Utilizing Sonographic Measurements to Assess Abdominal Adiposity

THESIS

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By

A. Nicole Stigall, B.S., RDMS, RVT

Graduate Program in Allied Medicine

The Ohio State University

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Thesis Committee

Kevin D. Evans, Ph.D., Advisor

Colleen K. Spees, Ph.D.

Randee L. Hunter, Ph.D.

Abstract

Approximately 93 million adults and over 13 million children and adolescents across the U.S. are considered overweight or obese.[1] Healthcare expenditures are shown to be 81% greater in obese adults versus those of normal-weight.[2] Obesity has been linked to several chronic health conditions and severe disease risks. These health concerns include risk for cardiovascular disease, type 2 diabetes, some cancers, and metabolic syndrome.[3] The prevalence of type 2 diabetes and hypertension has steadily increased in the United States and the prevalence of metabolic syndrome is estimated at more than 30%.[4]UUnderstanding the trends in metabolic syndrome and examining those who are at an increased risk for metabolic conditions is paramount.[4]

Therefore, it is essential that accurate and reliable tools are used and implemented to assess patients at risk for metabolic syndrome. Currently body mass index (BMI), waist circumference (WC), and dual-energy x-ray absorptiometry (DXA) are believed to be appropriate screening measures. Expanding on the work of Hamagawa et al.[5], and Suzuki et al.[6], this work adds evidence for providing a cost effective, portable, accurate, and non-ionizing approach to assess an individuals' abdominal adiposity. This approach uses diagnostic medical sonography (DMS) as a tool for assessing abdominal

adiposity in hopes of this method being adopted to help determine an individual's risk for metabolic conditions. Participants provided several anthropometric measures as well as imaging data, to determine if sonographic measures of abdominal fat could be an accurate screening technique for gauging the risk for heart disease, stroke, and diabetes. Measurements were taken on a GE Logiq i laptop ultrasound unit to indirectly asses the participants' subcutaneous fat and visceral fat. These measures were then compared to corresponding measures of BMI, WC, and DXA (android percent body fat, subscores). Additionally, a mesenteric fat thickness measurement was taken and compared to the WC measure. This method was then applied in the pediatric population to gauge for adaptability and feasibility.

These measures demonstrated moderately positive association and were statistically significant. A Type III Test of Fixed Effects demonstrated a highly significant change over time for BMI, DMS measures of subcutaneous fat, visceral fat, and mesenteric fat. WC measures and the DXA (android % body fat, subscores) showed no significant change over time. Pearson's correlation coefficients indicated a mostly moderate to high association between the DXA (android % body fat, subscores) and DMS measurements of visceral fat, subcutaneous fat, and mesenteric fat layers. The visceral minimum measures did not demonstrate a high correlation to the DXA (android % body fat, subscores). DMS is an indirect imaging tool that could be used in correlation with other measures to help determine an individual's risk for metabolic syndrome. The value of DMS for gauging abdominal obesity and the risk for metabolic disease is that it is relatively inexpensive, noninvasive, and valid indirect assessment tool.

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Vita

May 14, 1993…………………Tacoma, Washington

2011…………………………..Marysville High School, Ohio

2015…………………………..A.A. General Studies, The Ohio State University

2017…………………………..B.S. Radiological Sciences, Diagnostic Medical Sonography, The Ohio State University

2017…………………………..Diagnostic Medical Sonographer/Vascular Technologist, The Ohio State Wexner Medical Center

2017-Present………………….Diagnostic Medical Sonographer/Vascular Technologist, The Bing Cancer Center, Ohio Health

2017-Present………………….Graduate Research Associate, Manager of Laboratory of Investigatory Imaging, The Ohio State University

Publications

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Chapter 1:
Introduction

1.1 Obesity Epidemic

The obesity epidemic has become increasingly rampant throughout the United States (US). According to the Centers for Disease Control (CDC), the prevalence of adult obesity has reached 39.8%, while obesity among children has reached rates of 13.9%, 18.4% and 20.6% in children ages 2-5 years, 6-11 years, and 12-18 years respectively.[1] This epidemic has affected over 93 million adults and over 13 million children and adolescents across the U.S.[1] The trend of obesity has significantly increased over the past 15 years (Figure 1.1).[1]

Not only is obesity affecting our population's health across all age groups but also has underlying contributions to several health conditions such as cardiovascular disease, type 2 diabetes, and metabolic syndrome. Obesity has concomitant effects on the cost of medical care throughout the US as well. Obesity contributes to medical conditions that can result in higher utilization of medical expenditures.[7] Overweight and obese patients are prone to increased inpatient stays, medical complications, and post-surgical complications.[7] Previous researchers compared medical costs of different body mass index (BMI) categories over an 18-month period.[8] The results showed a 1.9% increase in medical costs per one-unit increase of BMI.[8] In 2008 alone, the estimated annual medical cost of health conditions, related to obesity, was $147 billion.[1] As the cost of health expenditures continues to rise for these chronic and severe conditions brought on by obesity and metabolic syndrome, healthcare professionals continue to look for ways to provide preventative medicine and education to the patient population. Therefore, trying to alert healthcare providers as well as patients to the prevalence and ramifications of obesity is paramount.

