Sex Differences in Body Composition

Miriam A. Bredella

Abstract Body composition differs between men and women. Men have more lean mass, and women have more fat mass than men. Men are more likely to accumulate adipose tissue around the trunk and abdomen, whereas women usually accumulate adipose tissue around the hips and thighs. Less is known about sex differences in ectopic fat depots. Advances in imaging allow the *noninvasive* assessment of abdominal and femorogluteal fat compartments, intramyocellular lipids, intrahepatic lipids, pericardial adipose tissue, and neck adipose tissue including brown adipose tissue and tongue adipose tissue. In this review, sex differences of regional adipose tissue, muscle mass, ectopic lipids, and brown adipose tissue and their effects on cardiometabolic risk will be discussed. In addition, novel imaging techniques to quantify these body composition compartments *noninvasively* will be described.

Introduction

There is a great interest in the potential physiologic differences between males and females that may affect the prevention, diagnosis, and treatment of obesity and diabetes. Although males and females are both susceptible to obesity, the incidence and health consequences differ between the sexes (Power and Schulkin 2008) as do the patterns of fat distribution (Lemieux et al. 1993). Men have more lean mass, and women have more body fat than men of the same BMI, and men are more likely to accumulate adipose tissue around the trunk and abdomen, whereas women usually accumulate adipose tissue around the hips and thighs. Less is known about sex differences in ectopic fat depots. Advances in imaging allow the *noninvasive* assessment of abdominal and femorogluteal fat compartments (Bredella et al. 2010, 2013; Machann et al. 2005), intramyocellular lipids (Bredella et al. 2010; Machann et al.

M.A. Bredella (✉)
Department of Radiology, Division of Musculoskeletal Radiology and Interventions, Massachusetts General Hospital, Boston, MA, USA

Harvard Medical School, Boston, MA, USA
e-mail: mbredella@mgh.harvard.edu

F. Mauvais-Jarvis (ed.), *Sex and Gender Factors Affecting Metabolic Homeostasis, Diabetes and Obesity*, Advances in Experimental Medicine and Biology 1043, https://doi.org/10.1007/978-3-319-70178-3_2

2004, 2008; Torriani et al. 2005, 2007), intrahepatic lipids (Machann et al. 2008; Bredella et al. 2010; Dichtel et al. 2016), pericardial adipose tissue (Nichols et al. 2008; Wheeler et al. 2005), and neck adipose tissue including brown adipose tissue (Cypess et al. 2009; Saito et al. 2009; Torriani et al. 2014) and tongue adipose tissue (Godoy et al. 2016). In this review, sex differences of regional adipose tissue, muscle mass, ectopic lipids, and brown adipose tissue and their effects on cardiometabolic risk will be discussed. In addition, novel imaging techniques to quantify these body composition compartments *noninvasively* will be described.

Abdominal Adipose Tissue

Women have a higher percentage of body fat than men of the same BMI and a relatively higher proportion of body fat in the femorogluteal region, compared to more fat in the abdominal region in men (Lemieux et al. 1993). Studies have shown that the distribution of body fat has a greater impact on cardiometabolic risk than excess total adiposity. While the male pattern of abdominal fat accumulation is associated with increased cardiometabolic risk, the female pattern of fat distribution around the femorogluteal area might be relatively protective (Bjorntorp 1985, 1992; Goodpaster et al. 1997; Ohlson et al. 1985; Snijder et al. 2005). Within the abdomen, fat can accumulate in the subcutaneous area, subcutaneous adipose tissue (SAT) or in the deep abdomen, visceral adipose tissue (VAT). Multiple studies have demonstrated that VAT is associated with increased cardiometabolic risk (Bjorntorp 1992; Bjorntorp and Rosmond 1999; Tchernof and Despres 2013). Advances in imaging allow the detailed assessment of subcutaneous and visceral fat compartments (Bredella et al. 2009, 2010; Machann et al. 2005).

Dual-energy X-ray absorptiometry (DXA) is a technique that is routinely used for osteoporosis screening (Blake and Fogelman 2007) and is therefore readily available. It is associated with minimal radiation exposure and is relatively inexpensive. DXA is able to assess body composition, such as fat and lean mass, which has been shown to correlate closely with measures obtained by computed tomography (CT) or magnetic resonance imaging (MRI) in individuals of normal weight (Fuller et al. 1999; Glickman et al. 1985; Levine et al. 1985). However, we have demonstrated that in the extremes of the weight spectrum—obesity and anorexia nervosa—DXA underestimates trunk fat, a surrogate for VAT, as well as thigh fat, and this error increases with increasing weight (Bredella et al. 2010a). Advances in DXA technology now allow the assessment of VAT and abdominal SAT, using an algorithm that is based on changes in gray-scale values and special modeling techniques (Micklesfield et al. 2012). We performed a study testing this new technique in women across the weight spectrum. DXA was less accurate in quantifying VAT and SAT when used in subjects with extremely low weight and more accurate in overweight and obese women (Bredella et al. 2013).

CT and MRI are considered the gold standard for detailed assessment of body composition, including abdominal fat compartments (Abate et al. 1994; Rossner

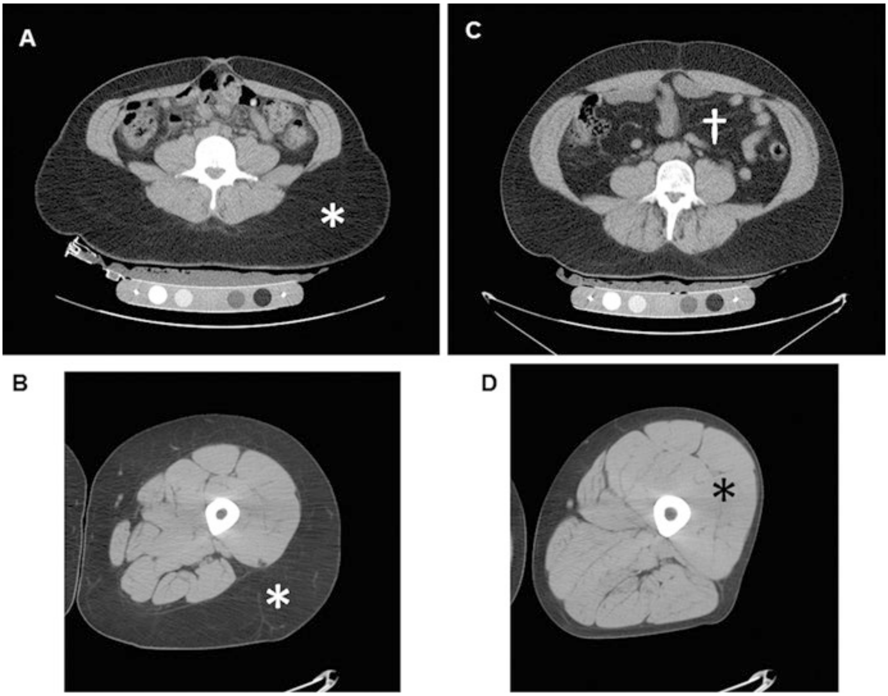

Fig. 1 Body composition of the abdomen and thigh assessed by CT in a 39-year-old woman (**a**, **b**) and 37-year-old man (**c**, **d**) with obesity (BMI, 33 kg/m^2) who were otherwise healthy. The woman has more subcutaneous adipose tissue in the abdomen and thigh (*white asterisks*), while the man has more visceral adipose tissue (*cross*) and muscle mass (*black asterisk*). The woman had a better metabolic profile compared to the man (serum LDL cholesterol 57 mg/dL vs 147 mg/dL; HDL cholesterol 68 mg/dL vs 32 mg/dL; triglycerides 45 mg/dL vs 159 mg/dL; insulin 4.9 μU/mL vs 7.0 μU/mL; HOMA-IR 0.98 vs 7.00)

et al. 1990) (Fig. 1). Studies using CT have shown that men have up to twice as much VAT compared to women (Kvist et al. 1988). Machann et al. (2005) used whole body MRI to assess sex differences in body composition in 150 healthy volunteers (90 women, 60 men) across a wide age range (19–69 years) who were at risk for developing type 2 diabetes mellitus (T2DM). At similar age and BMI, women had significantly higher %total adipose tissue, lower %VAT, and higher %SAT. Women had more fat in the lower extremities compared to men (Machann et al. 2005). In a study examining premenopausal women, Lemieux et al. (1994) found that although women had more total body fat than men, they had lower VAT assessed by CT, and this was associated with a better metabolic risk profile (Lemieux et al. 1994). Fox et al. (2007) examined 3,001 subjects from the Framingham Heart Cohort (1,452 women, 1,549 men, mean age 51 years) who underwent CT of the abdomen. Among men and women, abdominal SAT and VAT were significantly associated with blood pressure, fasting plasma glucose, triglycerides, high-density lipoprotein cholesterol, and increased odds of hypertension, impaired fasting glucose, T2DM, and the metabolic syndrome, with stronger correlations between VAT and most cardiometabolic risk factors. In women, VAT was more strongly associated with cardiometabolic risk factors compared to men with larger effect sizes. There were significant sex interactions with increasing volumes of SAT and VAT being consistently and more strongly associated with more adverse cardiometabolic risk factors in women than in men (Fox et al. 2007). These studies suggest that although women have more VAT, it confers greater cardiometabolic risk compared to men.

