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Adipose Tissue Quantification by Imaging Methods: A Proposed Classification

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Abstract

Recent advances in imaging techniques and understanding of differences in the molecular biology of adipose tissue has rendered classical anatomy obsolete, requiring a new classification of the topography of adipose tissue. Adipose tissue is one of the largest body compartments, yet a classification that defines specific adipose tissue depots based on their anatomic location and related functions is lacking. The absence of an accepted taxonomy poses problems for investigators studying adipose tissue topography and its functional correlates. The aim of this review was to critically examine the literature on imaging of whole body and regional adipose tissue and to create the first systematic classification of adipose tissue topography. Adipose tissue terminology was examined in over 100 original publications. Our analysis revealed inconsistencies in the use of specific definitions, especially for the compartment termed “visceral” adipose tissue. This analysis leads us to propose an updated classification of total body and regional adipose tissue, providing a well-defined basis for correlating imaging studies of specific adipose tissue depots with molecular processes.

Keywords

body composition; computed tomography; magnetic resonance imaging; body fat

Introduction

Increased adipose tissue mass is the primary phenotypic characteristic of obesity. The amount and distribution of adipose tissue is associated with many of the adverse consequences of obesity, such as coronary artery disease and type 2 diabetes (1–4).

Recently, it has been discovered that adipose tissue is not a single homogeneous compartment, but rather a tissue with specific regional depots with varying biological functions (5–7). Moreover, individual adipose tissue compartments have stronger associations with physiological and pathological processes than does total adipose tissue mass (6,8–11).

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Although there is intense and increasing interest in regional adipose tissue compartments, there is still little available information or formal consensus on the nomenclature of regional adipose tissue depots. Whereas computerized axial tomography (CT) and magnetic resonance imaging (MRI) are often used to quantify adipose tissue volumes, authors vary greatly in their definition of the adipose tissue compartments they measure.

Here we review some of the complexities posed by quantification of adipose tissue by imaging methods, focusing on classification issues. The first section is an overview of differences between adipose tissue and the group of molecular-level components referred to collectively as fat. The next section explores traditional adipose tissue classification systems. We then critically examine imaging-related terminology used in metabolic research. As part of our review, in each section, we recommend what we believe is appropriate adipose tissue terminology for providing a unified imaging-based classification. We conclude with recommendations for future research.

Adipose Tissue vs. Fat

Imaging methods, CT and MRI, quantify “adipose tissue” volume as voxels or volume elements. While often referred to as “fat” according to the five-level body composition model, adipose tissue and fat are different components (12). The distinction between fat and adipose tissue in common usage is usually irrelevant, and the terms are almost always used interchangeably. However, in the body composition and metabolism field, “fat” and “adipose tissue” are distinct and different compartments (Figure 1) (12), and their taxonomic separation is important when measuring their mass and metabolic characteristics.

A component at the tissue-organ body composition level (12), adipose tissue is a specialized loose connective tissue that is extensively laden with adipocytes. Adipose tissue has mainly been viewed as an energy storage depot, thermal insulator, and mechanical cushion in mammals. The 70-kg Reference Man has 15 kg of adipose tissue, representing 21% of body mass (13). The percentage is higher in women, the elderly, and overweight subjects. Adipose tissue is anatomically distributed throughout the human body, and the pattern of adipose tissue distribution is influenced by many factors, including sex, age, genotype, diet, physical activity level, hormones, and drugs (14–19).

In contrast to adipose tissue, the molecular level or chemical component fat is usually lipid in the form of triglycerides (12). Although fat is found primarily in adipose tissue, fat also exists in other tissues, especially in pathological conditions such as hepatic steatosis and various forms of lipodosis. Triglycerides in other tissues, such as in skeletal muscle, can be quantified by magnetic resonance spectroscopy (20). The most widely used current method for quantifying fat in vivo is DXA, whereas chemical analysis is used in vitro (21,22). Adipose tissue contains ~80% fat; the remaining ~20% is water, protein, and minerals (13).

Investigators in the field of metabolism often quantify fat or adipose tissue and find that the total mass of the two compartments in adults is similar, but not identical (23–27). This review concentrates on regional and total body adipose tissue, not fat or lipid, as quantified by the two main imaging methods, CT and MRI.

Traditional Adipose Tissue Classification

Classical anatomy was mainly organ-centered, without recognizing the specialized organ-like functions of different tissues. This was especially true of adipose tissue, which only recently has been recognized as an “endocrine organ” (28). We reviewed many 19th and early 20th century anatomy texts and found a conspicuous lack of detail in regard to adipose tissue classification.