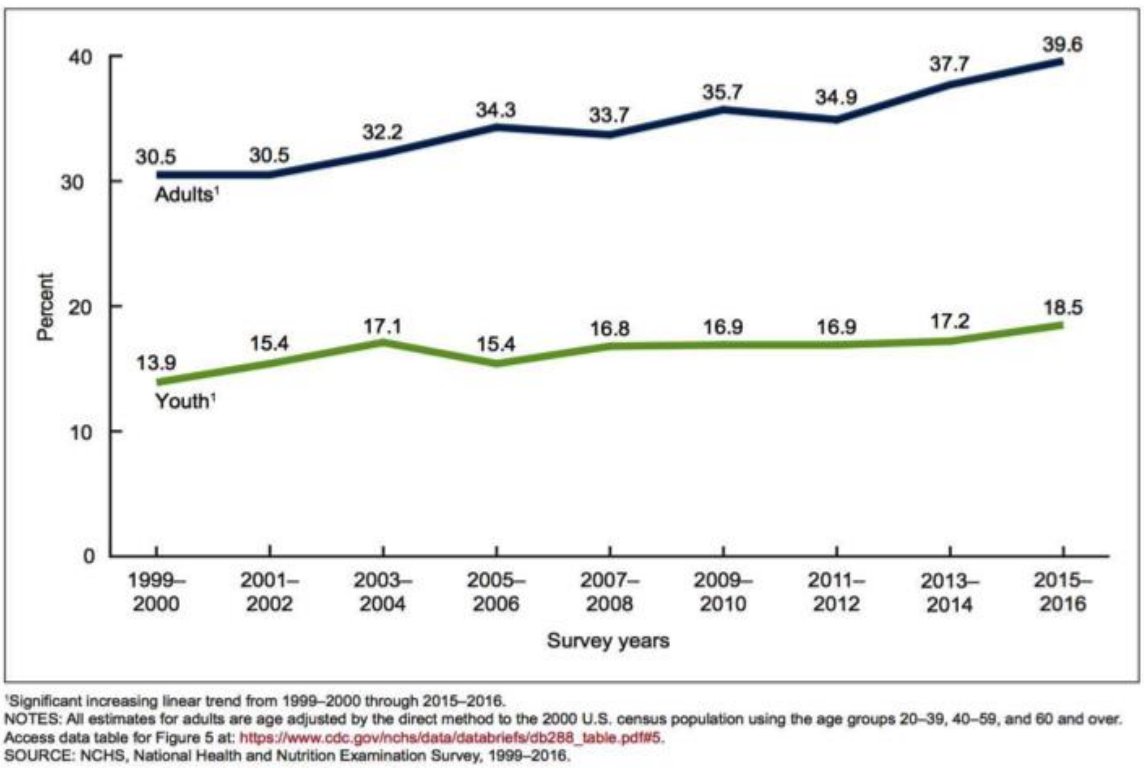

Figure 1.1 Obesity trends among adults aged 20 and over and youth aged 2-19 years

1.2 Obesity Categories

Obesity has been described as excess body fat or an accumulation of fat that presents a risk to health.[9] There are multiple methods used to measure or categorize obesity, such as, waist circumference (WC), skin fold thickness, underwater weighing, and percent body fat measures. Some sources say that a waist circumference is the best method of measuring obesity, due to the significance of abdominal obesity in relation to severe health risks.[9] An increase in abdominal fat has been associated with an increase of risk factors including metabolic conditions.[9] However, one of the most common means for categorizing obesity is through the use of BMI. A BMI is based on a person's height and weight to determine their specific category.[1] When a person's weight is higher than what is considered normal for their height, they may be described as overweight or obese.[1] Obesity is frequently subdivided into BMI categories.[10] These categories can be seen in Table 1.1.[10] These categories help to describe the categorization of obesity and underweight measures, which helps to improve the estimation of a person's risk for disease or illness based on BMI.

Classification	BMI(kg/m^2)	
	Principal cut-off points	**Additional cut-off points**
Underweight	**<18.50**	**<18.50**
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	**18.50 - 24.99**	**18.50 - 22.99**
		23.00 - 24.99
Overweight	**≥25.00**	**≥25.00**
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	**≥30.00**	**≥30.00**
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	≥40.00	≥40.00

Table 1.1 Obesity classification based on BMI

1.3 Metabolic Syndrome

Obesity has been linked to several risk factors including, cardiovascular disease, dyslipidemia, hypertension, type 2 diabetes, some cancers, and other risk factors.[2] Some of these risk factors, including, but not limited to abdominal obesity, raised blood pressure, insulin resistance, and atherogenic dyslipidemia, have been grouped together, to form what is known as metabolic syndrome.[2] It has become evident that cardiovascular disease risk has an associated linkage with metabolic syndrome and multiple chronic disease, even more than has been previously reported.[4] Poor personal lifestyle choices leading to risks for cardiovascular disease, chronic disease, and metabolic syndrome may not be independent of one another and may in fact share underlying causes.[9] The National Cholesterol Education Program Adult Treatment Panel III (ATP III) has defined criteria for metabolic syndrome.[9] Their criterion consists of six components including abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, insulin resistance ± glucose intolerance, proinflammatory, and prothrombotic states.[2] Metabolic syndrome can be a predictor for early onset diabetes and cardiovascular disease.[2] According to ATP III, when any three of the following five risk factors are met, metabolic syndrome can be diagnosed: waist circumference over 102 cm in men or over 88 cm in women, blood pressure over 130/85 mmHg, fasting triglyceride level over 1.7 mmol/L, fasting high-density lipoprotein, HDL cholesterol level less than 1.04 mmol/L in men or <1.30 mmol/L in women, and a fasting glucose over 6.1 mmol/L (Table 1.2)[9]. A schematic presentation of metabolic syndrome is included in Figure 1.2.

Between 2003-2012, the occurrence of metabolic syndrome in adults was 33% in the US .[11] The increased prevalence of type 2 diabetes and hypertension, will likely increase the proportion of adults who will likely meet the criteria for metabolic syndrome.[4] Moore, et al.[4], explored the prevalence of metabolic syndrome from 1988-2012. In that study, 51,371 participants over the age of 18 were followed over that time frame. Results showed that the prevalence of metabolic syndrome in men rose from 25.6% to 33.4% and from 25% to 34.9% in women, regardless of race or ethnicity.[4] Additionally, it was observed that by 2012, more than one-third of the U.S. population met the criteria for metabolic syndrome.[4] This extreme occurrence of metabolic syndrome, demonstrates an increased rate of individuals, at risk of developing severe chronic health conditions and diseases. As a result of the rising metabolic syndrome and obesity rates, the importance of early clinical treatment has become even more imperative.

ATP III Clinical Identification of Metabolic Syndrome	
Risk Factor	Defining Level
Abdominal obesity, given as waist circumference*†	
Men	>102 cm
Women	>88 cm
Triglycerides	≥1.7 mmol/L
HDL cholesterol	
Men	<1.04 mmol/L
Women	<1.30 mmol/L
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥6.1 mmol/L