Muscle Mass

Skeletal muscle plays a critical role in regulating glucose homeostasis being responsible for the majority of basal and insulin-stimulated glucose uptake. Impaired insulin action at the level of skeletal muscle is central to the clinical manifestations of insulin resistance and T2DM (DeFronzo and Tripathy 2009). Furthermore, sarcopenia, the age-related decline in skeletal muscle mass, quality, and function, may represent an underappreciated contribution to increased risk of T2DM (Larsen et al. 2016; Park et al. 2009), and patients with T2DM show a greater decline in leg muscle mass, strength, and function compared with healthy controls (Leenders et al. 2013). Lean or fat-free mass can be assessed using DXA (Fuller et al. 1999; Levine et al. 1985); however, we have shown that DXA overestimated thigh muscle mass and this error increases with increasing weight (Bredella et al. 2010). CT and MRI are considered the gold standard for quantifications of skeletal muscle mass (Beneke et al. 1991; Borkan et al. 1983; Engstrom et al. 1991; Mitsiopoulos et al. 1985) (Fig. 1).

Sex differences in muscle mass become apparent during puberty, with boys having larger muscles than girls (Kanehisa et al. 1994; Tanner et al. 1981). Gallagher et al. (1985) assessed sex differences in skeletal muscle mass by DXA in 148 women and 136 men. Men had higher muscle mass than women, and this difference was greater in the upper compared to the lower body. With aging a larger magnitude decrease of muscle was observed in men compared to women (Gallagher et al. 1985). Janssen et al. (1985) performed whole body MRI in 468 men and women from 18 to 88 years. Men had significantly higher skeletal muscle mass than women in both absolute terms and relative terms relative to body mass (38% vs 31%). The sex differences were greater in the upper (40%) than lower (33%) body. Aging was associated with loss of muscle mass, independent of sex, with greater loss of muscle in the lower body (Janssen et al. 1985).

A study examining 1,433 subjects (658 men and 775 women), 60 years or older, who participated in the Fifth Korea National Health and Nutritional Examination Survey 2010, found a higher prevalence of sarcopenic obesity in women compared to men (31.3% vs 19.6%) (Oh et al. 2015). Men and women with sarcopenic obesity had higher fasting insulin, HOMA-IR, and serum triglycerides (Oh et al. 2015). Ochi et al. (2010) examined 496 healthy middle-aged to elderly men and women with CT of the thigh to assess muscle mass corrected for body weight and carotid ultrasound to assess carotid intima-media thickness (IMT) and brachial-ankle pulse wave velocity (baPWV). High relative muscle area was inversely associated with carotid IMT and baPWV in men but not in women (Ochi et al. 2010). In a study from the National Health and Nutrition Examination Survey III examining 4,652 elderly men and women (mean age 70.6 ± 0.2 years), the prevalence of sarcopenic obesity was lower in women compared to men (18.1% vs 42.9%). However, in women but not in men, sarcopenic obesity was associated with increased mortality, and women with sarcopenia had higher mortality risk compared to men, regardless of the presence of obesity (Batsis et al. 2014). The reported sex differences in muscle mass with higher morbidity and mortality in women emphasize the importance of maintaining muscle mass with aging, especially in women who are at greater risk for developing sarcopenic obesity due to higher fat and lower muscle mass.

Intramyocellular Lipids

Within skeletal muscle, lipids occur between muscle fibers, called extramyocellular lipids (EMCL), and within muscle cells, called intramyocellular lipids (IMCL). IMCL have been shown to play a critical role in the pathogenesis of insulin resistance (Shulman 2000, 2014). IMCL can be quantified using proton MR spectroscopy (1H-MRS), and several studies have shown higher IMCL as determined by 1H-MRS in states of insulin resistance, T2DM, and disorders of lipid metabolism. The ability to distinguish IMCL from EMCL is based on their difference in geometric arrangements within muscle which is associated with different bulk magnetic susceptibility, which leads to a spectroscopic frequency separation between the two pools (Boesch 2007; Boesch and Kreis 2000; Boesch et al. 1997; Goodpaster et al. 2000) (Fig. 2).

Machann et al. (2005) performed 1H-MRS for quantification of IMCL within soleus muscle and whole body MRI for quantification of adipose tissue depots in 150 healthy volunteers. Men had significantly higher IMCL compared to women, despite similar BMI and age. In women but not in men, IMCL were positively associated with total adipose tissue, VAT, and abdominal SAT and inversely associated with lower extremity adipose tissue (Machann et al. 2005).

However, not only the quantity but also the composition of the IMCL pool plays an important role for cardiometabolic risk. Fatty acid composition in patients with insulin resistance and the metabolic syndrome is characterized by high levels of saturated fatty acids and low levels of polyunsaturated fatty acids (Vessby et al. 2002; Warensjo et al. 2005). Therefore, techniques that could assess lipid components and the degree of unsaturation in vivo may provide important information on cardiometabolic risk. The composition of muscle lipids can be quantified using localized 2D correlation spectroscopy (L-COSY) (Thomas et al. 2005; Velan et al. 2007, b). To study sex difference in skeletal muscle composition, Velan et al. (2008) examined eight healthy normal-weight premenopausal women and eight

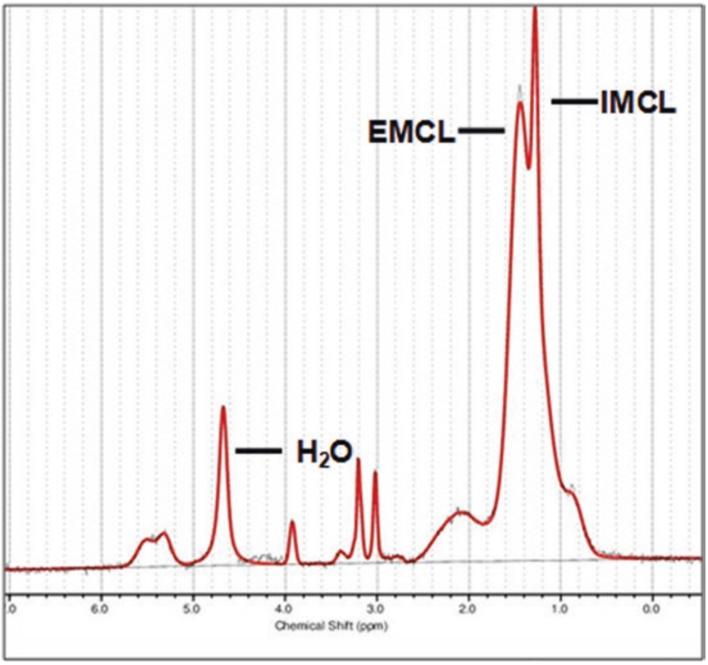

Fig. 2 Proton MR spectroscopy (1H-MRS) of soleus muscle for assessment of intramyocellular lipid content. 1H-MRS spectrum shows IMCL and EMCL resonances. *IMCL* (intramyocellular lipids) methylene protons at 1.3 ppm; *EMCL* (extramyocellular lipids) methylene protons at 1.5 ppm; *H_2O* residual water signal

normal-weight age-matched men using L-COSY of soleus muscle to determine the amount of saturated and unsaturated fatty acids. Women had a lower degree of unsaturation within IMCL and EMCL compared to men (Velan et al. 2008). These findings might contribute to increased cardiometabolic risk in women.

