Rapid Body Composition Measurements Reveal Detailed Metabolic Changes in Large Scale Population Studies

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Introduction

Body composition measurements, such as adipose tissue compartments, muscle volumes, and muscle tissue composition are increasingly important in research and clinical context. Up until recently many MR-protocols in combination with analysis methods for segmenting muscle and fat compartments in the body were laborious and time-consuming. This has hindered implementation in large cohorts and in clinical applications. In this article we present a rapid and robust MR-protocol for body composition profiling and initial clinically relevant findings. This MR-protocol enables accurate measurements of visceral adipose tissue, abdominal subcutaneous adipose tissue, thigh muscle volumes, as well as other specific biomarkers such as liver and intra-muscular fat content. The MR-protocol and analysis method were applied and quality assured in the vast UK Biobank imaging cohort showing excellent results in terms of compliance and scan precision.

The UK Biobank imaging study

The UK Biobank is a very large and detailed prospective study following about 500,000 volunteers in the UK for over 25 years. Participants were aged from 40 to 69 when recruited between 2006 and 2010. The ambitious study collects data ranging from questionnaires and physical measurements to genome-wide genotyping. In 2014 an imaging sub-study was added to the biobank and the plan is to scan 100,000 participants by 2021. Participants are ineligible for imaging if they have metal or electronic implants, had surgery within six weeks before imaging, or if they have medical conditions that would make it difficult to conduct the imaging, such as hearing or breathing problems. The UK Biobank imaging sub-study includes detailed MR examinations of the brain, heart, abdomen, and body (neck to knee), as well as ultrasound and dual-energy X-ray absorptiometry (DXA). The North West Multicentre Research Ethics Committee (MREC), UK, approved the study and written informed consent was obtained.

<table>
<thead>
<tr>
<th></th>
<th>First slab (neck region)</th>
<th>Slabs two to four (torso region)</th>
<th>Slab five (upper leg region)</th>
<th>Slab six (lower leg region)</th>
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<tbody>
<tr>
<td>Repetition time (ms)</td>
<td>6.69</td>
<td>6.69</td>
<td>6.69</td>
<td>6.69</td>
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<tr>
<td>Echo time (ms)</td>
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<td>2.39 &amp; 4.77</td>
<td>2.39 &amp; 4.77</td>
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<tr>
<td>Bandwidth (Hz)</td>
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<td>440</td>
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<td>440</td>
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<td>Slices (-)</td>
<td>64</td>
<td>44</td>
<td>72</td>
<td>64</td>
</tr>
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<td>2.23 x 2.23 x 4.5</td>
<td>2.23 x 2.23 x 3.5</td>
<td>2.23 x 2.23 x 4</td>
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<tr>
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<td>224 x 174</td>
<td>224 x 162</td>
<td>224 x 156</td>
</tr>
<tr>
<td>Breath-hold time (s)</td>
<td>–</td>
<td>17</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 1: Summary of the 6-minute Dixon VIBE-based neck to knee body composition MR-protocol presented per region.
obtained from all participants prior to study entry [1, 2]. The research presented in this communication has been conducted using the UK Biobank Resource under Application Number 6569.

**A body composition MR-protocol**

All eligible participants were imaged using 1.5T MAGNETOM Aera MR-scanners (Siemens Healthcare, Erlangen, Germany). The participants were imaged in supine position with the arms along the sides, initial isocentering was performed with the laser crosshair on the participant’s clavicles and no localizer sequence was used. The MR-protocol was based on T1-weighted VIBE Dixon and had a total cranio-caudal coverage of 1.1 m divided over six overlapping slabs of axial 3D spoiled gradient dual-echo images. The acquired images covered a region between the neck and the knees. Detailed protocol parameters are presented in Table 1 and the parameters differed between the slabs depending on which anatomical region was being imaged. Over the torso region (slabs two to four) imaging was performed during 17 s expiration breath-hold. The total time for the MR body composition protocol was about 6 minutes. Reconstruction of Dixon water and Dixon fat images was performed using the integrated scanner software. Examples of the reconstructed water and fat images are shown in Figures 1A, B for two participants.