Table 1.2 ATP III clinical identification factors of metabolic syndrome

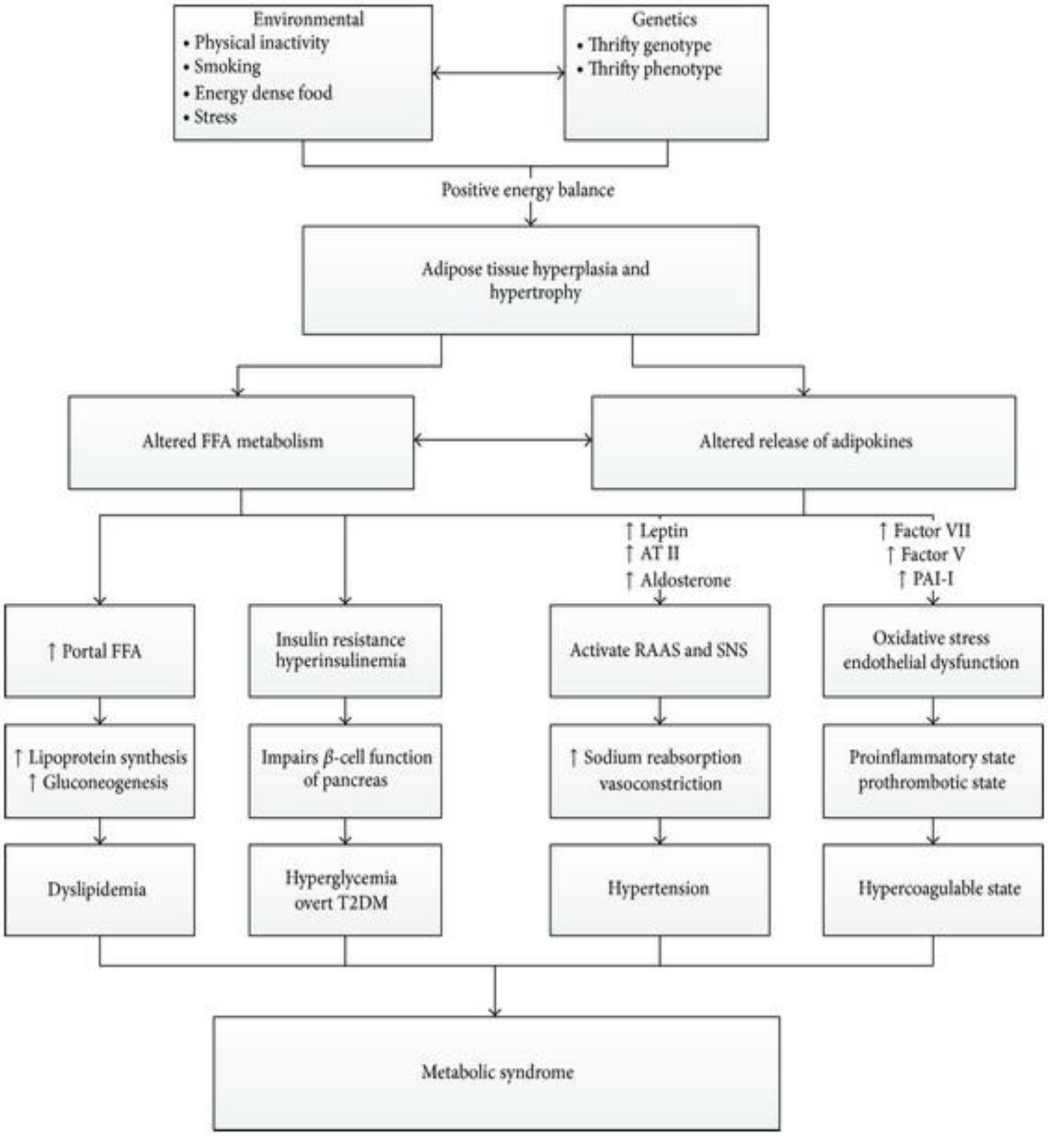

Figure 1.2 Schematic presentation of metabolic syndrome. (FFA: free fatty acid, ATII: angiotensin II, PAI-1: plasminogen activator inhibitor-1, RAAS: renin angiotensin aldosterone system, SNS: sympathetic nervous system.)[55]

1.4 Metabolic Syndrome and Abdominal Adiposity

Understanding the implications of metabolic syndrome, the risk factors, and fat distribution have become increasingly important for developing a timely treatment for patients.[12] Increased abdominal fat distribution has been associated with metabolic syndrome and increased risk of other pathological conditions, including prostate, breast and colorectal cancer. More specifically, an increased visceral adiposity, known as visceral obesity has been associated with a variety of medical disorders.[12] Increased visceral adiposity or this body composition phenotype, has been connected with inflammation, insulin resistance, and myocardial dysfunction.[13] BMI may be the choice for defining obesity, however, it may not fully define the risk for metabolic syndrome or cardiovascular disease .[13] Visceral adiposity measures has been suggested as a complimentary measure to assess body composition and help to determine risk of previously described chronic health concerns.

In a multi-ethnic study of atherosclerosis (MESA), 6,400 individuals who were free of clinical cardiovascular disease, at time of enrollment, were studied. From the main cohort, researchers took 1,511 individuals with baseline measures of visceral adiposity and evaluated how visceral and subcutaneous fat distribution affected their risk for metabolic syndrome, across different BMI categories.[13] The participants were followed over 11 years and had 5 different office exam visits. At visits 2 and 3, they were randomly selected to receive Computed Tomography (CT). Of those individuals, 253 participants without metabolic syndrome or dysglycemia were re-imaged at exam 4.This set of CT images were used to quantitatively analyze subcutaneous and visceral fat thickness which was compared to other anthropometric measures.[12] The results demonstrated that visceral fat was strongly associated with incidences of metabolic syndrome, regardless of weight, initial weight, race, age or sex. Neither BMI nor waist circumference were as closely associated with visceral fat .[12] These results indicated that quantifying and assessing visceral adiposity may be needed for measuring and establishing a patient's metabolic risk, especially at the very early stages of development. BMI and WC are too simple of measurements when determining and establishing metabolic syndrome risk. Therefore, quantifiable measures of visceral adiposity are needed in addition to traditional BMI and WC measures.

1.5 Sonographic Measurement of Abdominal Adiposity

Visceral adiposity plays a critical role in the risk for metabolic syndrome. The ability to establish the risk of metabolic syndrome early on, requires a practical, reliable and easy instrument. Imaging provides a useful and practical tool to assess the amount of visceral and subcutaneous fat tissues within the abdomen. Although, dual-energy X-ray absorptiometry (DXA) and CT have been utilized, both of these modalities rely on=ionizing radiation. Additionally, these modalities can be costly and inconvenient. The equipment is stationary, requiring patients to travel to the equipment. The table size is non-adjustable, making it difficult for patients of a larger body habitus to lay flat and still. Diagnostic medical sonography (DMS) is a diagnostic medical imaging modality that can distinctively quantify visceral and subcutaneous fat, with non-ionizing radiation[14] Hamagawa et al.[5], described a protocol that utilizes DMS to measure abdominal adipose tissues. This protocol was then enhanced by Woldemariam, et al.[15] In Woldemariam's pilot study, he suggested that optimizing the protocol for scanning visceral and subcutaneous fat has the potential for DMS to be used as a screening tool for metabolic syndrome.[15]

In a study conducted by, Riberiro-Filho, et al.[14], one hundred obese women were analyzed to compare methods of assessment of visceral fat compared to CT. These women had an anthropometric evaluation, bioelectrical impedance, DXA, abdominal DMS and CT. Sonography was the best alternative method compared to CT, for the assessment of female intra-abdominal fat in regards to accuracy and reproducibility.[14] It is possible that DMS can be utilized as a reliable, non-ionizing method for accurately measuring visceral adiposity, in hopes of determining risk for metabolic conditions.

This research looks to explore the use of diagnostic medical sonography to assess and measure abdominal adiposity in overweight and obese adults and to compare these measures to BMI, WC and DXA (android % BF subscore). Additionally, this research aims to use this same optimized protocol and methodology of diagnostic medical sonography measures of subcutaneous and visceral fat thickness to determine if DMS could be a tool for assessing abdominal adiposity in children as well.