Intrahepatic Lipids

A complication of obesity is nonalcoholic fatty liver disease (NAFLD), fatty infiltration of the liver in the absence of alcohol use. NAFLD encompasses a spectrum that ranges from simple steatosis to nonalcoholic steatohepatitis (NASH). NASH is associated with the development of fibrosis, cirrhosis, and hepatocellular carcinoma and is expected to become the most common indication for liver transplantation by 2020 (Charlton 2008; Williams et al. 2011; Wree et al. 2013). While sex differences in gastrointestinal diseases are increasingly recognized, there are few data on sex differences in NAFLD. Advances in MRI technology allow the accurate quantification of hepatic lipid content *noninvasively*, and we have developed pulse sequences

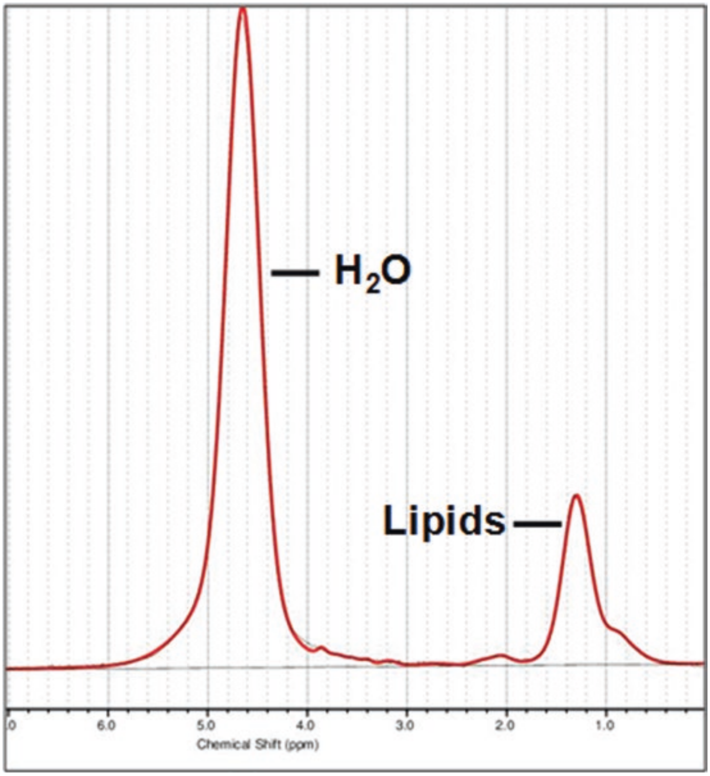

Fig. 3 Breath-hold single voxel proton MR spectroscopy (1H-MRS) of the right hepatic lobe for assessment of intrahepatic lipids. 1H-MRS spectrum shows lipids (1.3 ppm) and unsuppressed water (4.7 ppm) resonances

for proton MR spectroscopy (1H-MRS) that allow assessment of hepatic lipids in a single breath-hold (Bredella et al. 2010; Dichtel et al. 2016) (Fig. 3).

Machann et al. (2005) performed 1H-MRS for quantification of hepatic lipid content in 150 healthy volunteers across a wide age range (19–69 years) who were at risk for developing T2DM. There was no significant difference in hepatic lipid content between men and women at similar BMI. However, in women, intrahepatic lipids were positively associated with age, VAT, and abdominal SAT, while in men intrahepatic lipids only correlated with VAT (Machann et al. 2005). Westerbacka et al. (2004) assessed intrahepatic lipids in 66 men and 66 women using 1H-MRS. There was no significant difference in intrahepatic lipid content between men and women. Intrahepatic lipids were positively associated with measures of serum insulin, independent of age, BMI, and intra-abdominal and subcutaneous fat with no sex differences observed (Westerbacka et al. 2004).

Fatty infiltration of the liver can also be assessed using computed tomography (CT) by measuring liver attenuation in Hounsfield units (HU) which correlates with hepatic lipid content assessed by 1H-MRS (Bredella et al. 2010). North et al. (2012)

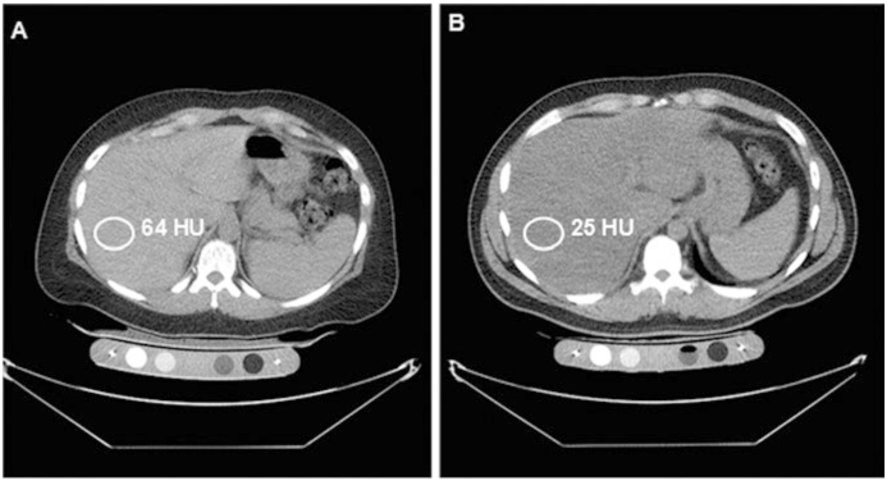

Fig. 4 Non-contrast CT of the liver for assessment of intrahepatic lipid content in the right hepatic lobe in a 39-year-old woman with obesity (BMI, 31 kg/m^2) (**a**) and a 37-year-old man with the same BMI (**b**). CT attenuation was lower in the man compared to the woman, consistent with fatty infiltration. Images are presented by using the same window and level

examined liver attenuation by CT as a marker of fatty infiltration in 1,242 men and 1,477 women who participated in the NHLBI Family Heart Study. Men had significantly lower liver attenuation, consistent with fatty infiltration, compared to women (Fig. 4). In both sexes fatty infiltration was associated with VAT, serum triglycerides, and measures of insulin resistance; however, the association of fatty liver infiltration with VAT and HOMA-IR had a stronger magnitude of effect in women. Fatty infiltration of the liver was associated with alcohol consumption and BMI only in men, while no such associations were observed in women (North et al. 2012).

Lonardo et al. (Lonardo and Trande 2000) studied men and women with and without fatty liver, assessed by ultrasound, to determine sex differences in predictors of fatty infiltration. BMI was an independent predictor of fatty infiltration in either sex. Measures of impaired glucose tolerance were predictors of liver fatty infiltration in women but not in men, while elevations in serum triglycerides were predictors of fatty infiltration in men but not in women. Moreover, central adiposity was a predictor of fatty liver in women but not in men. These findings suggest that there are sex-specific pathways for fatty infiltration of the liver (Lonardo and Trande 2000). An understanding of the underlying mechanisms responsible for these sex differences in intrahepatic fat accumulation may lead to improved therapeutic strategies for the prevention and treatment of NAFLD and NASH.

Pericardial Adipose Tissue

Recent studies have identified pericardial adipose tissue (PAT), the fat around the heart, as a novel risk factor for coronary artery disease (CAD), atrial fibrillation, carotid intima-media thickness, and carotid stiffness (Brinkley et al. 2011; Lee et al. 2016; Rosito et al. 2008; Schlett et al. 2012; Soliman et al. 2010). PAT is a unique fat depot given its anatomic proximity to the myocardium, coronary arteries, and atrial conduction system (Friedman et al. 2014). In addition to storing lipids, PAT also secretes adipokines and inflammatory cytokines (Baker et al. 2006; Cheng et al. 2008) which, given the proximity to the coronary arteries and shared blood supply with the coronary artery wall, may lead to acceleration of atherosclerosis (Fantuzzi and Mazzone 2007; Yudkin et al. 2005). PAT can be accurately quantified using CT (Ding et al. 2008).

The incidence of cardiovascular disease (CVD) differs by sex, and although CVD and heart disease are more prevalent in older men than women (Arnold et al. 2005), women suffering from CVD have a higher mortality compared to men. Differences in PAT volume between men and women may account for some of the observed sex differences in manifestations of CVD.