Among typical approaches we did find in early texts, one is based on simple anatomic adipose tissue groupings not defined by traditional anatomic landmarks. According to this approach, adipose tissue can be typically organized into simple categories such as subcutaneous adipose tissue, organ-surrounding adipose tissue, interstitial adipose tissue, and adipose tissue in bone marrow (29). Subcutaneous adipose tissue is known to gross anatomists as superficial fascia and is defined as the adipose tissue layer found between the dermis and the aponeuroses and fasciae of the muscles. Adipose tissue is sometimes named specifically for the organ it surrounds, as in “perirenal adipose tissue.” Interstitial adipose tissue, however, is interspersed or infiltrated among the cells of different tissues so tightly that it is not readily dissectible (30).

This simple adipose tissue classification system served anatomists well for the past centuries, particularly because the main early focus was on organs, and little clinical pathology was directly attributable to or found within the adipose tissue compartment.

Adipose tissue is also named according to special biological functions, such as white, mammary gland, brown, and bone marrow adipose tissues (31). White adipose tissue functions mainly as an energy reservoir, insulator, and as a source of recently discovered hormones (32). Thermogenesis is the main function of brown adipose tissue found in many small mammals. Mammary gland adipose tissue plays an important role in epithelial cell growth and milk production, whereas bone marrow adipose tissue might participate in hematopoiesis and osteogenesis (31).

This classification provided a clear and useful approach for organizing some of the recognized biological functions of adipose tissue. However, important metabolic properties of adipose tissue depots, such as visceral adipose tissue, cannot easily be accommodated. Also, the groupings in this approach represent a hybrid that includes anatomic regions (e.g., mammary glands) and functional properties (e.g., heat production by brown adipose tissue and energy storage by white adipose tissue), with the potential for overlap.

Adipose Tissue Classification in Radiology

The prevailing confusion and, to some extent, outdated terminology concerning adipose tissue in the medical literature prompted us to review papers on imaging of adipose tissue compartments related to metabolic activity and disease. Using Medline, we examined over 100 articles with the terms “total,” “regional,” and “visceral” adipose tissue or fat published between 1979 and 2002. Two categories were identified, those that evaluated whole body and those that evaluated regional adipose tissue.

Whole-Body Imaging Studies

While investigators usually provided clear definitions of adipose tissue depots, some reports lacked adequate detail to evaluate component characteristics. Most articles did not indicate whether or how adipose tissue depots other than subcutaneous and visceral adipose tissue were measured, even though they collectively contribute to total-body adipose tissue (33,34).

Overall, the reports were concordant on a number of measurement procedures when applied to whole-body multislice CT and MRI. First, even though its boundary is clearly visible and thus easily quantified, bone marrow adipose tissue was usually not included in imaging studies of total-body adipose tissue (35). This is likely because most investigators have little interest in bone marrow adipose tissue estimates.

Second, adipose tissue in the head, feet, and hands is difficult to distinguish from adipose tissue in bone marrow with commonly applied MRI sequences, and these tissues are usually labeled

as nonadipose tissue (36,37). Nevertheless, a trained analyst can isolate subcutaneous adipose tissue from bone marrow with high resolution MRI.

Third, scattered adipocytes are found within many organs and tissues, especially skeletal muscle. Unless these adipocytes clump together and form a larger mass, they may be below the commonly applied resolution of CT and MRI, relegating them to measurement within the nonadipose tissue component. While these small adipose tissue clumps are now below the current imaging threshold, it should be possible in the future with MRI to establish a separate estimate of the lipid content of scattered adipocytes by subtracting intramyocellular lipid content measured by ^1H magnetic resonance spectroscopy from total tissue lipid content measured by chemical shift imaging (20,38,39). These advanced methods are revolutionizing the study of in vivo biology and redefining the study of human anatomy.

Thus, “total-body” adipose tissue measured by imaging methods in the current published literature is usually different from the actual volume of adipose tissue determined by dissection and histological analysis. Nevertheless, the potential exists with developing techniques to accurately quantify total body adipose tissue in vivo.

Some whole-body imaging studies grouped adipose tissue compartments according to metabolic activity. Barnard et al. subdivided total body adipose tissue into “subcutaneous” and “internal” (i.e., visceral, paravertebral, and intermuscular) with further partitioning of visceral adipose tissue into retro- and intraperitoneal components (33,35). This partition of total-body adipose tissue assumes that subcutaneous adipose tissue and internal adipose tissue differ in their metabolic activities. Thomas et al. (34), in their imaging studies, separated internal adipose tissue into two compartments, visceral adipose tissue and nonvisceral adipose tissue.