Chapter 2:
Abdominal adiposity measured by Sonography as a tool for determining disease risk

2.1 Introduction

Excessive body fatness is a significant health risk for adults in the US, and the prevalence of obesity between 2011 and 2014 was estimated to be 36.5%[16] In addition, overweight and obesity have been linked to deleterious health conditions such as heart disease, stroke, type 2 diabetes, and many types of cancer.[17] Specifically, increased risk for obesity-related diseases can be attributed to the deposit of fat in the adipose layer and can be centered around the abdomen. Abdominal adiposity has extensively been linked to cancers of the breast, endometrium, colorectum, kidney, pancreas, esophagus, gallbladder, ovaries, thyroid, and potentially the prostate.[18] Given the varied health risks and all-cause mortality associated with increased body fatness and specifically abdominal adiposity, it is important to use validated body composition measures to objectively assess adiposity in human studies. BMI is a noninvasive and widely accepted weight classification system associated with risk of disease. BMI and WC were the metrics of choice for a study to determine the influence of abdominal adiposity for both cardiovascular disease and cancer, which followed a cohort of 44,636 women over a 16-year period.[19] During that time, 3507 deaths were identified, including 751 deaths attributed to cardiovascular disease and 1748 deaths due to cancer.[19] This linkage between abdominal adiposity and cancer has been carefully researched to determine the biological mechanisms that trigger these varied cancer risks. Several mechanisms have been suggested, but the current evidence seems to point to hormonally stimulated cancers due to stored abdominal fat.[20] It is for this reason that screening techniques have been used to categorize patients with abdominal adiposity and use BMI, WC, and other subjective measures as clinical measures. Table 2.1 provides an example of BMI categories used to stratify levels of obesity.[1] These levels of obesity could be used as a tool to determine the potential risk for disease. Given that BMI and WC are commonly used clinically, they may not be the best screening tools because of their level of reliability.

Classification	BMI (kg/m^2)
Healthy weight	18.5-24.9
Overweight	25-29.9
Obesity I	30-34.9
Obesity II	35-39.9
Obesity III	40 or more

Table 2.1 Body fat classifications for patient based on body mass index (BMI)

Imaging has also been used to provide a more objective and precise means for screening patients for abdominal adiposity. CT, magnetic resonance imaging (MRI), DXA, and DMS have all been suggested as more accurate means for measuring the level of abdominal adiposity.[12] In most clinical practices, the use of DXA is considered a quick means for collecting screening data that is more accurate than BMI or WC.[21] Although DXA is a very low dose of ionizing radiation for the patient, other non-ionizing radiation techniques are considered advantageous. MRI and DMS represent those non-ionizing choices to measure abdominal adiposity; however, some argue that DMS lacks reproducible measures. [12]

Nonetheless, studies have been published using DMS for the purpose of measuring abdominal adipose.[15,5,6,22] Perhaps the Hamagawa et al.[5] study was the most seminal as it looked at the ability of sonographically measured visceral fat to predict metabolic syndrome in a cohort of patients. Besides BMI, WC, and other biomarkers, DMS was compared with coronary angiography for predictive value. The use of DMS to measure the visceral fat depth of 185 patients who had undergone coronary angiography was a nonionizing alternative that had significant value.[5] The concern for reproducibility of making sonographic visceral fat depth measures was explored by Bazzocchi et al.[22] in a cohort of 45 males and 45 females, with varied ultrasound equipment. In their study, they found that the highest level of precision was associated with patients in a fasting state, holding their breath during imaging, and using the imaging protocol with newer ultrasound equipment.[23]

Given the epidemic of obesity and the possible relationship of abdominal adipose to cardiovascular disease or cancer, a non-ionizing imaging method is needed to reliably screen patients. Compared with DXA, DMS provides a noninvasive, portable, and relatively less expensive examination that requires less time to complete. The objective of this study was to determine the strength of relationship between DMS measures of subcutaneous and visceral fat with other associated measures of adiposity in a cohort of overweight cancer survivors. The research question was as follows: Which combination of DMS measures was strongly correlated with DXA measures of body fat and non-imaging measures of adiposity? A secondary question was, what was the intra-rater reliability of DMS measures of abdominal adiposity? These exploratory studies needed to be completed to confidently proceed with properly screening patients at risk for diseases linked to abdominal adiposity.

2.2 Methodology

A phase 2 randomized clinical trial design was used to stage a longitudinal study of cancer survivors who were invited to participate in a bio-behavioral intervention for 1 year. These phase 2 participants were recruited to the longitudinal study, and the list of participants was 80, 67 of whom would receive DMS measures at baseline. Based on the registration list, the statistical power was set a priori at an alpha of 0.05, a moderate effect size of 0.5, and power of 0.598. The inclusion criteria for baseline data measures were having had a diagnosis of cancer and successfully completing a physician-supervised treatment plan. The larger study was approved by the university's internal review board and was targeted specifically for adults (18 years and older). Patients were invited to come for 1 day of data collection at the university's sponsored clinical research center. Those patients consented to the study and were asked to report in the morning fasting for biometric and imaging data collection.

Subject Population

DMS and DXA scanning were done concurrently, and at the same appointment, trained research dietitians collected BMI and WC measures on each participant, research nurses completed DXAs. Due to scheduling conflicts, only 67 patients received DMS measures. Selectively, the DMS, DXA, BMI, and WC data were used for this baseline analysis.

DXA Protocol

The participants were also given a DXA examination on a GE Lunar iDXA (Waukesha, WI) with the patient supine on the examination table. The DXA equipment was operated by a registered nurse who was trained to complete DXA examinations. The onboard software, enCORE 2011 (version 13.6), was used to analyze DXA images. A researcher credentialed in bone density and with clinical experience checked the data analysis process. The body fat percentage (%BF) was generated specifically as a specialized report from the enCORE software. The DXA equipment was carefully monitored for quality control and quality assurance as outlined in the literature.[24,25]

The DXA examination allowed for a series of body fat analyses to be generated. To properly match our sonographic measurements, the android region was chosen. Stults-Kolehmainen et al.[26] described the android subscore of %BF, which consists of the area between the ribs and the pelvis and is totally enclosed by the trunk region.[26] For the purposes of this study, the android subscore that is derived from DXA is listed as DXA-android %BF.