In a study of 1,155 participants (522 men, 633 women, mean age 63 years) of the Framingham Heart Study, who were free of CVD, Rosito et al. (2008) found significantly higher PAT volume by CT in men compared to women, despite similar age and BMI (Fig. 5). However, PAT was positively associated with systolic and diastolic blood pressure and fasting glucose in women but not in men. In addition, there were significant sex interactions between PAT and serum triglycerides, HDL cholesterol, the presence of hypertension, impaired fasting glucose, T2DM, and the metabolic syndrome, with larger effect sizes in women compared to men, which

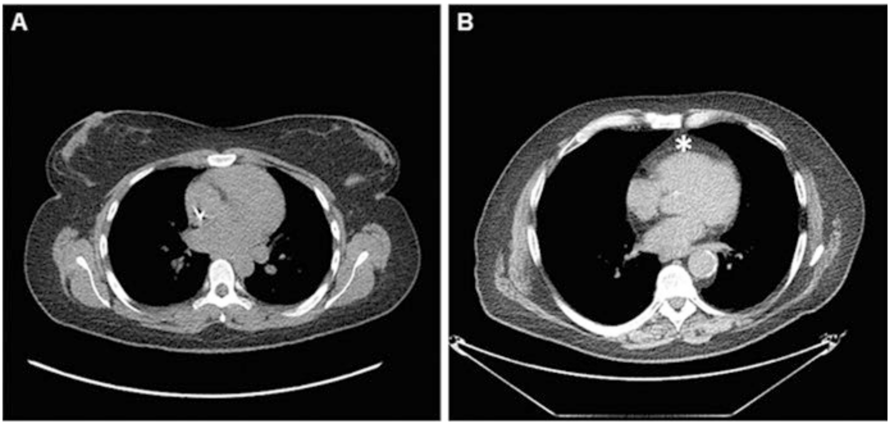

Fig. 5 Non-contrast CT of the chest for assessment of pericardial adipose tissue in a 33-year-old woman with obesity (BMI 31 kg/m^2) (**a**) and an age- and BMI-matched man (**b**). The man had higher pericardial adipose tissue area (*asterisk*) compared to the woman despite the same BMI

were independent of BMI. These data suggest that PAT is associated with more adverse risk factor profiles in women than men (Rosito et al. 2008). In another study examining 1946 participants (1,067 men, 879 women, mean age 44.0 ± 6.4 years) of the Framingham Heart Study, Friedman et al. (2014) examined the relationship between PAT and atrial conduction as measured by P wave indices. In men and women, PAT was significantly associated with P duration in analyses after adjusting for visceral or intrathoracic fat. Among women, PAT was associated with P wave area after adjustment for intrathoracic and visceral fat and with P wave terminal force after adjustment for visceral fat. In multivariable models adjusting for BMI, pericardial fat remained associated with P wave duration and P wave terminal force in women and P wave amplitude and P wave terminal force in men (Friedman et al. 2014). Brinkley et al. (2011) examined 5,770 participants (2,719 men, 3,051 women, mean age 62.1 ± 10.2 years) from the Multi-Ethnic Study of Atherosclerosis (MESA) cohort who underwent CT for PAT and ultrasound for assessment of carotid stiffness. In men and women, PAT was positively associated with parameters of arterial stiffness, independent height, demographics, behavioral factors, blood pressure, metabolic factors, medication use, CRP, BMI, and waist circumference. However, the effect size was larger in women. In an exploratory analysis examining whether the relationship between PAT and carotid stiffness was altered by total or abdominal obesity, the association between PAT and carotid stiffness was twofold stronger in women who were nonobese, while in men there was no difference in the associations among the obesity subgroups. These findings suggest that excess PAT is more detrimental when the overall amount of body fat is low or normal and these changes are more pronounced in women (Brinkley et al. 2011).

Neck Adipose Tissue

Fat accumulation in the neck—usually estimated by neck circumference—has been found to be a strong marker of metabolic disease, independent of BMI or waist circumference (Preis et al. 2010). In contrast to the well-defined abdominal fat compartments, VAT and SAT, less is known about discrete fat compartments in the neck and potential sex differences in neck adipose tissue. In a retrospective study, we determined specific neck adipose tissue compartments by CT in 151 women and 152 men across a wide range of age (mean age 55 ± 17 years; range 18–91 years) and BMI (28 ± 6 kg/m^2, range 16–47 kg/m^2) (Torriani et al. 2014). There were 101 subjects in each BMI category (normal weight, overweight, obese), and there were no age differences between sexes in each category. Neck adipose tissue was assessed by CT. Measures of cardiovascular (CV) risk and the presence or absence of the metabolic syndrome were determined. We identified three discrete fat compartments in the neck: subcutaneous/superficial neck adipose tissue (NATsc), located between the skin and deep cervical fat and two intermuscular fat compartments; posterior cervical neck adipose tissue (NATpost), located between the sternocleidomastoid, scalene, and trapezius muscle; and perivertebral neck adipose tissue

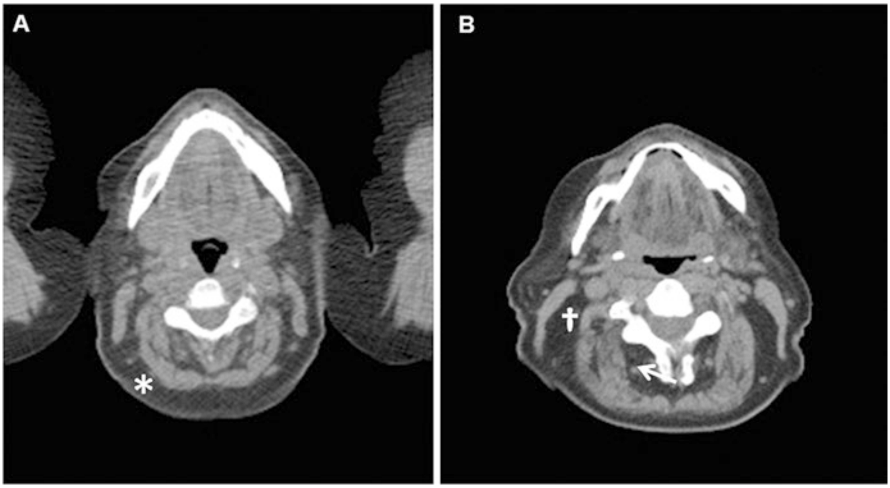

Fig. 6 CT of the neck for assessment of neck adipose tissue (NAT) in a 56-year-old woman and a 56-year-old man with the same BMI (35 kg/m^2). The woman had more subcutaneous NAT (*asterisk*), and the man had more intermuscular adipose tissue [posterior NAT (*cross*) and perivertebral NAT (*arrow*)]. The man but not the woman had serum measures consistent with the metabolic syndrome

(NATperivert), fat interspersed between muscles surrounding the cervical vertebral body. There was no difference in neck adipose tissue in lean men and women. However, overweight and obese women had significantly higher subcutaneous neck fat compared to men, despite being age and BMI matched. Conversely, overweight and obese men had significantly higher intermuscular neck adipose tissue depots (NATpost and NATperivert) compared to obese women (Fig. 6). NATpost and NATsc were associated with measures of cardiometabolic risk, which was stronger in women compared to men. In both sexes, NATsc was associated with the metabolic syndrome even after adjusting for BMI. In both sexes NATpost had the highest prevalence ratio for the metabolic syndrome, but this persisted only in women after additional adjustment for BMI. Also NATperivert only remained a significant predictor of the metabolic syndrome in women after adjustment for BMI (Torriani et al. 2014). Similar to the abdomen, women have more subcutaneous fat in the neck and men more intermuscular fat. Accumulation of neck adipose tissue is associated with higher risk of the metabolic syndrome in women compared to men.

Brown Adipose Tissue

Advances in positron emission tomography (PET) combined with computed tomography (CT) technology allow the *noninvasive* assessment of brown adipose tissue (BAT) in humans. Because of its metabolic activity, BAT can be visualized by [18F] fluorodeoxyglucose (FDG) uptake using FDG-PET/CT (Chen et al. 2016; Sampath et al. 2016).

BAT is the major site for nonshivering thermogenesis during cold exposure, and BAT is believed to contribute to the control of body temperature, energy expenditure, and adiposity (Cannon and Nedergaard 2004; Lowell and Spiegelman 2000). Nonshivering thermogenesis is mediated by the expression of uncoupling protein 1 (UCP1) which is expressed exclusively in the mitochondrial membrane of BAT (Cannon and Nedergaard 2004).

BAT is regulated by environmental, nutritional, endocrine and neural factors (Thuzar and Ho 2016) and is stimulated during cold exposure. Therefore, personalized cooling protocols are recommended in prospective and longitudinal studies using FDG-PET/CT for the quantification of BAT (Chen et al. 2016). BAT is also regulated by sex steroids (Lopez and Tena-Sempere 2016). Ovariectomy in rats causes atrophy of BAT depots, an effect reversed by estrogen replacement, suggesting that estrogen stimulates BAT mass (Pedersen et al. 2001; Rodriguez-Cuenca et al. 2007).