Although adipose tissue in the female breast functions differently from other subcutaneous regions in several respects (31), most investigators consider mammary adipose tissue a portion of the subcutaneous compartment. Localized fat pads, such as the synovia, were formerly classified as mechanical adipose tissue but are now considered by most investigators to be components of subcutaneous adipose tissue.

A number of reviews explore the well-developed technical aspects of imaging methods and their validity in quantifying total-body and subcutaneous adipose tissue (30,40–42). The coefficients of variation (CV) for repeated subcutaneous adipose tissue measurements by CT and MRI are similar and in the range of ~2% (43–45).

The subcutaneous adipose tissue of the lower trunk and the gluteal-thigh region has a thin fascial plane dividing it into superficial and deep portions, as shown in Figure 2 (46–49). In recent studies, both morphological and metabolic differences were found between these two adipose tissue layers (10,50,51). The majority of deep subcutaneous adipose tissue is located in the posterior half of the abdomen, whereas superficial subcutaneous adipose tissue is evenly distributed around the abdominal circumference (10).

These collected reports led us to propose a practical total-body and regional adipose tissue classification system based on the well-defined fascial planes listed in Table 1. Total-body adipose tissue can be first divided into two main measurable components, subcutaneous and internal. Subcutaneous adipose tissue is well defined and has clear anatomic demarcations, as noted in the table. Internal adipose tissue is divided into visceral and nonvisceral components.

Among the nonvisceral components, some perimuscular adipose tissue regions are specially named. For example, when distributed among muscles, they are named as inter-muscular adipose tissue, and when adjacent to bones, they are named as paraosseal adipose tissue. The fascial planes separating perimuscular adipose tissue from adjacent adipose tissue

compartments are sometimes, but not always, visible when images are prepared using typical MRI acquisition sequences (Figure 3A). These fascial planes are visible in most subjects when high-resolution images are prepared (Figure 3B). Additionally, the perimuscular and intramuscular adipose tissue depots are small and are thus not accurately measurable by traditional cadaver dissection. Recently, advanced digital photography (30) and microdissection (52) methods have provided a means of accurately estimating the areas or volumes of these difficult-to-dissect adipose tissue compartments and can be applied in human cadaver or animal studies to serve as the imaging-method criterion.

Absolute and relative visceral adipose tissues have been associated with the greatest health risk (53,54). Authors vary widely in their definitions and descriptions of visceral adipose tissue. Some reports did not provide any anatomic demarcations of visceral adipose tissue compartments (11,55–67). Contrary to the simple view of visceral adipose tissue held by many authors, there are important differences in the metabolic and functional properties of depots within the “visceral adipose tissue” compartment. Accordingly, in the following section, we present a critical review of previous visceral adipose tissue studies, along with a detailed classification of visceral adipose tissue.

Visceral Adipose Tissue

The word “viscera” originates from Latin (68) and is defined as “organs in the cavities of the body” (68–70). Because there are three main body cavities, it is reasonable to assume that visceral adipose tissue (VAT) consists of adipose tissue (AT) distributed in the three body cavities: intrathoracic (ITAT), intraabdominal (IAAT), and intrapelvic (IPAT). The physical location of these three cavities is from cephalad to caudad, and axial image acquisition provides the landmarks for roughly separating ITAT from IAAT and IAAT from IPAT. Accordingly, investigators have studied the metabolic characteristic of visceral adipose tissue found in these three different compartments. Most investigators report visceral adipose tissue as IAAT or the sum of IAAT and IPAT.

The CVs of visceral adipose tissue estimates by imaging methods are well studied and extensively reviewed. The CVs for VAT measurements by MRI are ~9% to 18% (44,45,71, 72) and by CT are ~2% (43). The lower CV of CT is usually ascribed to a shorter image acquisition time, and CT is thus less vulnerable to image artifacts produced by peristaltic gastrointestinal tract movement (73). The signal intensity of MRI pixels from the same tissue may vary from region to region due to magnetic field heterogeneity. There may also be some sequence-related artifacts with MRI, such as chemical shift and blood flow artifacts. These effects collectively lower the accuracy and precision of MRI visceral adipose tissue estimates, particularly as image analysis requires establishing the irregular boundaries between VAT and other tissues and organs.

As a stimulus for review and as a means of evoking the prevailing confusion in the literature, we now examine earlier studies in the context of VAT as the sum of three distinct components.