Sonography Protocol

The patients were all imaged on a GE Logiq 9 ultrasound machine with a 9.0 (6- to 8-MHz) linear transducer. The protocol was standardized using 8 MHz, gain 30, depth 7 cm, and acoustic output power set at 100%. Patients were asked to lay supine on the examination table, and they had to hold their breath for a series of sagittal and transverse images of the abdomen. The images were captured by skilled sonographers according to the Suzuki et al.[6] protocol. A cine clip in the sagittal plane was taken in the same manner on all patients for further post-examination analysis. Each cine clip began at the xiphoid process (Figure 2.1) and continued down the linea alba and concluded at the umbilicus. In addition, a transverse static sonographic image was taken at the level indicated for the WC. This is adapted from the Bazzocchi et al.[23] scanning protocol to assess the layers of adiposity at the same area as the WC (Figure 2.2) was taken. The ultrasound equipment was carefully monitored for quality control of the transducers by taking tissue-mimicking phantom measurements for axial and lateral resolution. DMS post examination measurements were taken at the xiphoid, umbilicus, and the waist to determine the depth of adiposity as outlined by previous researchers.[15,5,6,22] At each location, subcutaneous fat and visceral fat were measured (Figure 2.3). All image analyses were completed by a credentialed abdominal sonographer. The measurements were made on the GE Logiq 9 ultrasound equipment using the onboard measurement system. For all patient DMS cases, five measurements were taken at each location (xiphoid, umbilicus, waist), eliminating the highest and lowest of the five measurements. An average was calculated for the three remaining measurements to address the issue of measurement error. All the images were stored on the equipment and easily rebooted for subsequent measurements by staff to address interrater reliability.

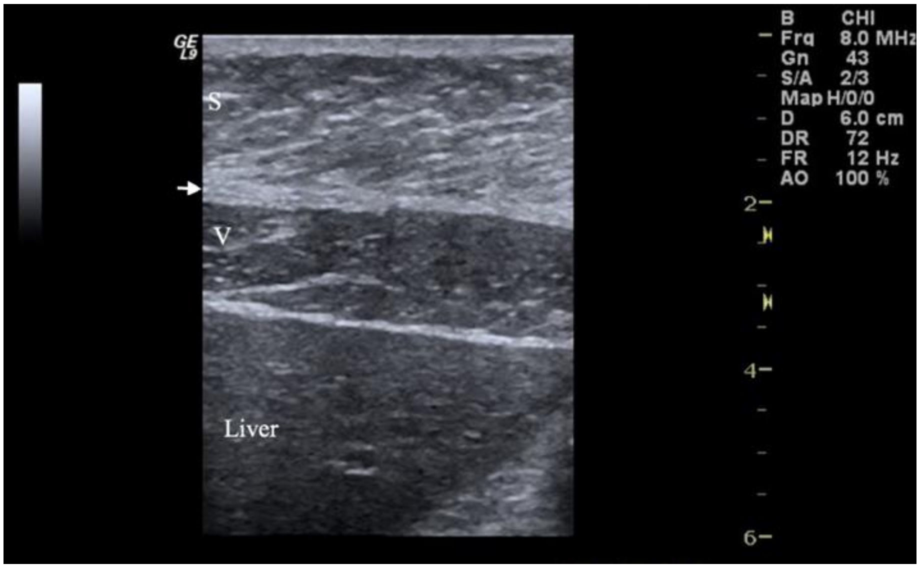

Figure 2.1 Sonographic image demonstrating a sagittal image at the xiphoid. Subcutaneous fat (S), visceral fat (V), linea alba (arrow) and liver are shown.

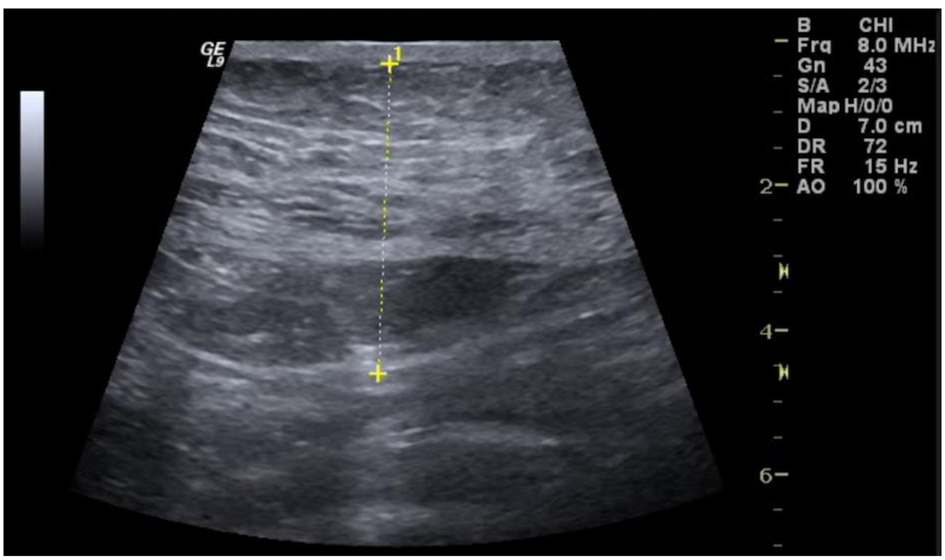

Figure 2.2 Sonographic image in the transverse plane demonstrating the mesenteric fat thickness measurement.

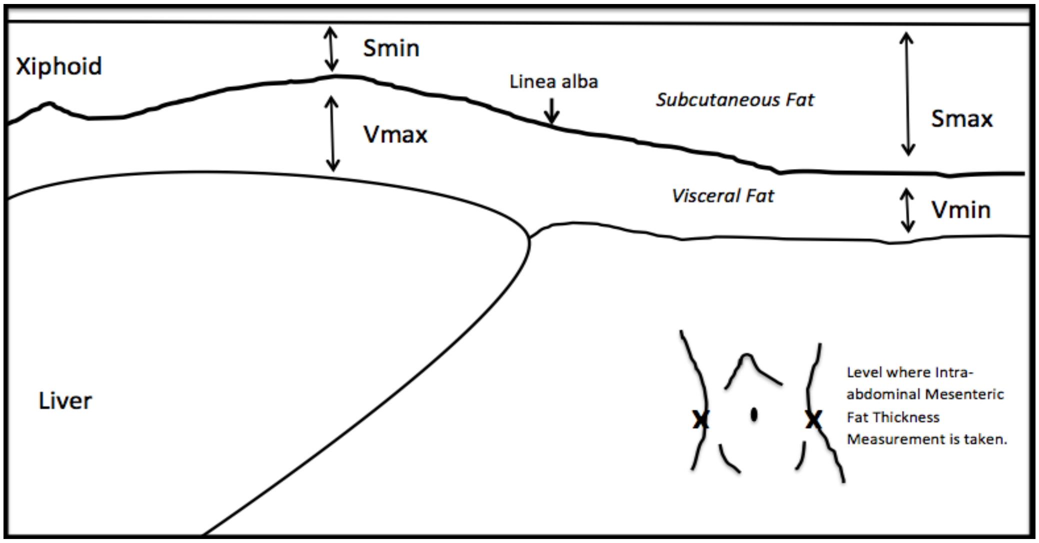

Figure 2.3 Diagram demonstrating the location of each sonographic measurement

2.3 Clinical Evaluation

The BMI (height and weight) as well as WC measurements, taken at the level of the iliac crests, were averaged and reported for further data analysis. Table 2.1 provides the classification for BMI that was used in this study.