Several studies in humans performed under thermoneutral conditions have demonstrated sex differences of BAT with significantly higher prevalence and volumes of BAT in women (Cypess et al. 2009; Au-Yong et al. 2009; Ouellet et al. 2011; Zhang et al. 2014). Cypess et al. (2009) analyzed 3,640 consecutive clinical FDG-PET/CTs performed under thermoneutral conditions for various diagnostic reasons and found a higher prevalence of BAT-positive scans in women (7.5%) compared to men (3.1%). Moreover, women had significantly higher BAT mass and activity compared to men (Cypess et al. 2009). Similar results were found in a study by Au-Yong et al. of 3,614 consecutive patients who underwent FDG-PET/CTs under thermoneutral conditions (Au-Yong et al. 2009). Prevalence of BAT-positive scans in women was 7.2% and 2.8% in men (Au-Yong et al. 2009). Ouellet et al. (2011) also found a higher prevalence of BAT in women compared to men in 6,652 clinical FDG-PET/CTs performed under thermoneutral conditions. However, the difference diminished with age, and sex was not an independent determinant of BAT prevalence after adjusting for covariates, such as age, BMI, lean body weight, diabetes, or outdoor temperature. However, BAT mass and activity remained significantly higher in women compared to men, even after controlling for covariates (Ouellet et al. 2011). In the largest study to date, Zhang et al. (2014) examined 31,088 FDG-PET/CTs performed under thermoneutral conditions for routine medical checkup or cancer surveillance and found a significantly higher prevalence of BAT in women (2.36%) compared to men (0.7%). This sex difference was higher in the medical checkup group (female 3.16% vs male 0.77%) and lower in the cancer surveillance group (female 1.59% vs male 0.61%) (Zhang et al. 2014). However, prospective studies employing standardized cooling protocols did not confirm sex differences in BAT (Saito et al. 2009; Yoneshiro et al. 2011). Saito et al. (2009) performed FDG-PET/CTs in 56 healthy volunteers after a 2-h cooling protocol and found no sex difference in BAT prevalence (Saito et al. 2009). In a larger prospective study, Yoneshiro et al. (2011) performed 162 FDG-PET/CTs after a 2-h cooling protocol and found no significant sex difference in the prevalence of BAT (Yoneshiro et al.

2011). These studies suggest that sex differences in BAT observed in the retrospective studies might be due to a difference in sensitivity to environmental temperature (Thuzar and Ho 2016).

Tongue Adipose Tissue

The tongue plays an important role in upper airway patency, and increased tongue size and accumulation of adipose tissue within the tongue have been associated with a higher risk for obstructive sleep apnea (OSA) (Kim et al. 2014; Schwab et al. 1995). Men have a higher prevalence of OSA than women, and sex differences in tongue fat accumulation might represent a mechanism for sex differences in OSA. Godoy et al. (Godoy et al. 2016) assessed CT attenuation in HU as a measure of tongue fatty infiltration and measures of airway patency in 104 women and 102 men across the weight spectrum (range 16–47 kg/m^2, mean 28 ± 6 kg/m^2). Fatty infiltration of the tongue was higher in men compared to women (Fig. 7) and was associated with measures of decreased upper airway patency independent of age and BMI, suggesting higher upper airway, soft tissue burden, and narrower airways in males versus females (Godoy et al. 2016).

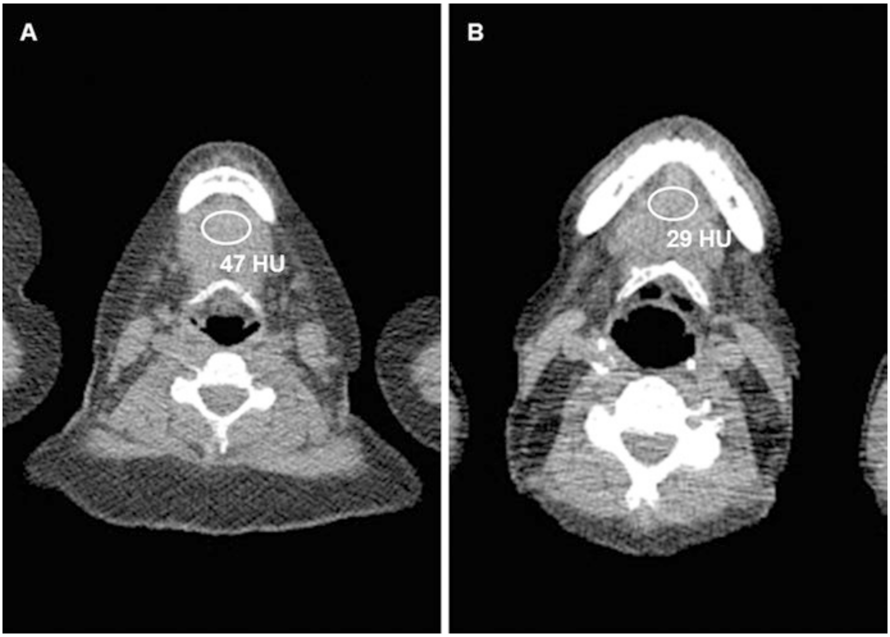

Fig. 7 Non-contrast CT of the neck for assessment of tongue adipose tissue in a 63-year-old woman (BMI, 34 kg/m^2) (**a**) and 63-year-old man with similar BMI (BMI, 35 kg/m^2) (**b**). The man had lower CT attenuation of the tongue compared to the woman, consistent with fatty infiltration. Images are presented by using the same window and level

Summary

Body composition differs between men and women. Men have more VAT and higher inter- and intramuscular adipose tissue and pericardial and tongue adipose tissue, which is associated with increased cardiometabolic risk, despite higher muscle and lean mass. Women on the other hand have more femoral SAT and neck SAT and potentially more BAT. This female pattern of fat distribution is associated with improved cardiometabolic risk at similar BMI. However, ectopic fat deposition within the abdomen, muscle, pericardium, and neck is more strongly associated with adverse cardiometabolic risk in women compared to men.

Disclosure The author has nothing to disclose.

References

Abate, N., Burns, D., Peshock, R. M., Garg, A., & Grundy, S. M. (1994). Estimation of adipose tissue mass by magnetic resonance imaging: Validation against dissection in human cadavers. *Journal of Lipid Research, 35*, 1490–1496.

Arnold, A. M., Psaty, B. M., Kuller, L. H., Burke, G. L., Manolio, T. A., Fried, L. P., Robbins, J. A., & Kronmal, R. A. (2005). Incidence of cardiovascular disease in older Americans: The cardiovascular health study. *Journal of the American Geriatrics Society, 53*, 211–218.

Au-Yong, I. T., Thorn, N., Ganatra, R., Perkins, A. C., & Symonds, M. E. (2009). Brown adipose tissue and seasonal variation in humans. *Diabetes, 58*, 2583–2587.

Baker, A. R., Silva, N. F., Quinn, D. W., Harte, A. L., Pagano, D., Bonser, R. S., Kumar, S., & McTernan, P. G. (2006). Human epicardial adipose tissue expresses a pathogenic profile of adipocytokines in patients with cardiovascular disease. *Cardiovascular Diabetology, 5*, 1.

Batsis, J. A., Mackenzie, T. A., Barre, L. K., Lopez-Jimenez, F., & Bartels, S. J. (2014). Sarcopenia, sarcopenic obesity and mortality in older adults: Results from the National Health and Nutrition Examination Survey III. *European Journal of Clinical Nutrition, 68*, 1001–1007.

Beneke, R., Neuerburg, J., & Bohndorf, K. (1991). Muscle cross-section measurement by magnetic resonance imaging. *European Journal of Applied Physiology and Occupational Physiology, 63*, 424–429.

Bjorntorp, P. (1985). Regional patterns of fat distribution. *Annals of Internal Medicine, 103*, 994–995.

Bjorntorp, P. (1992). Metabolic abnormalities in visceral obesity. *Annals of Medicine, 24*, 3–5.

Bjorntorp, P., & Rosmond, R. (1999). Visceral obesity and diabetes. *Drugs, 58*(Suppl 1), 13–18; discussion 75–82.

Blake, G. M., & Fogelman, I. (2007). Role of dual-energy X-ray absorptiometry in the diagnosis and treatment of osteoporosis. *Journal of Clinical Densitometry, 10*, 102–110.

Boesch, C. (2007). Musculoskeletal spectroscopy. *Journal of Magnetic Resonance Imaging, 25*, 321–338.

