Progress in Nuclear Magnetic Resonance Spectroscopy 73 (2013) 56–80

Contents lists available at SciVerse ScienceDirect

Progress in Nuclear Magnetic Resonance Spectroscopy

journal homepage: www.elsevier.com/locate/pnmrs

Whole body fat: Content and distribution

E.L. Thomas [a,*], J.A. Fitzpatrick [a], S.J. Malik [b], S.D. Taylor-Robinson [c], J.D. Bell [a]

[a] *Metabolic and Molecular Imaging Group, MRC Clinical Sciences Centre, Imperial College London, London, UK*
[b] *Division of Imaging Sciences and Biomedical Engineering, King's College London, King's Health Partners, St. Thomas' Hospital, London, UK*
[c] *Division of Diabetes, Endocrinology and Metabolism, Department of Medicine, Imperial College London, London, UK*

Edited by David Gadian and David Neuhaus

ARTICLE INFO

Article history:
Received 21 January 2013
Accepted 23 April 2013
Available online 13 May 2013

Keywords:
Adipose tissue
Ectopic Fat
^{1}H MR Spectroscopy
IMCL
IHCL
Visceral fat
MRI

ABSTRACT

Obesity and its co-morbidities, including type II diabetes, insulin resistance and cardiovascular diseases, have become one of the biggest health issues of present times. The impact of obesity goes well beyond the individual and is so far-reaching that, if it continues unabated, it will cause havoc with the economies of most countries. In order to be able to fully understand the relationship between increased adiposity (obesity) and its co-morbidity, it has been necessary to develop proper methodology to accurately and reproducibly determine both body fat content and distribution, including ectopic fat depots. Magnetic Resonance Imaging (MRI) and Spectroscopy (MRS) have recently emerged as the gold-standard for accomplishing this task. Here, we will review the use of different MRI techniques currently being used to determine body fat content and distribution. We also discuss the pros and cons of MRS to determine ectopic fat depots in liver, muscle, pancreas and heart and compare these to emerging MRI techniques currently being put forward to create ectopic fat maps. Finally, we will discuss how MRI/MRS techniques are helping in changing the perception of what is healthy and what is normal and desirable body-fat content and distribution.

Contents

* Corresponding author. Address: Metabolic and Molecular Imaging Group, MRC Clinical Sciences Centre, Imperial College, Du Cane Road, London W12 0HS, UK. Tel.: +44 0208 383 3772.
E-mail address: louise.thomas@csc.mrc.ac.uk (E.L. Thomas).

0079-6565/$ - see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.pnmrs.2013.04.001

1. Introduction

Obesity has become one of the major health concerns of modern times. It is estimated that over 700 million people across the world are currently either overweight or obese [1]. In the UK alone, latest studies show that over 60% of the adult population is either overweight (with a body mass index (BMI) between 25–30 kg/m^2) or obese (with a BMI between 30–40 kg/m^2), while 30.3% of children (aged 2–15) are overweight or obese. This increase in body adiposity is closely associated with a number of non-communicable diseases, including type-2 diabetes, hypertension, cardiovascular disorders and some forms of cancer. Indeed, type-2 diabetes is today a major worldwide problem, with more than 346,000,000 diabetics across the planet and these figures may double by 2030 [1]. In some countries, levels of diabetes now affect over 20% of the adult population. The social and economic impact of the obesity pandemic, and its co-morbidities, cannot be overstated, and at this rate is likely to have a severe impact on healthcare provision in many economies [2].

Adipose tissue (or body-fat) is a multifaceted and complex organ [3]. Besides functioning as a system for excess energy deposition, protection from the cold and everyday hazards, adipose tissue produces an assortment of molecular messengers (adipokines), which influence a diverse array of functions, including appetite, fertility, neuronal development and plasticity, inflammatory responses, and the action of other hormones, including insulin [4]. Yet, despite these positive functions, a close association between excess body adiposity and the development of non-communicable diseases has been reported in many epidemiological studies [5]. Moreover, these associations are further strengthened if age and physical activity (or the lack of it) are included in the paradigm.

