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Abstract

18F-FDG-PET have been used in detecting human brown adipose tissue (BAT) for several years. As this research method is very expensive, time consuming and exposes the subjects to ionizing radiation, alternative research methods are needed. The aim of this study was to compare MR spectroscopy and IR thermoscopy as research methods of the activity of brown adipose tissue's baseline metabolism and to examine whether PET, MRI and MR Spectroscopy could be supplemented with infrared (IR) imaging. The study was undertaken in 24 healthy volunteers of which 19 were women. The mean age (±SD) was 48 ± 5 years and BMI was 27,5 ± 5,7 kg/m2. Both IR thermography and MR spectroscopy were measured at room temperature. As expected, there was no association between IR temperatures and fat fraction in the total study population. The association between IR and MRS fat fraction was significant only in subjects with BMI less than 30.

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Short title: BAT MRS and thermal imaging

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In a recent review of Acta Physiologica, Rodriguez et al[1] suggests that the metabolically active brown adipose tissue (BAT) can be detected studied using ^{18}F-FDG-PET/CT. Although this method is commonly used in BAT research, it is very expensive and time-consuming and exposes the subjects to ionizing radiation. Therefore, more affordable and radiation-free methods have been developed, such as thermal infrared imaging (IR) and magnetic resonance spectroscopy (MRS) [2].

IR has been used for studying BAT function in small animals, and increasingly also in humans. Moreover, Jang et al [3] claim to have validated the utility of IR thermography in detecting human BAT against ^{18}F-FDG-PET. While these studies have found IR imaging to be a feasible method for the study of BAT activity, most of the study populations have been very homogenous in terms of BMI, age and sex. None of the human studies have validated IR thermometry against a method which truly measures the tissue temperature. Moreover, the effect of insulating fat under the skin has not been addressed in any of them which also Gatidis et al [4] have criticized. They showed that the thickness of the supraclavicular subcutaneous adipose tissue influences the supraclavicular skin temperature and proposed alternative thermographic methods to evaluate the possibility of BAT detection. It has been shown that MRS is capable of temperature detection [2] and also differentiating brown and white adipose tissue by several features, e.g. fat fraction, noninvasively [5]. Moreover, the fat fraction of BAT measured in ambient conditions by MRS is shown to be associated with BAT metabolic activity measured by ^{18}F-FDG-PET during acute cold exposure [6].

We performed IR imaging and MRS on female and male patients (n = 20, 15F/5M) with varying age and BMI (age 48 ± 5 years, BMI 28.1 ± 5.3 kg/m^2) to compare the feasibility of these two methods in studying of BAT. We postulate that MRS of the supraclavicular fat depot is more suitable for heterogeneous study populations than IR imaging of the skin.

Healthy Caucasian volunteers were studied and the subjects spent a minimum of 5 minutes at room temperature prior to imaging. They had not had a symptomatic infection on the day of imaging and not been physically active or consumed food, alcohol or caffeine for one hour prior to the imaging. Sweat was swiped from the area of interest immediately before imaging. There was no air conditioning in the study room.

A FLIR A325 IR camera was used for the IR thermography (FLIR A325, 3.2 megapixel, FLIR Systems Australia Pty Ltd, Melbourne, Vic., Australia). IR imaging was performed on the manubrium sterni of the study subjects at ambient room temperature (see Figure 1). The distance was set to 1 m for an optimal field of view. Subjects were scanned in sitting position with arms adducted, head in a neutral position and the subject looking straight ahead. The head, neck and shoulders were unclothed. The emissivity was set at 0.98. The IR images were analyzed using Matlab-based Biosignal Scientist software (Thermidas Oy, Oulu, Finland). Regions of interest (ROIs) were determined in five different areas as shown in Figure 1. Orientation of M. sternocleidomastoideus was used as a guideline to determine and set the most optimal ROIs for IR scanning. The software indicated the mean and standard deviation of the temperature within the ROI.

The MRS of subcutaneous and supraclavicular fat was measured at room temperature as described previously [5]. Half of the supraclavicular spectra were acquired on the right hand side and half on the left. MRS of liver was also performed. The supraclavicular and subcutaneous spectra were analyzed and fat fraction was calculated as described previously.[6] T1 effects were not taken into account since the repetition time was relatively long compared to the T1 relaxation times of water and lipids. To determine the temperature, the frequency difference ($f_{\Delta wf}$) between the water and CH_2 (methylene) resonance peaks was assessed first using jMRUI software [7]. The methylene resonance peak could be determined confidently in only 8 of the 20 liver spectra. The median $f_{\Delta wf}$ in liver (3.40555 ppm) was taken to be equivalent to a temperature of 37°C. The relation between the change of temperature (T) and the $f_{\Delta wf}$ was supposed to be -0.01 ppm/°C as in [2]. Thus the formula to convert $f_{\Delta wf}$ into temperature became T[°C] = 37.0[°C] - ($f_{\Delta wf}$ – 3.40555)[ppm]/0.01[ppm/°C].

Statistical analyses were performed as described previously [6].