Boesch, C., & Kreis, R. (2000). Observation of intramyocellular lipids by 1H-magnetic resonance spectroscopy. *Annals of the New York Academy of Sciences, 904*, 25–31.

Boesch, C., Slotboom, J., Hoppeler, H., & Kreis, R. (1997). In vivo determination of intramyocellular lipids in human muscle by means of localized 1H-MR-spectroscopy. *Magnetic Resonance in Medicine, 37*, 484–493.

Borkan, G. A., Hults, D. E., Gerzof, S. G., Robbins, A. H., & Silbert, C. K. (1983). Age changes in body composition revealed by computed tomography. *Journal of Gerontology, 38*, 673–677.

Bredella, M. A., Utz, A. L., Torriani, M., Thomas, B., Schoenfeld, D. A., & Miller, K. K. (2009). Anthropometry, CT, and DXA as predictors of GH deficiency in premenopausal women: ROC curve analysis. *Journal of Applied Physiology, 106*, 418–422.

Bredella, M. A., Ghomi, R. H., Thomas, B. J., Torriani, M., Brick, D. J., Gerweck, A. V., Misra, M., Klibanski, A., & Miller, K. K. (2010a). Comparison of DXA and CT in the assessment of body composition in premenopausal women with obesity and anorexia nervosa. *Obesity (Silver Spring), 18*, 2227–2233.

Bredella, M. A., Hosseini Ghomi, R., Thomas, B. J., Miller, K. K., & Torriani, M. (2010b). Comparison of 3.0 T proton magnetic resonance spectroscopy short and long echo-time measures of intramyocellular lipids in obese and normal-weight women. *Journal of Magnetic Resonance Imaging, 32*, 388–393.

Bredella, M. A., Hosseini Ghomi, R., Thomas, B. J., Ouellette, H. A., Sahani, D. V., Miller, K. K., & Torriani, M. (2010c). Breath-hold 1H-magnetic resonance spectroscopy for intrahepatic lipid quantification at 3 tesla. *Journal of Computer Assisted Tomography, 34*, 372–376.

Bredella, M. A., Gill, C. M., Keating, L. K., Torriani, M., Anderson, E. J., Punyanitya, M., Wilson, K. E., Kelly, T. L., & Miller, K. K. (2013). Assessment of abdominal fat compartments using DXA in premenopausal women from anorexia nervosa to morbid obesity. *Obesity (Silver Spring), 21*, 2458–2464.

Brinkley, T. E., Hsu, F. C., Carr, J. J., Hundley, W. G., Bluemke, D. A., Polak, J. F., & Ding, J. (2011). Pericardial fat is associated with carotid stiffness in the multi-ethnic study of atherosclerosis. *Nutrition, Metabolism, and Cardiovascular Diseases, 21*, 332–338.

Cannon, B., & Nedergaard, J. (2004). Brown adipose tissue: Function and physiological significance. *Physiological Reviews, 84*, 277–359.

Charlton, M. (2008). Cirrhosis and liver failure in nonalcoholic fatty liver disease: Molehill or mountain? *Hepatology, 47*, 1431–1433.

Chen, K. Y., Cypess, A. M., Laughlin, M. R., Haft, C. R., Hu, H. H., Bredella, M. A., Enerback, S., Kinahan, P. E., Lichtenbelt, W., Lin, F. I., Sunderland, J. J., Virtanen, K. A., & Wahl, R. L. (2016). Brown Adipose Reporting Criteria in Imaging STudies (BARCIST 1.0): Recommendations for standardized FDG-PET/CT experiments in humans. *Cell Metabolism, 24*, 210–222.

Cheng, K. H., Chu, C. S., Lee, K. T., Lin, T. H., Hsieh, C. C., Chiu, C. C., Voon, W. C., Sheu, S. H., & Lai, W. T. (2008). Adipocytokines and proinflammatory mediators from abdominal and epicardial adipose tissue in patients with coronary artery disease. *International Journal of Obesity, 32*, 268–274.

Cypess, A. M., Lehman, S., Williams, G., Tal, I., Rodman, D., Goldfine, A. B., Kuo, F. C., Palmer, E. L., Tseng, Y. H., Doria, A., Kolodny, G. M., & Kahn, C. R. (2009). Identification and importance of brown adipose tissue in adult humans. *The New England Journal of Medicine, 360*, 1509–1517.

DeFronzo, R. A., & Tripathy, D. (2009). Skeletal muscle insulin resistance is the primary defect in type 2 diabetes. *Diabetes Care, 32*(Suppl 2), S157–S163.

Dichtel, L. E., Eajazi, A., Miller, K. K., Torriani, M., & Bredella, M. A. (2016). Short- and long-term reproducibility of intrahepatic lipid quantification by 1H-MR spectroscopy and CT in obesity. *Journal of Computer Assisted Tomography, 40*, 678–682.

Ding, J., Kritchevsky, S. B., Hsu, F. C., Harris, T. B., Burke, G. L., Detrano, R. C., Szklo, M., Criqui, M. H., Allison, M., Ouyang, P., Brown, E. R., & Carr, J. J. (2008). Association between non-subcutaneous adiposity and calcified coronary plaque: A substudy of the Multi-Ethnic Study of Atherosclerosis. *The American Journal of Clinical Nutrition, 88*, 645–650.

Engstrom, C. M., Loeb, G. E., Reid, J. G., Forrest, W. J., & Avruch, L. (1991). Morphometry of the human thigh muscles. A comparison between anatomical sections and computer tomographic and magnetic resonance images. *Journal of Anatomy, 176*, 139–156.

Fantuzzi, G., & Mazzone, T. (2007). Adipose tissue and atherosclerosis: Exploring the connection. *Arteriosclerosis, Thrombosis, and Vascular Biology, 27*, 996–1003.

Fox, C. S., Massaro, J. M., Hoffmann, U., Pou, K. M., Maurovich-Horvat, P., Liu, C. Y., Vasan, R. S., Murabito, J. M., Meigs, J. B., Cupples, L. A., D'Agostino, R. B., Sr., & O'Donnell, C. J.

(2007). Abdominal visceral and subcutaneous adipose tissue compartments: Association with metabolic risk factors in the Framingham Heart Study. *Circulation, 116*, 39–48.

Friedman, D. J., Wang, N., Meigs, J. B., Hoffmann, U., Massaro, J. M., Fox, C. S., & Magnani, J. W. (2014). Pericardial fat is associated with atrial conduction: The Framingham Heart Study. *Journal of the American Heart Association, 3*, e000477.

Fuller, N. J., Hardingham, C. R., Graves, M., Screaton, N., Dixon, A. K., Ward, L. C., & Elia, M. (1999). Assessment of limb muscle and adipose tissue by dual-energy X-ray absorptiometry using magnetic resonance imaging for comparison. *International Journal of Obesity and Related Metabolic Disorders, 23*, 1295–1302.

Gallagher, D., Visser, M., De Meersman, R. E., Sepulveda, D., Baumgartner, R. N., Pierson, R. N., Harris, T., & Heymsfield, S. B. (1985). 1997 Appendicular skeletal muscle mass: Effects of age, gender, and ethnicity. *Journal of Applied Physiology, 83*, 229–239.

Glickman, S. G., Marn, C. S., Supiano, M. A., & Dengel, D. R. (1985). 2004 Validity and reliability of dual-energy X-ray absorptiometry for the assessment of abdominal adiposity. *Journal of Applied Physiology, 97*, 509–514.

Godoy, I. R., Martinez-Salazar, E. L., Eajazi, A., Genta, P. R., Bredella, M. A., & Torriani, M. (2016). Fat accumulation in the tongue is associated with male gender, abnormal upper airway patency and whole-body adiposity. *Metabolism, 65*, 1657–1663.

Goodpaster, B. H., Thaete, F. L., Simoneau, J. A., & Kelley, D. E. (1997). Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. *Diabetes, 46*, 1579–1585.

Goodpaster, B. H., Theriault, R., Watkins, S. C., & Kelley, D. E. (2000). Intramuscular lipid content is increased in obesity and decreased by weight loss. *Metabolism, 49*, 467–472.

Janssen, I., Heymsfield, S. B., Wang, Z. M., & Ross, R. (1985). 2000 Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *Journal of Applied Physiology, 89*, 81–88.

Kanehisa, H., Ikegawa, S., Tsunoda, N., & Fukunaga, T. (1994). Cross-sectional areas of fat and muscle in limbs during growth and middle age. *International Journal of Sports Medicine, 15*, 420–425.