Detailed studies of adipose tissue content *and distribution* suggest that the latter plays an important part in these associations [6]. Indeed, a number of adipose-tissue related sub-phenotypes have now been identified, including '*thin on the outside fat on the inside*' (TOFI) and '*fat-fit*' subjects, which indicate the importance of having accurate and reproducible measurements of both the total body-fat and its distribution [7]. For example, in the case of TOFI, subjects with normal BMI (<24.9 kg/m^2) but increased abdominal obesity, have increased risk of developing insulin resistance and type II diabetes, while the "fat-fit", subjects with BMI > 30 kg/m^2 appear metabolically normal despite their elevated body adiposity [8].

In order to understand these somehow paradoxical findings, it is important to get a better definition of the different concepts/words involved in many of these associations, including 'adipose tissue', 'body-fat' and 'ectopic fat'. The use of the words 'fat' or 'body-fat' has become synonymous with obesity, and in general refers to the fat found immediately under the skin covering substantial parts of the surface of the body. Strictly speaking, this fat layer is actually 'subcutaneous adipose tissue' and is part of a larger organ: adipose tissue, which makes up a significant part of our bodies. Adipose tissue can also be found surrounding organs such as the liver, pancreas, kidneys and the heart, to some degree. It is also found in muscles and other areas of the body including part of the orbital cavities. All these fat depots, which in many instances are not in direct physical contact with each other, appear to work in a coordinated manner, and are normally referred to as 'total adipose tissue'. Besides these fat depots, fat can also be accumulated <u>within</u> certain organs and tissue, including liver, pancreas, heart and muscle, and these deposits are technically known as 'ectopic fat depots'. Some of these depots have recently been shown to be important independent risk factors for disease development and clearly deserve closer scrutiny if the underlying mechanism that underpins the associations between increased body adiposity is to be unravelled [9].

The need for an accurate and reproducible method to determine levels of different fat depots, including ectopic fat, has driven the scientific community to investigate the potential use of imaging technologies, including CT, magnetic resonance imaging and spectroscopy (MRI/MRS). Thus, in the last two decades MRI/MRS have become the gold-standard for such studies, especially as the scientific community moves into the post-genomic era and an understanding is sought of the gene-environment interactions that contribute to the determination of fat content and distribution in different subjects and their role in the reported gender and ethnic differences. With this in mind, we will review the use of MRI and MRS in the study of adipose tissue and ectopic fat and how these techniques are helping us to get a better understanding of the role of body fat not only in disease development, but also in the process of achieving optimal health.

2. Indirect methods for body-fat measurements

A number of techniques are currently available to assess body fat content. Indirect methods include: body-mass-index (BMI), skinfold anthropometry, bioelectrical impedance, underwater weighing, and body water dilution [10]. While there are pros and cons for all of these methodologies, the one thing they have in common is that they give little or no information concerning adipose tissue distribution. Moreover, most of these techniques are based on indirect measurements of either body water or body volume and necessitate equations to convert these into total fat measurements. While these methodologies do provide valuable information, particularly at a population level, they are not always applicable to all ethnic groups or to subjects with extremes of body types. This is mainly due to the fact that they were derived from specific populations, generally Caucasian. More importantly, they say nothing about intra-abdominal (also known as 'visceral fat') or ectopic fat levels, two crucial factors in the association between body adiposity and disease development. We will therefore not discuss these methods further.

2.1. Direct methods for body-fat measurements

2.1.1. CT and MRI to measure adipose tissue content and distribution

The fact that different fat depots within the body appear to contribute, to a differing extent, to the risk of developing non-communicable diseases, has made it clear that measuring total body fat content alone was not sufficient. This has necessitated the development and implementation of new techniques that could accurately measure body fat content and distribution and which could be applicable to all populations and body types.

The first technique used which appeared to meet all of these criteria was CT scanning. Total adipose tissue content could be measured as well as individual adipose tissue depots, particularly intra-abdominal adipose tissue depot [11–14]. However, a major drawback of CT scanning is the radiation dose it delivers, which greatly limits its application, particularly for longitudinal studies