VAT = ITAT + IAAT + IPAT—Although viscera are distributed throughout all body cavities, very few investigators defined VAT in humans as the sum of ITAT, IAAT, and IPAT (74–76). This definition of VAT is applied in the animal literature (77). It is not known whether the three VAT components have distinct metabolic characteristics. The least studied of these three components is ITAT. The ITAT is mainly distributed surrounding the heart, and the physiological role of ITAT is in an early stage of investigation. In animal studies, Marchington et al. (78) found that epicardial adipose tissue has a greater capacity for fatty acid release than adipose tissue elsewhere in the body. Cardiac adipose tissue may supply energy for the adjacent myocardium and serve as a buffer against toxic levels of free fatty acids.

IPAT is usually quantified together with IAAT. However, when studied separately from IAAT, the metabolic properties of IPAT and IAAT differ (49,79). Part of the reason for this metabolic difference is that IAAT represents both extra- and intraperitoneal adipose tissue, whereas IPAT represents mainly extraperitoneal adipose tissue (49).

VAT = IAAT + IPAT—The VAT compartment as defined in some reports included IAAT and IPAT (33,34,37,79) that ranged anatomically from the femoral heads to the liver dome or base of the lungs. Whole-body CT and MRI scans usually consisted of multiple slices at predefined intervals (e.g., 5 cm). With the 5-cm intervals often used in MRI protocols, VAT was frequently defined as located within the seven slices extending from two below and four above the L4–L5 level (37). The IAAT and IPAT components are anatomically connected, and it is thus reasonable to study them together.

VAT = IAAT—Most of the reviewed earlier studies defined VAT as IAAT only, with a range from 5 cm below L4–L5 to the slice corresponding to the superior border of the liver (8,9,40, 80–87). Some investigators additionally divided VAT into intraperitoneal and retroperitoneal adipose tissue (9,82,83,86,87). Because the parietal peritoneum rarely is visible on cross-sectional images (73), some investigators adopted an arbitrary method in which the marker was used to draw a straight line across the anterior border of L4–L5 and the psoas muscles, continuing on a tangent toward the posterior borders of the ascending and descending colon, and extending to the abdominal wall. However, the lack of exact boundaries between the intraperitoneal and retroperitoneal space renders this subdivision only an approximation. Some investigators referred to “abdominal VAT” instead of “VAT” to indicate that they were actually measuring IAAT (34,36,88,89).

VAT = Intraperitoneal Adipose Tissue—A few studies defined VAT solely as intraperitoneal adipose tissue, which is drained by the portal vein, whereas blood from retroperitoneal adipose tissue empties into the inferior vena cava (90,91). Although limiting the definition of VAT to intraperitoneal adipose tissue is inconsistent with the term “viscera,” the relationships between intraperitoneal adipose tissue and metabolic disorders have aroused considerable research interest. Abate et al. (91) proposed that metabolic differences exist between intraperitoneal and retroperitoneal adipose tissue. Although the fatty acid component of omental and mesenteric sites is not different from subcutaneous and retroperitoneal sites (36), it is currently hypothesized that the direct exposure of liver cells through the portal circulation to high concentrations of free fatty acids and/or other metabolites derived from intraperitoneal adipose tissue is responsible for the increased frequency of dyslipidemia, hyperinsulinemia, and other metabolic complications associated with abdominal obesity (43, 92).

Ideally the study of VAT should include all adipose tissue in the thoracic, abdominal, and pelvic cavities. However, many investigators are interested only in some subdivisions of VAT. Accordingly, it is reasonable to suggest that any VAT depot under study should be accurately named and characterized to avoid further confusion. Metabolic characteristics can be attributed to IAAT as a whole (9,82,83,86,87,90,91), although this may simply reflect the relatively large amount of highly active intraperitoneal adipose tissue (e.g., mesenteric and omental) found in this compartment. With increasing evidence of metabolic differences between intraperitoneal and extraperitoneal adipose tissues, it is reasonable to consider the intraperitoneal adipose tissue of both the abdominal and pelvic regions together, particularly because these compartments are contiguous.

We summarize the main VAT components in Table 2 and propose this as a classification and nomenclature for future studies. Because there is no adipose tissue adjacent to the pleura, we use pericardium instead of pleura to further separate the adipose tissue components of the

thoracic cavity (Figure 4). In the studies we reviewed, rather than measuring total extraperitoneal adipose tissue, most investigators only quantified retroperitoneal adipose tissue because it could be easily separated from intraperitoneal adipose tissue by an arbitrary line.

The traditional CT and MRI protocols now in use are not capable of separating all of the compartments listed in Table 2. On the other hand, retroperitoneal components such as pararenal adipose tissue are clearly visible on some conventionally acquired MRI scans (Figure 5). With a smaller field of view, higher resolution, and thinner slices, it may be possible to separate all of the adipose tissue depots from one another with the expectation of major technical advances in the future.

