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Measurement of brown adipose tissue mass using a novel dual-echo magnetic resonance imaging approach: A validation study

Milja Holstila[a], *Kirsi A. Virtanen*[b], *Tove J. Grönroos*[b], *Jukka Laine*[c], *Virva Lepomäki*[b], *Jani Saunavaara*[a], *Irina Lisinen*[b], *Markku Komu*[a], *Jarna C. Hannukainen*[b], *Pirjo Nuutila*[b,d], *Riitta Parkkola*[a,*], *Ronald J.H. Borra*[a,b,e]

[a] *Medical Imaging Centre of Southwest Finland, Turku University Hospital, Turku, Finland*
[b] *Turku PET Centre, University of Turku and Turku University Hospital, Turku, Finland*
[c] *Department of Pathology, University of Turku and Turku University Hospital, Turku, Finland*
[d] *Department of Medicine, University of Turku and Turku University Hospital, Turku, Finland*
[e] *A.A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, MA, USA*

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ABSTRACT

Objective. The aim of this study was to evaluate and validate magnetic resonance imaging (MRI) for the visualization and quantification of brown adipose tissue (BAT) in vivo in a rat model. We hypothesized that, based on differences in tissue water and lipid content, MRI could reliably differentiate between BAT and white adipose tissue (WAT) and could therefore be a possible alternative for ^{18}F-Fluorodeoxyglucose Positron Emission Tomography (^{18}FDG-PET), the current gold standard for non-invasive BAT quantification.

Materials/Methods. Eleven rats were studied using both ^{18}FDG-PET/CT and MRI (1.5 T). A dual echo (in-and-out-of-phase) sequence was used, both with and without spectral presaturation inversion recovery (SPIR) fat suppression (DUAL-SPIR) to visualize BAT, after which all BAT was surgically excised. The BAT volume measurements obtained via ^{18}FDG-PET/CT and DUAL-SPIR MR were quantitatively compared with the histological findings. All study protocols were reviewed and approved by the local ethics committee.

Results. The BAT mass measurements that were obtained using DUAL-SPIR MR subtraction images correlated better with the histological findings ($P = 0.017$, $R = 0.89$) than did the measurements obtained using ^{18}FDG-PET/CT ($P = 0.78$, $R = 0.15$), regardless of the BAT metabolic activation state. Additionally, the basic feasibility of the DUAL-SPIR method was demonstrated in three human pilot subjects.

Conclusions. This study demonstrates the potential for MRI to reliably detect and quantify BAT in vivo. MRI can provide information beyond that provided by ^{18}FDG-PET imaging, and its ability to detect BAT is independent of its metabolic activation state. Additionally, MRI is a low-cost alternative that does not require radiation.

Abbreviations: MRI, magnetic resonance imaging; BAT, brown adipose tissue; WAT, white adipose tissue; ^{18}FDG-PET, ^{18}F-Fluorodeoxyglucose positron emission tomography; CT, computed tomography; FDG, fluorodeoxyglucose; SPIR, spectral presaturation inversion recovery.

* *Corresponding author*. Medical Imaging Centre of Southwest Finland. Tel.: +358 2 313 0148; fax: +358 2 313 2950.
E-mail address: riitta.parkkola@tyks.fi (R. Parkkola).

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1. Introduction

1.1. Background

Two types of adipose tissue are present in the human body: brown and white adipose tissue. The predominant adipose tissue type, white adipose tissue (WAT), is the primary site of regular energy storage, whereas the thermogenic metabolic activity of brown adipose tissue (BAT), which is innervated by the sympathetic nervous system, is more acutely induced by dieting and cold temperatures [1,2]. Long-term cold exposure is believed to increase the volume of BAT [3–5], while short-term cold exposure causes metabolic activation [1,6]. The important role of BAT, as determined by in vivo study, in cold-induced thermogenesis in human adult energy balance has attracted tremendous interest recently, especially because changes in BAT may have a role in the pathogenesis of type 2 diabetes and obesity [7–9].

BAT has been reported to account for 11.8% of the resting metabolic rate, albeit with high individual variation [10]. The amount of brown adipose tissue is inversely correlated with body-mass index, which strongly suggests that brown adipose tissue may have a role in adult human metabolism [2,11]. Additionally, outside temperature, sex, body mass index and diabetic status have all been shown to affect the glucose-uptake activity of BAT in humans [12,13].

