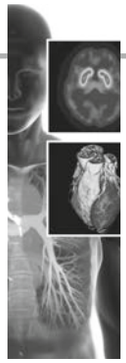

How promising is thermal imaging in the quest to combat obesity?

"*The potential widespread use of thermal imaging means that the exact contribution of specific environmental, dietary and lifestyle interventions on brown adipose tissue thermogenesis can now be quantified.*"

KEYWORDS: brown adipose tissue ■ development ■ thermogenesis

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The causes of obesity, ultimately the long-term consequence of an imbalance between energy intake and output, are numerous. Whatever its cause(s), obesity is affecting increasing numbers of individuals at earlier ages. One debate that has persisted since the 1980s, following the pioneering studies of Rothwell and Stock, is that inadequate thermogenesis within brown adipose tissue (BAT) is a primary cause of excess weight gain [1]. This proposal was based largely on studies in rodents in which BAT is primarily located within the interscapular region. This so-called brown fat has a vital role in heat production, especially in human newborns, as well as in newborn and adult small mammals, and is characterized as possessing a UCP1, located within the inner mitochondrial membrane [2]. When activated, UCP1 enables the rapid generation of heat through the unmasking of GDP-binding sites and the subsequent free flow of electrons across the mitochondria. Consequently, when maximally activated BAT, can generate 300 W of heat per kg of tissue compared with 1 W from most other tissues [3]. This substantial ability of BAT to produce heat means that, in adult humans, a comparatively small amount of this tissue could potentially contribute to as much as 20% of total daily heat production [1]. BAT, therefore, remains a compelling target for anti-obesity therapies; however, there have been significant previous constraints on assessing BAT function directly in humans.

The recent innovations in the detection of BAT within humans using a combination of PET-CT and tissue biopsy have now established that the main site of human BAT is within the supraclavicular region. When stimulated, this can, indeed, make a significant contribution to daily heat production in healthy adult humans [4]. However, a number of factors, including the relatively large amounts of radiation exposure and high cost of PET-CT, limit this technique to a very small number of normal healthy subjects for ethical reasons. Similarly, biopsying BAT within the supraclavicular region is a technically challenging procedure and is of ethical concern as the loss of even a small amount of BAT could have negative implications for body weight regulation. It was with these significant issues in mind that we commenced our investigations into the feasibility of using thermal imaging to assess BAT thermogenesis.

"*Thermal imaging ... offers unique potential to directly assess brown adipose tissue function under resting and activated conditions, with rapid activation of brown adipose tissue occurring in response to modest thermal challenges...*"

From the outset, it was clear that the hottest spot on the body surface of healthy children, adolescents and adults was in the region colocating to the main depot of BAT – that is, with the supraclavicular region colocated with the depots identified in earlier studies using PET-CT and/or tissue biopsy [5]. This has been apparent in all subjects we have assessed and thus offers the exciting possibility that large-scale assessments of BAT thermogenesis can now be undertaken on a population-wide basis. The potential widespread use of thermal imaging means that the exact contribution of specific environmental, dietary and lifestyle interventions on BAT thermogenesis can now be quantified [6]. Thermal imaging, therefore, offers unique potential to directly assess BAT function under resting and activated conditions,

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with rapid activation of BAT occurring in response to modest thermal challenges, such as the placement of a hand into cool water.

Crucially, however, the standardization of protocols will be essential, as it has also become apparent that, as may be expected for such a metabolically active tissue, its temperature fluctuates throughout the day and night. This is in accord with rodent studies in which direct measurements of BAT temperature have been made [7]. Therefore, a number of technical and logistical challenges remain to be overcome in the use of thermal imaging to quantify BAT function. These include:

- Standardization of time of day and the environmental temperature at which measurements are made;
- Standardization of time since previous food and drink consumption;
- Standardization of image processing to enable direct comparable quantifications of the actual area/size of BAT deposits;
- Ensuring the subjects remain in a calm and natural state throughout the course of the study;
- Standardization of adequate exposure of the supraclavicular anatomical region for imaging;
- Further assessment of the potential impact of skin depth over the supraclavicular region on skin surface temperature immediately above BAT.

As these challenges are met, it will be possible to define the precise role for BAT in humans rather than having to rely on indirect conclusions based on rodents, in which BAT has a different location and may be under different types of control mechanisms. For example, BAT, at least as assessed from thermal imaging, is rapidly activated, presumably from immediate stimulation, by the sympathetic nervous system [5]. This swift responsiveness could explain, in part, why pharmacological compounds that have previously appeared promising in activating BAT in dogs, for example [8], have not had comparable long-term effects in humans. It may also now be feasible to ascertain how the main location of BAT fits in with its function. Although the temperature of blood supplying the brain would be maintained or increased as BAT is activated, this may only be a transient or intermittent response, which may not be amenable to long-term enhancement. Nevertheless, human studies in which thermal imaging combined with assessments of brain function can now be undertaken in order to establish whether these are closely linked, especially with respect to appetite control.

Further areas of future investigation would include quantification of the role of BAT in both exercise and dietary-induced thermogenesis; such studies will require further experimental modifications, as each will include thermogenic responses that originate from enhanced muscle and/or gut activity [9]. In addition, there are important developmental changes in BAT function that must be considered in establishing future studies [5]. Given the high prevalence of childhood obesity, which is potentially linked to compromised BAT function, intervention strategies focused on BAT in children can now be considered a real possibility.

It is rather surprising that, despite what are clear and distinct changes within the supraclavicular region (which colocates to BAT), other investigators using thermal imaging have not yet presented comparable data from their ongoing investigations. Although, this may be due, in part, to the focus of the majority of BAT research on adults, in whom its abundance is clearly much lower compared with children.

> *"Given the high prevalence of childhood obesity ... intervention strategies focused on brown adipose tissue in children can now be considered a real possibility."*

In summary, thermal imaging is already being utilized for an increasing number of medical-related applications [10]. Its potential to be used extensively to establish how promoting BAT function could prevent obesity could represent a step-wise shift in our ability to overcome this global health challenge.

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