Kim, A. M., Keenan, B. T., Jackson, N., Chan, E. L., Staley, B., Poptani, H., Torigian, D. A., Pack, A. I., & Schwab, R. J. (2014). Tongue fat and its relationship to obstructive sleep apnea. *Sleep, 37*, 1639–1648.

Kvist, H., Chowdhury, B., Grangard, U., Tylen, U., & Sjostrom, L. (1988). Total and visceral adipose-tissue volumes derived from measurements with computed tomography in adult men and women: Predictive equations. *The American Journal of Clinical Nutrition, 48*, 1351–1361.

Larsen, B. A., Wassel, C. L., Kritchevsky, S. B., Strotmeyer, E. S., Criqui, M. H., Kanaya, A. M., Fried, L. F., Schwartz, A. V., Harris, T. B., & Ix, J. H. (2016). Association of muscle mass, area, and strength with incident diabetes in older adults: The health ABC study. *The Journal of Clinical Endocrinology and Metabolism, 101*, 1847–1855.

Lee, J. J., Yin, X., Hoffmann, U., Fox, C. S., & Benjamin, E. J. (2016). Relation of pericardial fat, intrathoracic fat, and abdominal visceral fat with incident atrial fibrillation (from the Framingham Heart Study). *The American Journal of Cardiology, 118*, 1486–1492.

Leenders, M., Verdijk, L. B., van der Hoeven, L., Adam, J. J., van Kranenburg, J., Nilwik, R., & van Loon, L. J. (2013). Patients with type 2 diabetes show a greater decline in muscle mass, muscle strength, and functional capacity with aging. *Journal of the American Medical Directors Association, 14*, 585–592.

Lemieux, S., Prud'homme, D., Bouchard, C., Tremblay, A., & Despres, J. P. (1993). Sex differences in the relation of visceral adipose tissue accumulation to total body fatness. *The American Journal of Clinical Nutrition, 58*, 463–467.

Lemieux, S., Despres, J. P., Moorjani, S., Nadeau, A., Theriault, G., Prud'homme, D., Tremblay, A., Bouchard, C., & Lupien, P. J. (1994). Are gender differences in cardiovascular disease risk factors explained by the level of visceral adipose tissue? *Diabetologia, 37*, 757–764.

Levine, J. A., Abboud, L., Barry, M., Reed, J. E., Sheedy, P. F., & Jensen, M. D. (1985). 2000 Measuring leg muscle and fat mass in humans: Comparison of CT and dual-energy X-ray absorptiometry. *Journal of Applied Physiology, 88*, 452–456.

Lonardo, A., & Trande, P. (2000). Are there any sex differences in fatty liver? A study of glucose metabolism and body fat distribution. *Journal of Gastroenterology and Hepatology, 15*, 775–782.

Lopez, M., & Tena-Sempere, M. (2016). Estradiol and brown fat. *Best Practice & Research. Clinical Endocrinology & Metabolism, 30*, 527–536.

Lowell, B. B., & Spiegelman, B. M. (2000). Towards a molecular understanding of adaptive thermogenesis. *Nature, 404*, 652–660.

Machann, J., Haring, H., Schick, F., & Stumvoll, M. (2004). Intramyocellular lipids and insulin resistance. *Diabetes, Obesity & Metabolism, 6*, 239–248.

Machann, J., Thamer, C., Schnoedt, B., Haap, M., Haring, H. U., Claussen, C. D., Stumvoll, M., Fritsche, A., & Schick, F. (2005a). Standardized assessment of whole body adipose tissue topography by MRI. *Journal of Magnetic Resonance Imaging, 21*, 455–462.

Machann, J., Thamer, C., Schnoedt, B., Stefan, N., Stumvoll, M., Haring, H. U., Claussen, C. D., Schick, F., & Fritsche, A. (2005b). Age and gender related effects on adipose tissue compartments of subjects with increased risk for type 2 diabetes: A whole body MRI/MRS study. *Magma, 18*, 128–137.

Machann, J., Stefan, N., & Schick, F. (2008). (1)H MR spectroscopy of skeletal muscle, liver and bone marrow. *European Journal of Radiology, 67*, 275–284.

Micklesfield, L. K., Goedecke, J. H., Punyanitya, M., Wilson, K. E., & Kelly, T. L. (2012). Dual-energy X-ray performs as well as clinical computed tomography for the measurement of visceral fat. *Obesity (Silver Spring), 20*, 1109–1114.

Mitsiopoulos, N., Baumgartner, R. N., Heymsfield, S. B., Lyons, W., Gallagher, D., & Ross, R. (1985). 1998 Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. *Journal of Applied Physiology, 85*, 115–122.

Nichols, J. H., Samy, B., Nasir, K., Fox, C. S., Schulze, P. C., Bamberg, F., & Hoffmann, U. (2008). Volumetric measurement of pericardial adipose tissue from contrast-enhanced coronary computed tomography angiography: A reproducibility study. *Journal of Cardiovascular Computed Tomography, 2*, 288–295.

North, K. E., Graff, M., Franceschini, N., Reiner, A. P., Feitosa, M. F., Carr, J. J., Gordon-Larsen, P., Wojczynski, M. K., & Borecki, I. B. (2012). Sex and race differences in the prevalence of fatty liver disease as measured by computed tomography liver attenuation in European American and African American participants of the NHLBI family heart study. *European Journal of Gastroenterology & Hepatology, 24*, 9–16.

Ochi, M., Kohara, K., Tabara, Y., Kido, T., Uetani, E., Ochi, N., Igase, M., & Miki, T. (2010). Arterial stiffness is associated with low thigh muscle mass in middle-aged to elderly men. *Atherosclerosis, 212*, 327–332.

Oh, C., Jho, S., No, J. K., & Kim, H. S. (2015). Body composition changes were related to nutrient intakes in elderly men but elderly women had a higher prevalence of sarcopenic obesity in a population of Korean adults. *Nutrition Research, 35*, 1–6.

Ohlson, L. O., Larsson, B., Svardsudd, K., Welin, L., Eriksson, H., Wilhelmsen, L., Bjorntorp, P., & Tibblin, G. (1985). The influence of body fat distribution on the incidence of diabetes mellitus. 13.5 years of follow-up of the participants in the study of men born in 1913. *Diabetes, 34*, 1055–1058.

Ouellet, V., Routhier-Labadie, A., Bellemare, W., Lakhal-Chaieb, L., Turcotte, E., Carpentier, A. C., & Richard, D. (2011). Outdoor temperature, age, sex, body mass index, and diabetic status determine the prevalence, mass, and glucose-uptake activity of 18F-FDG-detected BAT in humans. *The Journal of Clinical Endocrinology and Metabolism, 96*, 192–199.

Park, S. W., Goodpaster, B. H., Lee, J. S., Kuller, L. H., Boudreau, R., de Rekeneire, N., Harris, T. B., Kritchevsky, S., Tylavsky, F. A., Nevitt, M., Cho, Y. W., & Newman, A. B. (2009). Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. *Diabetes Care, 32*, 1993–1997.

Pedersen, S. B., Bruun, J. M., Kristensen, K., & Richelsen, B. (2001). Regulation of UCP1, UCP2, and UCP3 mRNA expression in brown adipose tissue, white adipose tissue, and skeletal muscle in rats by estrogen. *Biochemical and Biophysical Research Communications, 288*, 191–197.

Power, M. L., & Schulkin, J. (2008). Sex differences in fat storage, fat metabolism, and the health risks from obesity: Possible evolutionary origins. *The British Journal of Nutrition, 99*, 931–940.

Preis, S. R., Massaro, J. M., Hoffmann, U., D'Agostino, R. B., Sr., Levy, D., Robins, S. J., Meigs, J. B., Vasan, R. S., O'Donnell, C. J., & Fox, C. S. (2010). Neck circumference as a novel measure of cardiometabolic risk: The Framingham Heart study. *The Journal of Clinical Endocrinology and Metabolism, 95*, 3701–3710.

Rodriguez-Cuenca, S., Monjo, M., Frontera, M., Gianotti, M., Proenza, A. M., & Roca, P. (2007). Sex steroid receptor expression profile in brown adipose tissue. Effects of hormonal status. *Cellular Physiology and Biochemistry, 20*, 877–886.

Rosito, G. A., Massaro, J. M., Hoffmann, U., Ruberg, F. L., Mahabadi, A. A., Vasan, R. S., O'Donnell, C. J., & Fox, C. S. (2008). Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: The Framingham Heart Study. *Circulation, 117*, 605–613.

