All necessary measurements were realized in Vienna at 3T MRI system and data processing was performed partially in Vienna and Brno.

1. Verification of MR system manufacturer FF quantification:

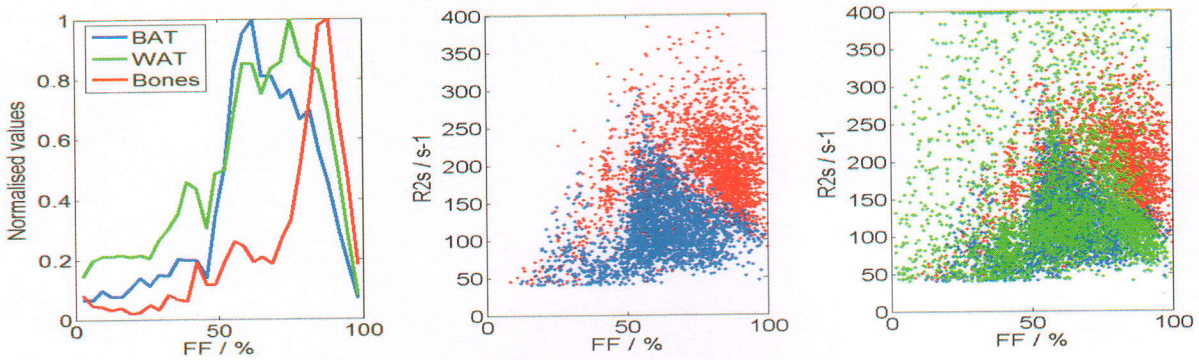
Two phantom objects were designed for the evaluation of the manufacturer WIP tool. In the first phantom, Intralipid 20% (20% I.V. Fat Emulsion) emulsion was selected as the basic substance. The combination of different ratios with saline solution resulted in the several different fat concentrations in the range between 0 – 20% of Fat Fraction. For higher FF values sunflower oil was mixed in different ratios with water, agar (Agargel™ SIGMA/A3301) and lecitine (emulgator). The homogenizer was used to mix thoroughly all substance components of final emulsion. The modified procedure to create the second phantom was successfully used in the evaluation of new 3PD (three-point Dixon) method FTSED [Korinek et al., 2017, JMRI]. The first type of phantoms (Intralipid + saline) was created in Vienna; on the other hand, the second phantom was realized in Brno (more complex preparation and necessity of homogenizer).

The phantoms were measured by multi-point Dixon (MPD) sequence VIBE (Volumetric interpolated breath-hold examination (VIBE) sequence) and spectroscopic sequences (STEAM, PRESS and HISTO). The MRI data were evaluated in Siemens WIP tool for

fat fraction quantification; besides, the MRI data were processed in the specialized MATLAB® toolbox for water/fat quantification (Hernando D, Hu H. Fat – Water toolbox v1, ISMRM 2012). The measurements showed, that for correct fat fraction quantification of Intralipid phantom in manufacturer proprietary WIP tool implementation of different, Intralipid specific, signal model is required. It ensures the correct fat fraction quantification. Besides the phantom measurements, the fat fraction quantification was confirmed by in-vivo measurements of specific parts in livers. The final manuscript is under preparation. The first results were published on the workshop on MR Studies in Rožnov pod Radhoštěm organized by IKEM (Prague) and MUW (Vienna). The part of these results was presented at the Annual Meeting of European Society for Magnetic Resonance in Medicine and Biology (ESMRMB) and published in the ESMRMB Book of Abstracts [Korinek et al., 2016, ESMRMB 2016].

2. Detection and characterization of BAT in humans

The detection and segmentation of total adipose tissue is generally provided directly by Dixon methods. One of the characteristic of metabolically active brown adipose tissue is increased water- (up to 50%) and reduced fat fraction when compared to white adipose or skeletal which is yield almost 100% of fat specific MR signal. This condition is often used in (semi)-automatic detection and segmentation However, the differentiation of brown adipose tissue (BAT) from white adipose tissue (WAT) by MRI turned out problematic and ambiguous based on the different FF values as is shown below. We tried more complex multi-parametric segmentation to distinguish the BAT from WAT and bone narrow (based on R2* and FF values). The results show, that automatic BAT detection is very problematic and in many cases impossible.



The second and more reliable way to detect a BAT is functional MRI method acquiring images before and during activation by cold exposure. This is achieved by cooling tubes placed on a patient body. The fat fraction will change (decrease) in the region containing BAT. The number of adult patients/volunteers with detectable amount of BAT in population is very low; therefore, the finding of suitable candidate for fMRI of BAT is complicated. In our case, the one volunteer was measured by fMRI in Vienna at 3T. The results confirm that fMRI is one of the possible suitable ways for BAT detection and quantification. The acquired

experiences will be used for next development on the field of BAT detection at MUW in Vienna.

Visits in Vienna:

1st visit: From 23 to 27 November, 2015. (Radim Kořínek, PhD)

2nd visit: From 15 to 19 January, 2016. (Radim Kořínek, PhD)

3rd visit: From 19 to 23 September, 2016. (Radim Kořínek, PhD)

4th visit: From 28 November to 2 December, 2016. (Radim Kořínek, PhD)

Visits in Brno:

1st visit: From 15 to 16 June, 2016. (Martin Krššák, PhD)

2nd visit: From 18 to 20 November, 2016. (Radka Tušková (Klepochová), PhD)

Workshops and Conferences:

- *Workshop on MR Studies in Roznov pod Radhostem (23.-25. June 2016). Presentation:* Kořínek R, Krššák M, Gajdošik M, Kannengiesser S. MRI based characterization of adipose tissue.

- *ESMRMB 2016 Congress, September 29 - October 1, 2016, Vienna/AT, 33rd Annual Scientific Meeting.*

Publications:

- R. Korinek, M. Gajdošík, S. Trattnig, M Krššák. Quantification of low fat fractions at 3T: comparison of water-fat imaging toolbox and MR spectroscopy. Book of Abstracts ESMRMB 2016 (e-only). Volume 29, Issue 1 Supplement, September 2016
Book of Abstracts ESMRMB 2016 (e-only) ISSN: 0968-5243 (Print) 1352-8661 (Online); (http://link.springer.com/journal/10334/29/1/suppl/page/1)

- Korinek R, Bartusek K, Starcuk Z Jr. Fast triple-spin-echo Dixon (FTSED) sequence for water and fat imaging. Magn Reson Imaging. 2016 Nov 24;37:164-170. doi: 10.1016/j.mri.2016.11.015. [Epub ahead of print].

In Brno 21st of January 2017

Radim Kořínek, PhD & Martin Krššák, PhD