The distribution of VAT is shown in photographs of the National Library of Medicine's Visible Woman and Visible Man (Figures 6–8) (93,94). Because VAT seems to be metabolically heterogeneous, a reasonable future goal is to separately examine specific compartments as outlined in Table 2.

Single-Slice Studies

In addition to volume quantification of VAT by multiple-slice and whole-body imaging protocols, VAT is often reported as the area of a single slice. Because of the cost of whole-body scans and concerns over exposure to radiation, single-slice studies have often been used, although they are less accurate (95). The single-slice CT and MRI studies are usually performed at the L4–L5 level, which, in addition to omental, mesenteric, and retroperitoneal compartments, includes many other smaller adipose tissue compartments. VAT and IAAT are terms that were often used interchangeably in earlier reports. It is important to recognize that single-slice studies only provide an area when reporting “VAT,” in contrast to the volumes reported in multiple-slice studies.

There is also some inconsistency in the anatomical boundaries used in single-slice studies. Clasey et al. (96), for example, used the innermost aspect of the abdominal and oblique muscle walls, rather than the midpoint or the outermost aspect of the muscle walls, for measuring “VAT.” The internal boundary of the muscle walls was used in most of the studies we reviewed and did not include intermuscular and paravertebral adipose tissues (44,51,61,62,66,79,81, 82,97–110), which we propose should be included as nonvisceral adipose tissue. These adipose tissue compartments increase in size with age (33) and can be large in obese subjects.

Summary

Investigators differ in their interests in and definitions of various adipose tissue compartments. A consistent and logical classification adapted to imaging methods will allow investigators to compare physiological and metabolic studies of adipose tissue and resolve some of the confusion in the current literature. Specifically, we propose the following:

- Refer to components evaluated by CT and MRI as “adipose tissue” instead of the chemical term “fat.” Because “body fat” is also measured (e.g., by DXA), this will leave no question as to what body constituent is actually being evaluated.
- Separate “total-body adipose tissue” into two categories: subcutaneous and internal. These are well demarcated and leave little room for confusion.
- Separate internal adipose tissue into two discrete components: “visceral” and “nonvisceral.” VAT should appropriately include two cavities: the thoracic and abdominopelvic cavity. The abdominopelvic cavity can be further divided into intraperitoneal and extraperitoneal regions.

- While there is some inconsistency in the anatomical boundaries in single-slice studies of the abdomen, we suggest that the inner boundary of the abdominal muscle wall should be used as the limit for VAT. This boundary does not include intermuscular and paravertebral adipose tissue, which should be included as nonvisceral adipose tissue.
- While, at present, the main imaging focus is on the total volume of adipose tissue structures, a growing interest centers on tissue quality. Chemical shift imaging can provide information on adipose tissue lipid content (38,39), and proton spectroscopy provides estimates of tissue-free fatty acid composition (111). These advanced magnetic resonance methods have great promise in the field of obesity research. Combining these tissue quality assessment methods with high-resolution image acquisition holds great future promise in adipose tissue quantification.

It was the purpose of this paper to clearly define the adipose tissue components in published reports using a precise classification. This will, over the long term, allow elucidation of the genetic and metabolic properties of specific adipose tissue depots, their interaction, and their overall orchestrated role in energy homeostasis.

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Nonstandard abbreviations

CT	computerized axial tomography
MRI	magnetic resonance imaging
CV	coefficients of variation

VAT	visceral adipose tissue
AT	adipose tissue
ITAT	intrathoracic adipose tissue
IAAT	intra-abdominal adipose tissue
IPAT	intrapelvic adipose tissue

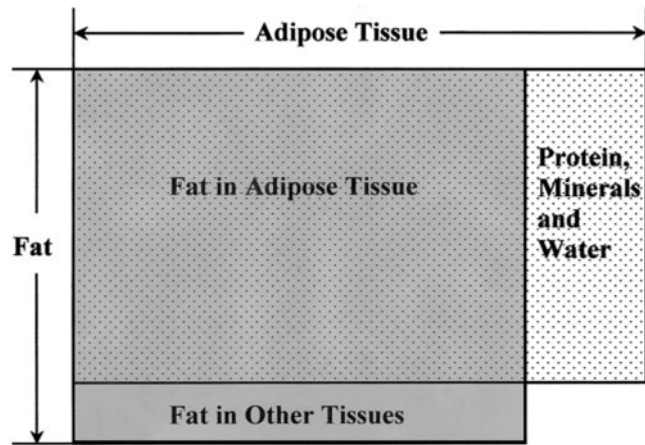


Figure 1.
The relationship between chemical fat (or lipid) and adipose tissue.