Rossner, S., Bo, W. J., Hiltbrandt, E., Hinson, W., Karstaedt, N., Santago, P., Sobol, W. T., & Crouse, J. R. (1990). Adipose tissue determinations in cadavers – a comparison between cross-sectional planimetry and computed tomography. *International Journal of Obesity, 14*, 893–902.

Saito, M., Okamatsu-Ogura, Y., Matsushita, M., Watanabe, K., Yoneshiro, T., Nio-Kobayashi, J., Iwanaga, T., Miyagawa, M., Kameya, T., Nakada, K., Kawai, Y., & Tsujisaki, M. (2009). High incidence of metabolically active brown adipose tissue in healthy adult humans: Effects of cold exposure and adiposity. *Diabetes, 58*, 1526–1531.

Sampath, S. C., Sampath, S. C., Bredella, M. A., Cypess, A. M., & Torriani, M. (2016). Imaging of brown adipose tissue: State of the art. *Radiology, 280*, 4–19.

Schlett, C. L., Ferencik, M., Kriegel, M. F., Bamberg, F., Ghoshhajra, B. B., Joshi, S. B., Nagurney, J. T., Fox, C. S., Truong, Q. A., & Hoffmann, U. (2012). Association of pericardial fat and coronary high-risk lesions as determined by cardiac CT. *Atherosclerosis, 222*, 129–134.

Schwab, R. J., Gupta, K. B., Gefter, W. B., Metzger, L. J., Hoffman, E. A., & Pack, A. I. (1995). Upper airway and soft tissue anatomy in normal subjects and patients with sleep-disordered breathing. Significance of the lateral pharyngeal walls. *American Journal of Respiratory and Critical Care Medicine, 152*, 1673–1689.

Shulman, G. I. (2000). Cellular mechanisms of insulin resistance. *The Journal of Clinical Investigation, 106*, 171–176.

Shulman, G. I. (2014). Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. *The New England Journal of Medicine, 371*, 1131–1141.

Snijder, M. B., Visser, M., Dekker, J. M., Goodpaster, B. H., Harris, T. B., Kritchevsky, S. B., De Rekeneire, N., Kanaya, A. M., Newman, A. B., Tylavsky, F. A., & Seidell, J. C. (2005). Low subcutaneous thigh fat is a risk factor for unfavourable glucose and lipid levels, independently of high abdominal fat. The Health ABC Study. *Diabetologia, 48*, 301–308.

Soliman, E. Z., Ding, J., Hsu, F. C., Carr, J. J., Polak, J. F., & Goff, D. C., Jr. (2010). Association between carotid intima-media thickness and pericardial fat in the Multi-Ethnic Study of Atherosclerosis (MESA). *Journal of Stroke and Cerebrovascular Diseases, 19*, 58–65.

Tanner, J. M., Hughes, P. C., & Whitehouse, R. H. (1981). Radiographically determined widths of bone muscle and fat in the upper arm and calf from age 3–18 years. *Annals of Human Biology, 8*, 495–517.

Tchernof, A., & Despres, J. P. (2013). Pathophysiology of human visceral obesity: An update. *Physiological Reviews, 93*, 359–404.

Thomas, M. A., Chung, H. K., & Middlekauff, H. (2005). Localized two-dimensional 1H magnetic resonance exchange spectroscopy: A preliminary evaluation in human muscle. *Magnetic Resonance in Medicine, 53*, 495–502.

Thuzar, M., & Ho, K. K. (2016). Mechanisms in endocrinology: Brown adipose tissue in humans: Regulation and metabolic significance. *European Journal of Endocrinology, 175*, R11–R25.

Torriani, M., Thomas, B. J., Halpern, E. F., Jensen, M. E., Rosenthal, D. I., & Palmer, W. E. (2005). Intramyocellular lipid quantification: Repeatability with 1H MR spectroscopy. *Radiology, 236*, 609–614.

Torriani, M., Thomas, B. J., Bredella, M. A., & Ouellette, H. (2007). Intramyocellular lipid quantification: Comparison between 3.0- and 1.5-T (1)H-MRS. *Magnetic Resonance Imaging, 25*, 1105–1111.

Torriani, M., Gill, C. M., Daley, S., Oliveira, A. L., Azevedo, D. C., & Bredella, M. A. (2014). Compartmental neck fat accumulation and its relation to cardiovascular risk and metabolic syndrome. *The American Journal of Clinical Nutrition, 100*, 1244–1251.

Velan, S. S., Durst, C., Lemieux, S. K., Raylman, R. R., Sridhar, R., Spencer, R. G., Hobbs, G. R., & Thomas, M. A. (2007a). Investigation of muscle lipid metabolism by localized one- and two-dimensional MRS techniques using a clinical 3T MRI/MRS scanner. *Journal of Magnetic Resonance Imaging, 25*, 192–199.

Velan, S. S., Ramamurthy, S., Ainala, S., Durst, C., Lemieux, S. K., Raylman, R. R., Spencer, R. G., & Thomas, M. A. (2007b). Implementation and validation of localized constant-time correlated spectroscopy (LCT-COSY) on a clinical 3T MRI scanner for investigation of muscle metabolism. *Journal of Magnetic Resonance Imaging, 26*, 410–417.

Velan, S. S., Said, N., Narasimhan, K., Papan, C., Bahu, A., Vargo, J. A., Raylman, R. R., Thomas, M. A., Rajendran, V. M., Spencer, R. G., & Alway, S. E. (2008). Gender differences in musculoskeletal lipid metabolism as assessed by localized two-dimensional correlation spectroscopy. *Magnetic Resonance Insights, 2008*, 1–6.

Vessby, B., Gustafsson, I. B., Tengblad, S., Boberg, M., & Andersson, A. (2002). Desaturation and elongation of Fatty acids and insulin action. *Annals of the New York Academy of Sciences, 967*, 183–195.

Warensjo, E., Riserus, U., & Vessby, B. (2005). Fatty acid composition of serum lipids predicts the development of the metabolic syndrome in men. *Diabetologia, 48*, 1999–2005.

Westerbacka, J., Corner, A., Tiikkainen, M., Tamminen, M., Vehkavaara, S., Hakkinen, A. M., Fredriksson, J., & Yki-Jarvinen, H. (2004). Women and men have similar amounts of liver and intra-abdominal fat, despite more subcutaneous fat in women: Implications for sex differences in markers of cardiovascular risk. *Diabetologia, 47*, 1360–1369.

Wheeler, G. L., Shi, R., Beck, S. R., Langefeld, C. D., Lenchik, L., Wagenknecht, L. E., Freedman, B. I., Rich, S. S., Bowden, D. W., Chen, M. Y., & Carr, J. J. (2005). Pericardial and visceral adipose tissues measured volumetrically with computed tomography are highly associated in type 2 diabetic families. *Investigative Radiology, 40*, 97–101.

Williams, C. D., Stengel, J., Asike, M. I., Torres, D. M., Shaw, J., Contreras, M., Landt, C. L., & Harrison, S. A. (2011). Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: A prospective study. *Gastroenterology, 140*, 124–131.

Wree, A., Broderick, L., Canbay, A., Hoffman, H. M., & Feldstein, A. E. (2013). From NAFLD to NASH to cirrhosis-new insights into disease mechanisms. *Nature Reviews. Gastroenterology & Hepatology, 10*, 627–636.

Yoneshiro, T., Aita, S., Matsushita, M., Okamatsu-Ogura, Y., Kameya, T., Kawai, Y., Miyagawa, M., Tsujisaki, M., & Saito, M. (2011). Age-related decrease in cold-activated brown adipose tissue and accumulation of body fat in healthy humans. *Obesity (Silver Spring), 19*, 1755–1760.

Yudkin, J. S., Eringa, E., & Stehouwer, C. D. (2005). "Vasocrine" signalling from perivascular fat: A mechanism linking insulin resistance to vascular disease. *Lancet, 365*, 1817–1820.

Zhang, Z., Cypess, A. M., Miao, Q., Ye, H., Liew, C. W., Zhang, Q., Xue, R., Zhang, S., Zuo, C., Xu, Z., Tang, Q., Hu, R., Guan, Y., & Li, Y. (2014). The prevalence and predictors of active brown adipose tissue in Chinese adults. *European Journal of Endocrinology, 170*, 359–366.

http://www.springer.com/978-3-319-70177-6

Sex and Gender Factors Affecting Metabolic
Homeostasis, Diabetes and Obesity
Mauvais-Jarvis, F. (Ed.)
2017, XXII, 627 p. 92 illus., 44 illus. in color., Hardcover
ISBN: 978-3-319-70177-6