**Body composition profiling**

The body composition profile of all participants was based on quantifying fat and muscle compartments such as visceral adipose tissue, abdominal subcutaneous adipose tissue, and thigh muscle volumes as well as intra-muscular and liver fat content (hepatic proton-
density fat fraction; PDFF). Body composition profiling was performed using the commercially available service AMRA® Profiler (AMRA Medical AB, Linköping, Sweden). The profiling consisted of the following steps:

1. automatic image calibration,
2. automatic labeling and registration of fat and muscle regions to the acquired image volumes,
3. quality control of anatomical regions and MR-data performed by trained analysis engineers at AMRA Medical, and
4. quantification of fat and muscle volumes based on the calibrated images.

Full details of the body composition profiling can be found in [2].

The semi-automated methods for analysing the body composition profile have up to now been shown to provide high repeatability and accuracy for adipose abdominal tissue volume, thigh muscle volumes, and liver fat content. When BMI was also included in the matching criteria the association of visceral adipose tissue volume and liver fat content to type 2 diabetes remained [5]. Cardiovascular disease is another disease relating to the metabolic syndrome. When we explored the body composition profiles for 213 participants with a history of cardiovascular events (angina, heart attack, or stroke) with age and gender matched controls with high blood pressure a strong disease association was found for multiple body composition parameters. Specifically, the visceral and total adipose tissue volume as well as liver fat content was significantly higher in the cardiovascular disease group whereas the muscle ratios were found to be lower, the association between visceral fat and cardiovascular disease remained when BMI was also included in the matching criteria [6].

As the inclusion in the UK Biobank imaging study continued we explored a larger group in 2017 (6 021 participants) and we found that the visceral adipose tissue volume was significantly associated with prior hospitalization [7]. An obese sub-population in this large group was further explored for the association to previous cardiovascular events and type 2 diabetes. In this case we found that visceral adipose tissue volume was significantly higher for both the diabetic and cardiovascular event groups. The participants that had reported previous diabetes had a lower muscle ratio and higher intra-muscular fat content than the participants without previous diabetes or cardiovascular events. The liver fat content was significantly higher in the diabetic group compared both controls and the cardiovascular event groups, no significant differences were observed comparing controls to the cardiovascular event group [8].

The non-alcoholic fatty liver disease spectrum is of growing concern and multiple pharmaceutical companies and research groups are working diligently to explore potential treatments to this worldwide epidemic. The disease spectrum is initially characterized by increased liver fat content (hepatic steatosis) and in the obese sub-population we explored if a fatty liver was associated
with increased health care burden (defined by the accumulated hospital nights). This analysis was slightly more complex as the association was significantly negative when controlling for visceral and total abdominal adipose tissue volumes (the models were also adjusted for age, sex, smoking, alcohol intake, and physical activity). The observation suggested that hepatic steatosis may have a link to visceral adiposity in participants with an increased health care burden in a phenotype presenting with high visceral adipose tissue volume together with low liver fat content [9].

Sarcopenia is a common problem in the aging population as well as in certain disease states, such as non-alcoholic steatohepatitis. In the UK Biobank imaging study DXA, which is typically used to diagnose sarcopenia, is also acquired and in 2016 we explored the relationship between the body composition profile derived from the MR-examination and the DXA-based biomarker for sarcopenia. We found that the total lean thigh muscle volume divided by the square of the height could be used to identify sarcopenic participants with an AUROC of 0.96. This suggests that sarcopenia can be characterized from this Siemens MR body composition protocol with high sensitivity and specificity [10].

**Conclusions**

In this article we have presented a robust and rapid neck to knee MR-protocol for Siemens MR-scanners that can deliver high technical success rates in large scale population studies. We have also presented initial clinical findings based on analysing the body composition profile in such a large population. We believe that this is a widely applicable method in a clinical and research setting investigating metabolic disease, muscle degenerative
disease, as well as metabolic components of other diseases. The simultaneous assessment of multiple important fat and muscle compartments increase the understanding of the complex interplay between disease development and metabolic processes.

References


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