All 67 patients had complete baseline data consisting of WC, BMI, DXA-android %BF, and DMS adiposity depth measurements. Based on the measurement parameters put forward by Suzuki et al.[6], the following measurements were made: subcutaneous minimum (Smin), subcutaneous maximum (Smax), visceral minimum (Vmin), and visceral maximum (Vmax) (Figures 2.3 and 2.4). In addition, a fifth measurement depth was taken, as proposed by Bazzocchi et al.[23], which is the intra-abdominal mesenteric fat thickness (IMT) (Figure 2.2) The IMT measurement was made at approximately the same level that the WC was taken with a cloth tape measurement. The trained clinical research staff placed a marker on the skin so that a transverse sonographic image could be lined up with the WC measurement location as close as possible. Occasionally, the image was taken just superior to the umbilicus due to its shadowing on the sonogram, which makes measurement impossible. These IMT measurements were compared with the other variables of interest using Pearson correlations to determine their strength of association. The sample size of 67 provides 80% power to detect a correlation of 0.334 between two fat measures based on a 2-sided hypothesis test with a significance level of .05 (G*Power, version 3.1.9.2)

Data Analysis

Two-way random intra-class correlation coefficients for absolute agreement were calculated to compare measurements made by an expert sonographer (>30 years of experience) with an intermediate sonographer (2 years of experience). The measurements from the expert sonographer were also compared with a novice (no sonography experience). Three measurements (for all five variables of interest) were made on nine (expert vs intermediate) and eight (expert vs novice) images.

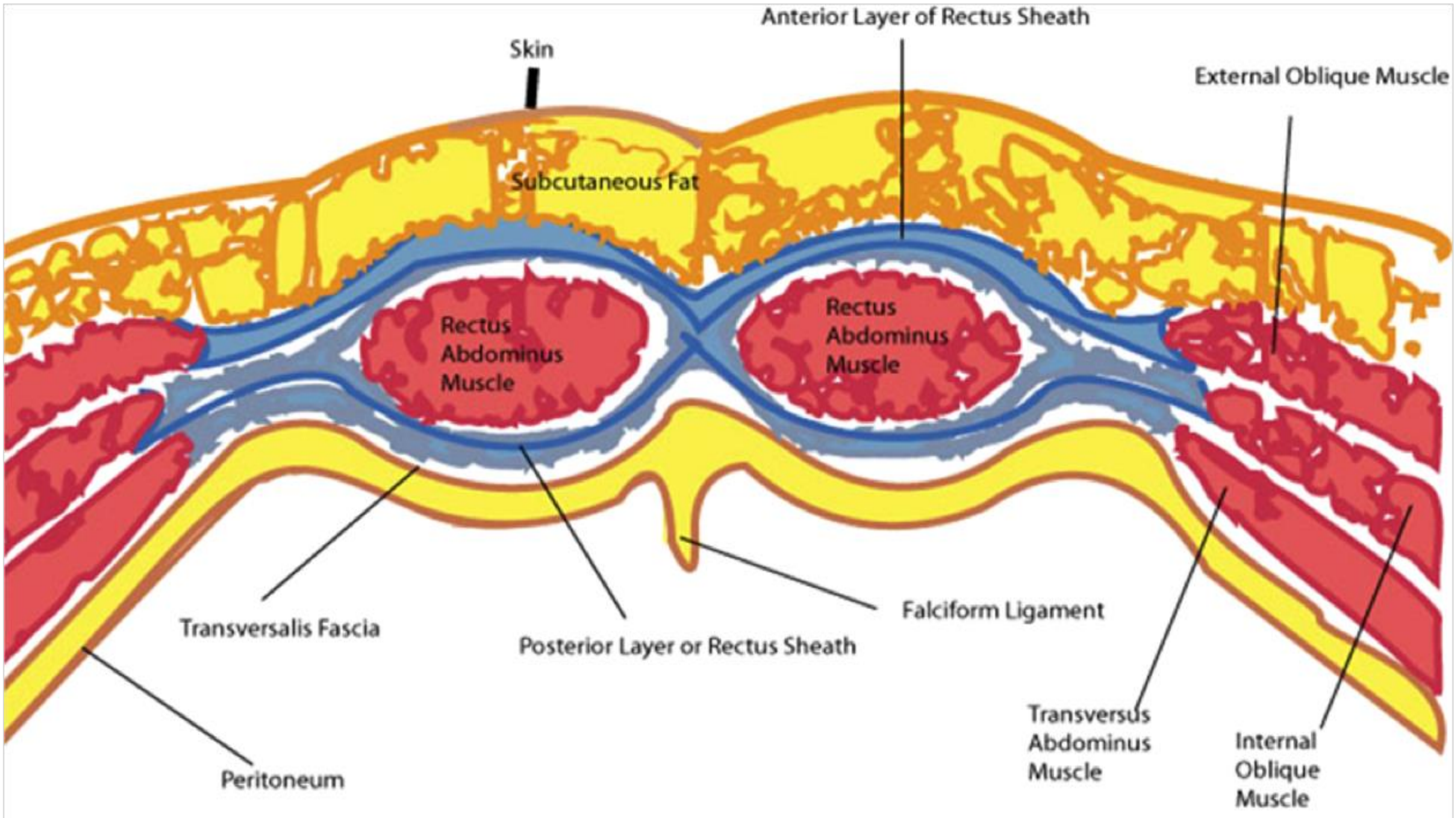

Figure 2.4 Cross-sectional view of abdominal wall anatomy

2.4 Results

Demographics of the patients who were imaged are included in Table 2.2. Most patients were women with a mean age of 50.0 years (SD ±11.00). The female cohort had a mean height of 1.65 m (SD ±0.07) and a mean mass of 91.5 kg (SD ±17.1). The cohort had a mean BMI of 33.4 kg/m^2 (SD ±5.4) and a mean WC of 108.0 cm (SD ±12.4). Table 2.2 provides a breakdown of BMI and WC for men and women. The adiposity depth measurements completed from the sonographic images at the xyphoid, umbilicus, and WC are also provided in Table 2.3. This table also includes descriptive statistics such as, BMI, WC, and percentage android fat of the participants prior to their intervention.

	Age (years)	Height (m)	Mass (kg)
Females (n = 64)	50.0 ± 11.00	1.65 ± 0.07	91.5 ± 17.1
Males (n = 3)	45.3 ± 21.7	1.76 ± 0.12	103.5 ± 10.9
Total (n = 67)	49.8 ± 11.4	1.66 ± 0.07	92.1 ± 17.0

Table 2.2 Subject characteristics of patients screened for disease reoccurrence based on adiposity.