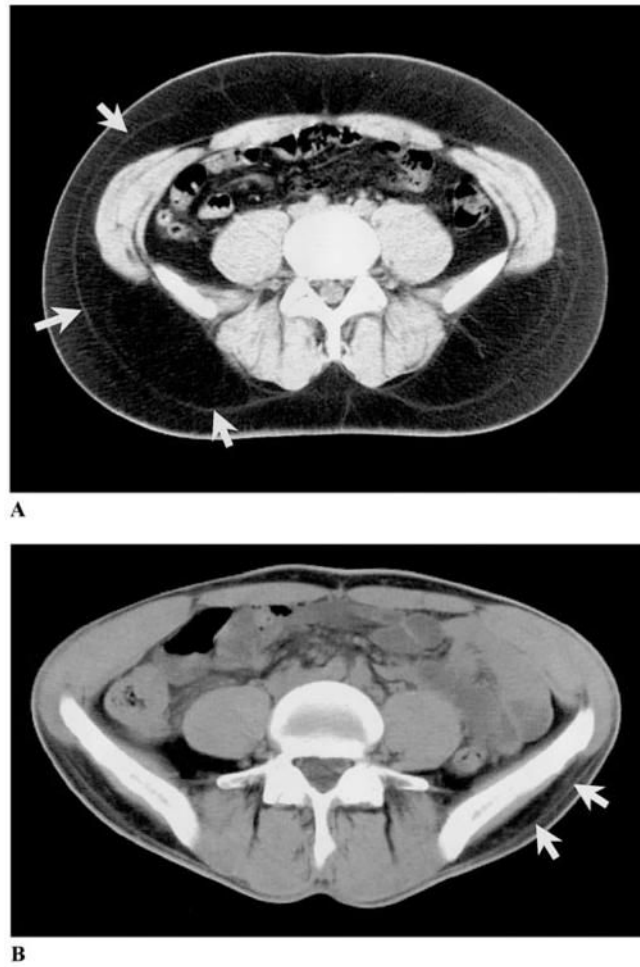
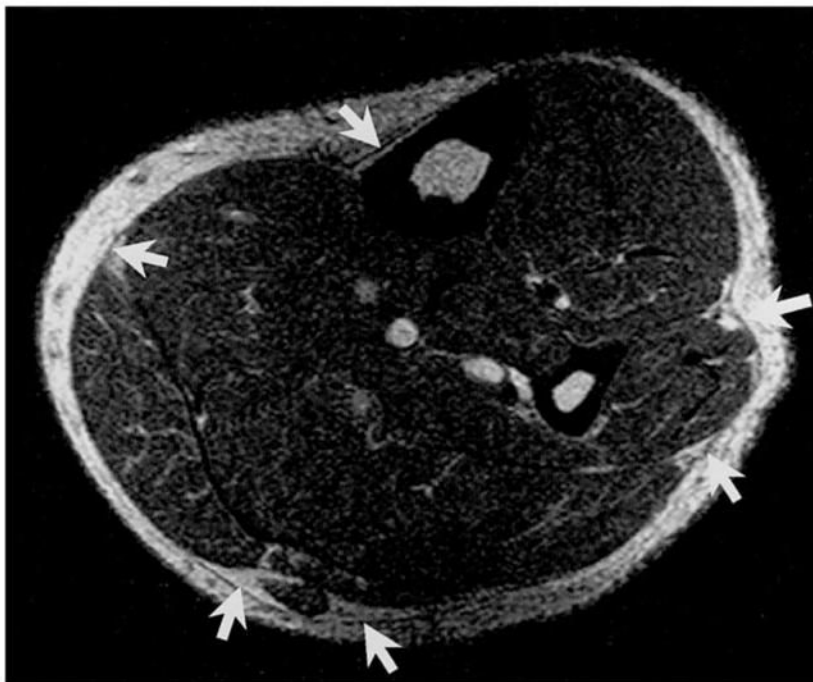


Figure 2. Abdominal axial CT scans of an obese (A) and a thin subject (B). Subcutaneous adipose tissue is divided into superficial and deep subcutaneous adipose tissue by a fascial plane, as indicated by the white arrows.

**A****B****Figure 3.**

(A) Arrows indicate the fascial planes separating perimysium from subcutaneous adipose tissue as observed on an axial leg typical resolution MRI scan. (B) Arrows indicate the fascial planes separating perimysium from subcutaneous adipose tissue as observed on an axial lower leg high resolution MRI scan. The intramuscular adipose tissue is clearer in image B than in image A.