To date, in vivo observations of BAT have been performed mainly using clinical ^{18} F-fluorodeoxyglucose positron emission tomography (^{18}FDG-PET); these observations have revealed that a substantial fraction of adult humans have areas of symmetrical high FDG uptake [14]. In adult humans, the most common location for BAT is the cervical–supraclavicular depot [11]. BAT can also be found in paravertebral, mediastinal, para-aortic, and suprarenal locations [11,12]. However, the visibility of subclavicular depots of BAT by ^{18}FDG-PET in humans has been validated by biopsies only recently [1]. In studies conducted after cold exposure, the prevalence of detectable BAT depots by ^{18}FDG-PET approaches 100% in healthy volunteers [6].

In clinical settings, MRI has been considered the most suitable modality for imaging and quantifying fat tissue due to its superior soft-tissue contrast and resolution. Some studies of BAT-containing tumors, such as pheochromocytomas [15] and hibernomas [16–19], have been reported, but none of them characterized BAT using MRI in healthy humans. In rats, several MR techniques, including magnetic spectroscopy [23,24], have been employed to quantify BAT using 4.7 T, 7 T and 9.4 T small bore animal MR systems [20–23]. The most promising approach seems to be in- and out-of-phase imaging [21,22,25]. Additionally, fat water mapping at a field strength of 3 T has been used to quantify BAT in mice [26].

These techniques are based on the fact that brown adipose tissue has a higher water content than WAT, which should allow the differentiation of BAT from the surrounding WAT tissue using in- and out-of-phase imaging [28]. Furthermore, while ^{18}FDG-PET/CT only identifies activated BAT that has increased metabolic activity (glucose uptake), MRI provides superior anatomical resolution and thus has the potential to determine BAT volume in a more reliable fashion, regardless of the activation state. To the best of our knowledge, no studies comparing MR in- and out-of-phase imaging with ^{18}FDG-PET and histology have been previously reported.

1.2. Rationale

In the current study, we aimed to validate our novel and rapid method of BAT imaging at 1.5 T magnetic field strength using in- and out-of-phase dual echo MR imaging combined with spectral presaturation inversion recovery (DUAL-SPIR) in a rat model by directly comparing the MR findings with those of ^{18}FDG-PET/CT and histology. Additionally, we aimed to demonstrate the feasibility of this technique for detecting BAT in the cervical–supraclavicular region of a healthy human subject.

2. Methods

2.1. Ethical approval

The animal study protocol was reviewed by Ethics Committee for Animal Experimentation at the University of Turku, Finland and was approved by the State Provincial Office of Western Finland (STH39A//ESLH-2006-11128/Ym-23).

2.2. Study animals and design

Eleven male Sprague–Dawley rats, weighing 325–400 g, bred at the animal facility of the University of Turku were housed under standard conditions (20±1 °C, humidity 55% ± 5%, lights on from 6:00 a.m. to 6:00 p.m.) with free access to standard food and tap water. Because our local Ethics Committee did not grant permission for cold exposure of the rats, they were not exposed to cold. On a given study day, an ^{18}FDG-PET/CT scan was performed first and was then followed by an MR study. The animals were anaesthetized via isoflurane inhalation during the ^{18}FDG-PET/CT scan and then euthanized by CO_2-gas prior to the MR studies. After the MR scan, the BAT tissue of the rats was located visually through careful dissection, and it was then removed and weighed. The removed BAT tissue was also immunohistochemically stained and analyzed. All of the rats were euthanized approximately 5 h prior to the BAT dissection and histological analysis.

2.3. ^{18}FDG-PET/CT studies

^{18}FDG-PET/CT scans were performed on eight rats using a hybrid PET/CT animal scanner, Siemens Inveon PET/CT (Siemens Medical Solutions, Knoxville, USA). ^{18}FDG (16.45 ± 0.64 MBq) was injected via a cannula inserted in the tail vein. The rats were anaesthetized with isoflurane 60 min prior to a 20-min static PET scan that was preceded by a low-resolution CT scan used for attenuation correction and anatomical reference. The body temperature was not actively influenced or regulated during either the 60-min biodistribution period of ^{18}FDG or the PET/CT scan. The images were reconstructed using an OSEM2D algorithm, and ROIs were drawn on the expected BAT tissue, WAT tissue, and heart muscle using the areas with high ^{18}FDG uptake and/or the CT anatomical