	Females (n = 64)	Males (n = 3)	Total (n = 67)
BMI	33.4 ± 5.5	33.7 ± 4.5	33.4 ± 5.4
Waist Circumference	107.6 ± 12.5	116.2 ± 9.1	108.0 ± 12.4
% Android Fat	52.0 ± 5.7	42.1 ± 8.3	51.6 ± 6.1
Subcutaneous Minimum	2.00 ± 0.83	1.54 ± 0.37	1.98 ± 0.82
Subcutaneous Maximum	3.36 ± 1.09	3.70 ± 0.53	3.37 ± 1.08
Visceral Minimum	0.52 ± 0.27	0.62 ± 0.28	0.53 ± 0.27
Visceral Maximum	1.87 ± 0.58	1.88 ± 0.27	1.87 ± 0.57
Mesenteric	4.05 ± 1.27	4.62 ± 0.48	4.07 ± 1.25

Table 2.3 Descriptive statistics of the patients screened for disease reoccurrence based on adiposity.

The Pearson correlations between the sonographic depth measurements and BMI, WC, and DXA-android %BF are provided in Table 2.4. The combination of the subcutaneous fat layer at both Smin and Smax were compared with BMI, WC, and DXA-android %BF and demonstrated moderately positive strength of association and were statistically significant. In addition, the combination of visceral fat layer at both Vmin and Vmax were compared with BMI, WC, and DXA-android %BF and demonstrated only a weakly positive association that was statistically significant. A total maximum mean score with DMS that combined Smax and Vmin was compared with BMI, WC, and DXA-android %BF and demonstrated a moderately positive association that was statistically significant. Lastly, the IMT-DMS mean value was compared with WC, which demonstrated a strong positive association that was statistically significant. Overall, both the intermediate and novice sonographers demonstrated high reliability compared with the expert, with the exception of the novice sonographer for the visceral minimum measurement (Table 2.5)

	Subcutaneous Total	Visceral Total	Maximum Total	*Intra-Abdominal Thickness*
BMI	0.655**	0.031	0.600**	
DXA (android % BF subscore)	0.515**	0.283*	0.500**	
Waist Circumference	0.567**	0.206	0.567**	0.524**
Intra-abdominal thickness			0.817**	

**p-value <.001

Table 2.4 Pearson's correlations comparing common measures of fat in a sample of obese cancer survivors.

	Smin	Smax	Vmin	*Vmax*	IMT
Intermediate	0.998	0.999	0.929	0.999	0.999
Novice	0.996	0.998	0.5	0.968	1

Table 2.5 Two-way random intra-class correlation coefficients for absolute agreement between an expert and an intermediate sonographer and an expert and a novice sonographer.

2.5 Discussion

Due to the increased trajectory of body fatness across the United States, the obesity epidemic remains the focus of Healthy People 2020 with the goal for Americans to achieve and maintain a healthy body weight.[26,27] To identify patients with overweight/obesity and increased risk for concomitant diseases, a nonionizing screening tool would be both practical and advantageous. The current study assessed a cohort of cancer survivors who were deemed to be overweight/obese and willing to complete body composition measures. As a group, the patients were on average classified at Obesity I based on a mean BMI of 33.4 (SD ±5.4). Since their abdominal adiposity was made up of both subcutaneous and visceral fat, the use of DXA-android %BF combines the varied layers of fat. In their study, Snijder et al.[28] used a Hologic QDR 1500 DXA unit to measure trunk fat; however, this was compared with CT at the same level.[28] Interestingly, in their study, CT was a better predictor of visceral fat than DXA in their group of patients. Similarly, the measurement of visceral fat that was completed with DMS in the current study did not have a strong correlation with the DXA-android %BF.[28] This is likely due to the inability of separating these levels of fat on a DXA, unlike what can be accomplished with CT and DMS. Since DMS is the nonionizing imaging choice compared with both DXA and CT, it has a higher likelihood of being chosen as a screening tool.

The use of intra-abdominal fat to predict obesity makes the current study's use of IMT an important factor. In a study by Jensen et al.[29], a sample of 21 participants were assessed with BMI, DXA, and CT, and their intra-abdominal fat was specifically analyzed. CT slices taken in the lumbar region were added to DXA values to predict intra-abdominal fat (subcutaneous and visceral fat combined). They found that a single-slice CT or other imaging technique with or without DXA data was the best predictor of intra-abdominal fat.[29] In the current study, we found, that IMT measurement from a sonographic image at the lower abdominal region was moderately correlated and statistical significantwith WC. Thishelps to support the hypothesis that the IMT measurement represents a nonionizing technique for obtaining a similar predictive measure of intra-abdominal fat. It is important to underscore that in present study, the measurement of IMT was similar to that in the Bazzocchi et al.[23] study. Given that L4 is generally at the level of the iliac crests, this would be comparable to the WC measurements that were made. The only exception to this level of measurement was when the scan aligned with the umbilicus, and the transducer was then moved superior to avoid the artifact.

In this study, mean total visceral fat measurement was not correlated with BMI or with the WC measurements. This could indicate a problem with classifying patients strictly by their BMI. Gallagher et al.[30], specifically looked at a cohort of patients (N = 1626) and used multiple measures, including DXA, to better classify fat ranges. The concern is that it may take multiple measures to accurately classify patients, especially those who have a BMI ≤35. Certainly, the patients in the current study are very comparable to those in the Gallagher study given they analyzed 1013 women with a mean age of 50 years.[30] Comparing the two study results helps in making the argument that multiple measures are needed for providing healthy body fat ranges, given that visceral fat is a contributor as well as measures of %BF. In the Gallagher et al.[30] study, the resulting model used multiple measures (DXA, BMI, and hydrostatic weighting) to propose a body fat range for women 40 to 59 years of age: BMI ≥30; African American = 39, Asian = 41, Caucasian = 41).[30]The present study suggests that DMS could provide even more specific data, which could improve this model, given the limitations of DXA as an ionizing imaging choice.

Interestingly, the use of WC and Vmax were shown to be very sensitive for predicting the presence and severity of coronary artery disease. Hamagawa et al.[5] found that a Vmax of 6.9 cm or higher but not a WC of 84.5 cm or higher did predict the number of diseased vessels. Other variables such as BMI, blood chemistry, medications, and coronary risk factors were not as sensitive a predictor. It is worth noting that sonographic measurements of Smin were also not a significant factor in the regression analysis.[5] It would seem that the use of nonionizing imaging such as DMS could provide important prognostic information for patients at risk for coronary artery disease and is worth further investigation.

Finally, it is important to consider that the present study's cohort were cancer survivors. The hope is that correctly classifying cancer survivors will set goals for reducing their risk for cancer reoccurrence. Balentine et al.,[31] followed 61 postsurgical patients who had a pancreatic adenocarcinoma and found that preoperative BMI was not a predictor of survival but that intra-abdominal fat thickness was the best predictor of survival.[31] In the Balentine et al.[31] study, CT was used to measure from the inferior edge of the left kidney to the abdominal wall to obtain the intra-abdominal fat depth. Although intra-abdominal fat thickness was highly correlated to overall survival for these pancreatic cancer patients, the use of ionizing radiation limits the translation of this work for a screening technique.