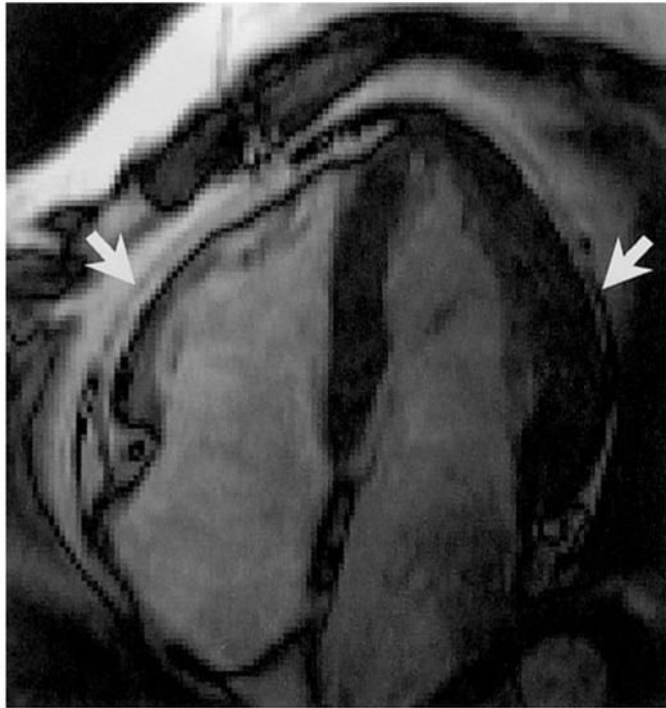


Figure 4. Arrows indicate the pericardium separating intrapericardial and extrapericardial adipose tissues on a gated cardiac image.



Figure 5. Arrows indicate the fascial planes separating pararenal from adjacent adipose tissue compartments on a typical resolution axial abdominal MRI scan.

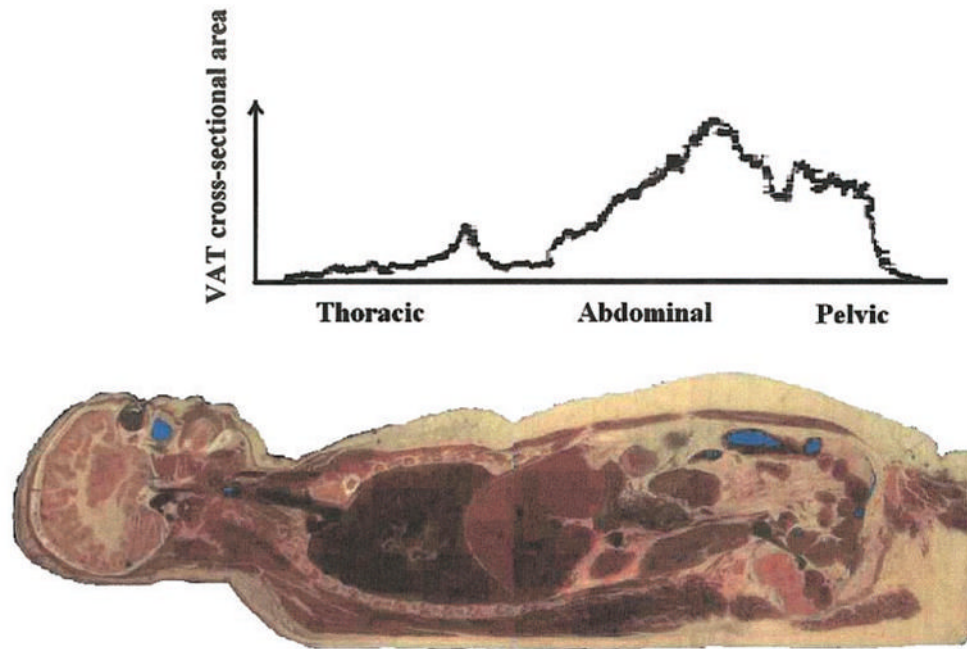


Figure 6. VAT distribution in the Visible Woman. Contiguous areas from 1-mm-thick slices are plotted across the thoracic, abdominal, and pelvic region. Reprinted with permission from the National Library of Medicine.