The skin IR temperature of ROIs 1 to 5 are presented in Figure 1. The average temperature of all ROIs was 33.6 ± 1.1°C. The mean fat fraction of supraclavicular adipose tissue was 72.2 ± 10.5% and the mean MRS temperature 32.9 ± 5.3°C. As MRS measures deep tissue and IR superficial skin, expectedly there was no association between IR temperature and fat fraction or IR temperature and MRS temperature of the supraclavicular adipose tissue in the total study

population. However, when the subjects were divided into obese (6 subjects) and non-obese (14 subjects) groups, the IR temperature distally from the typical BAT region (ROI 5) correlated with the MRS temperature ($\rho = 0.63$, $p = 0.016$) in the non-obese group. Interestingly, in the obese group there was an inverse significant correlation between the supraclavicular MRS temperature and IR temperature in the typical BAT regions (ROI 3, $\rho = -0.83$, $p = 0.042$ and ROI 4, $\rho = -0.89$, $p = 0.019$) and further distally (ROI 5, $\rho = -0.89$, $p = 0.019$). The distance between the voxel and skin correlated significantly with BMI ($\rho = 0.51$, $p = 0.023$).

We found that the associations between skin IR temperatures and MRS temperature being opposite in obese and non-obese subjects. It was considered that the inverse correlation of IR and MRS temperatures in the obese group might result from the greater tissue thickness and voxel distance from the skin. However, no correlation between IR and MRS temperatures in the total study population was found, when the distance was taken as co-variate. It might be, that the study population was too insufficient to disclose the correlation even though it exists. Gatidis et al[4], however, found a negative correlation between subcutaneal layer thickness and skin temperature in their study.

Thus, IR thermometry might be a feasible tool for the measurement of skin temperature and even a good surrogate for the estimation of BAT temperature in a lean study population or cell cultures. In an obese population the layer of subcutaneous fat insulation varies in its thickness and is therefore a seriously confounding factor in the IR thermometry of BAT. This is contradictory as BAT is thought to have a role in the treatment of obesity and still to measure its activity with IR thermometry the subjects must be lean. To our knowledge, this kind of comparison between different temperature measurement methods has not been previously applied. Confounding factors exist, e.g. the formula used for temperature conversion (1) and the small size of the study population. Even so, MRS thermometry remains the one of the few methods capable of detecting noninvasively not only the change but also the absolute tissue temperature, and certainly deserves to be developed and exploited further. As the BMI of study subjects influence the study results when imaging BAT with IR thermometry, studies with wide study population and obese study subjects in this field are needed. In conclusion, IR thermometry is not feasible for estimation of BAT temperature in diverse study population.

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Figures

Figure 1.

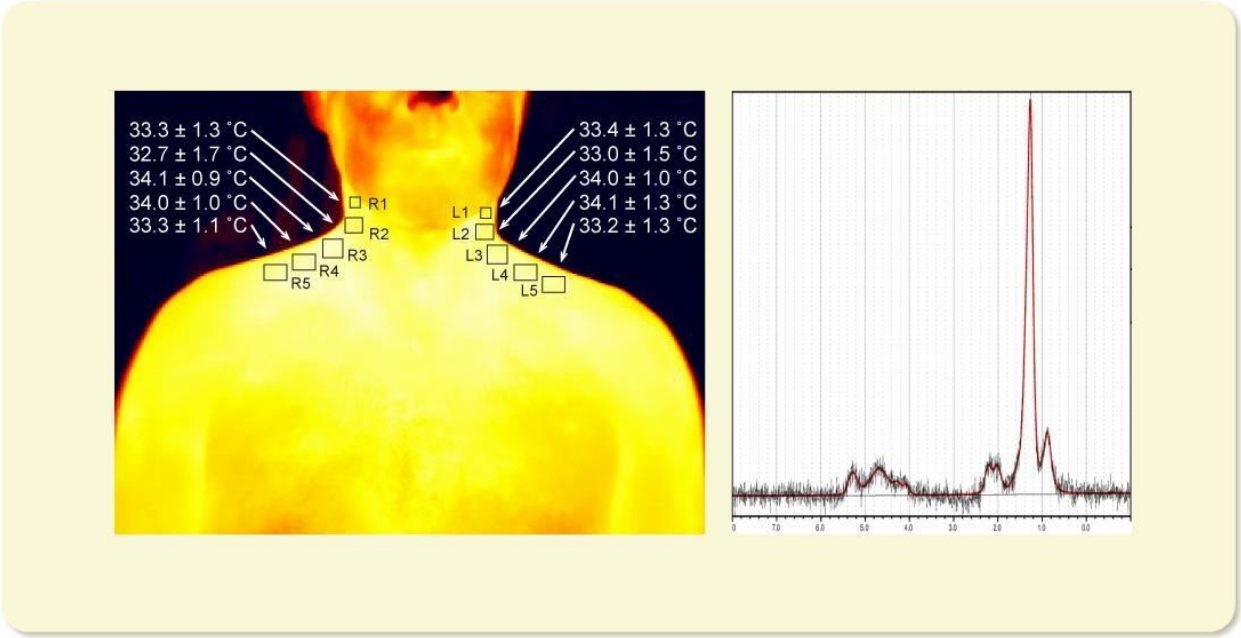

Figure 1. Left: Mean IR temperatures of ROIs 1 to 5 on both sides on a typical thermal image of a study subject. ROIs 3 and 4 are closest to the supraclavicular adipose tissue depot in which BAT is usually present. Right: a typical supraclavicular adipose tissue MR spectrum and LCModel fit printed in red.