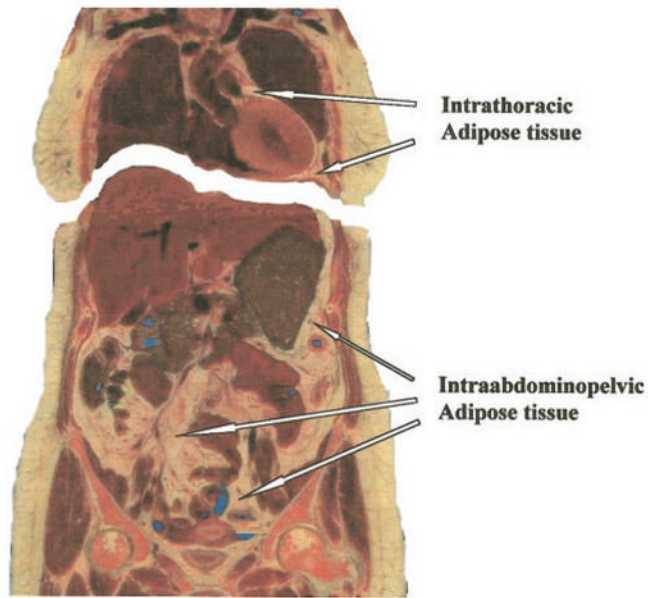


Figure 7.
The two VAT compartments in a coronal section of the Visible Man. Reprinted with permission from the National Library of Medicine.

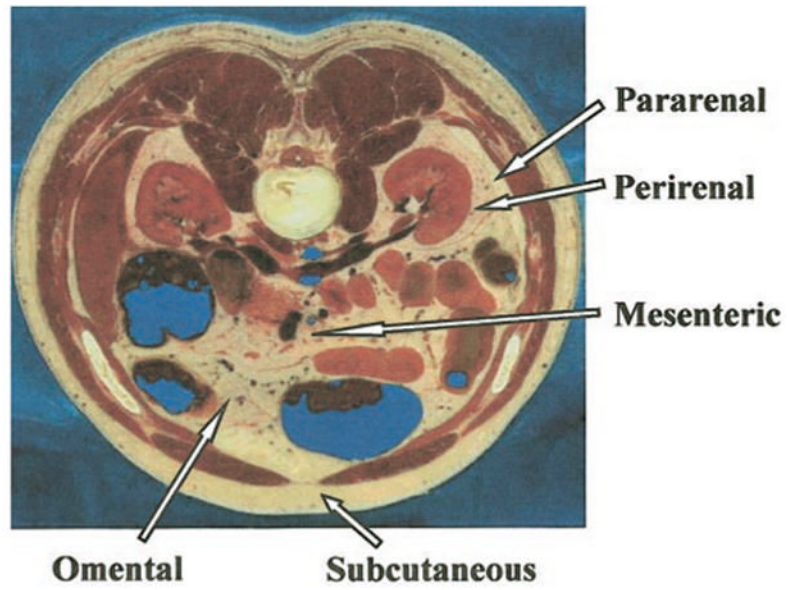


Figure 8. Main adipose tissue compartments in an axial section of the Visible Man. Reprinted with permission from the National Library of Medicine.

Table 1

Proposed classification of total body adipose tissue

Adipose tissue compartment	Definition
Total adipose tissue	Sum of adipose tissue, usually excluding bone marrow and adipose tissue in the head, hands, and feet.
Subcutaneous adipose tissue	The layer found between the dermis and the aponeuroses and fasciae of the muscles. Includes mammary adipose tissue.
Superficial subcutaneous adipose tissue	The layer found between the skin and a fascial plane in the lower trunk and gluteal-thigh area.
Deep subcutaneous adipose tissue	The layer found between the muscle fascia and a fascial plane in the lower trunk and gluteal-thigh areas.
Internal adipose tissue	Total adipose tissue minus subcutaneous adipose tissue.
Visceral adipose tissue (See Table 2)	Adipose tissue within the chest, abdomen, and pelvis.
Nonvisceral internal adipose tissue	Internal adipose tissue minus visceral adipose tissue.
Intramuscular adipose tissue	Adipose tissue within a muscle (between fascicles).
Perimuscular adipose tissue	Adipose tissue inside the muscle fascia (deep fascia), excluding intramuscular adipose tissue.
Intermuscular adipose tissue	Adipose tissue between muscles.
Paraosseal adipose tissue	Adipose tissue in the interface between muscle and bone (e.g., paravertebral).
Other nonvisceral adipose tissue	Orbital adipose tissue; aberrant adipose tissue associated with pathological conditions (e.g., lipoma).

Table 2

Proposed classification of visceral adipose tissue

Adipose tissue compartment

Visceral adipose tissue
 Intrathoracic adipose tissue
 Intrapericardial
 Extrapericardial
 Intraabdominopelvic
 Intraperitoneal (e.g., omental and mesenteric)
 Extraperitoneal
 Intraabdominal
 Preperitoneal
 Retroperitoneal (e.g., perirenal, pararenal, periaortic, and peripancreatic)
 Intrapelvic (e.g., parametrial, retropubic, paravesical, retrouterine, pararectal, retrorectal)