The use of DMS to objectively measure adiposity has a potential important role to play in screening patients for their risk of cardiovascular disease as well as certain cancers. The current study is limited because of the research design and the statistical power; however, it provides additional low-level evidence of the types of DMS measurements that are feasible to use in screening patients. Continued research is needed to determine what combination of variables and/or ratios might be of importance in screening obese patients for disease. Certainly, BMI continues to be suspect as a means for categorizing patients, as has been discussed in the articles provided, but it proved to be limited in its relationship to visceral fat deposits. The interrater reliability of these measurements would indicate that these DMS imaging metrics can be reliably completed by sonographers of varied experience. It would be important to provide appropriate training for clinicians so that reliable measures could be collected for all five variables of interest.

This cohort study adds to the evidence that DMS has an important potential role in providing nonionizing screening for obesity and informing patients on the need to reduce this risk factor. It also points to the potential for this technique to be used to screen children and adolescents for abdominal adiposity.

Chapter 3:
A Longitudinal Study to Assess Abdominal Adiposity by Sonography, DXA and BMI.

3.1 Introduction

Due to the increased risk for metabolic conditions in America’s obese populations, identifying patients at risk with a reliable and practical tool is vital to providing preventive health measures. Given the link between abdominal adiposity and metabolic syndrome, determining an individual’s risk for disease by measuring abdominal adiposity is greatly needed. The use of DMS has been shown to be a reliable and easily accessible tool when measuring abdominal adiposity.[32] DMS measures have the ability to identify health risks associated with increased abdominal adiposity and monitor changes in body composition[32] The use of DMS could be a more feasible and advantageous tool for routine clinical examinations due to its portability when compared to large and immobile imaging methods such as DXA, CT, and MRI. DMS provides a non-ionizing imaging method, is performed at levels that do not cause increased risk of bioeffects.[32] Bazzochchi, et al.[22] reports strong correlations between sonographic abdominal and CT adipose measurements. The current study continues to investigate the accuracy, reproducibility, and timeliness of sonographic adipose measures to help determine an individual’s risk for metabolic conditions.

3.2 Subject Population and Methods

Eighty obese cancer survivors (4 men and 76 women) were recruited to participate in the study. A randomized clinical trial design was used for a yearlong longitudinal study. All participants were known cancer survivors who were not currently receiving any form of active treatment within 2 years and met the criteria for obesity, based on BMI measurements. These participants were asked to come in for a day of data collection at a sponsored clinical research center pre-intervention for baseline data (month 0), 6 months post-intervention (month 6), and 12 months post-intervention (month 12). During each of their three visits, participants underwent several standard measures and imaging data collection, which included, blood draw, height and weight measures, waist circumference measures, skin carotenoid, walk test, stair climb, hand grip strength, DXA, and DMS images. However, for the purposes of this study, we focused on the DMA imaging, DXA imaging, BMI and waist circumferences measures.

Anthropometric Data

Height and weight were measured and then used to calculate BMI by the following formula[1]:

$$\text{Weight (kg) / Height}^2\ (\text{m}^2)$$

Waist circumference was measured at the superior border of the iliac crest. This measurement was conducted three times and averaged. The same registered dietician conducted all measurements for all three visits. DMS m and DXA measures were performed concurrently at each visit.

DMS was performed using a GE logiq 9 ultrasound machine with a 9.0(6-8 MHz) linear transducer for their baseline measurements. For visits two and three, DMS was performed using a GE logiq i ultrasound machine with a 9.0(6-8 MHz) linear transducer. Please reference, Stigall, et al.[33] and Woldemariam et al.[15], for the optimized protocol for scanning visceral and subcutaneous fat used in this study. A trained sonographer performed all images and data analysis.

DXA, which measures percent body fat, has been recognized as the gold standard for determine overall fat distributions. The DXA protocol can also be referenced in Stigall, et al. The examination was performed on a GE Lunar iDXA (Waukesha, WI). All images and equipment was operated by a trained Registered Nurse and images were analyzed by a credentialed Radiographer in Bone Density. Stults et al.[26] (2013) described the android sub-score of %BF, which consists of the area between the ribs and the pelvis, and is totally enclosed by the trunk region. The android sub-score of %BF, from the DXA analysis of percent body fat (%BF), was the metric used for data comparison. The use of an Android to Gynoid (A/G) ratio, as part of calculating %BF, has been reviewed by Imboden et al.[34] reference standards for body fat measures using GE dual energy x-ray absorptiometry in Caucasian adults. (Imboden MT, Welch WA, Swartz AM, et al., 2017).[34] This method not only requires low doses of radiation, but it also, does not have the ability to differentiate between the layers of fat (subcutaneous and visceral) within the abdominal region.

3.3 Analysis

Data Analysis

Statistical analyses were performed by a biostatistician. The associations of variables were determined by using trend graphs and Pearson correlation coefficients. The statistical power was set at a priori of p <0.05.

Each participant visit was analyzed over time and consisted of 8 main variables. These variables included BMI, WC, Subcutaneous Fat (Maximum and Minimum), Visceral Fat (Maximum and Minimum), DXA (android % body fat, subscore), and Intra-abdominal mesenteric fat thickness. All of these measures were analyzed longitudinally across all participant data. An example of the data collection form is included in Appendix A. Associations between variables were determined by using Pearson correlations. Intergroup comparisons were determined, using LS- Means Differences. Variable changes over time were also conducted using Type III Tests of Fixed Effects.

All DMS image analyses were completed by a credentialed sonographer. The DMS post-examination measurements were taken at the xiphoid, umbilicus, and the waist. Subcutaneous minimum fat and visceral fat maximum were measured at the level of the xiphoid. Subcutaneous fat maximum and visceral fat minimum were measured at the level of the umbilicus. Mesenteric fat thickness was measured at the level of the waist. Previous investigators have outlined these measurements. (Stigall et al., Woldemariam, et al.)[33,15]

3.4 Results

Due to scheduling conflicts, 77 out of the 80 participants, had sonographic images of their abdomen taken during at least one of their three visits. Of those participants, 67 received baseline images. Additionally, 53 participants had sonographic images performed at all three visits. Dropouts did occur due to cancer remission, and severe illness.

The trend graphs for waist circumference, BMI, and DMS measures of subcutaneous fat demonstrated similar behavior. See Figures 3.1 and 3.2. The trend graphs for the DXA (android % body fat, subscore), sonographic measures of visceral fat minimum, and sonographic measures of mesenteric fat demonstrated similar behavior to each other. See Figures 3.3 and 3.4. Sonographic measurements of the visceral fat maximum trended differently than the previous variables

Type III Test of Fixed Effects showed significant change over time for BMI, sonographic measures of subcutaneous fat, sonographic measures of visceral fat and sonographic measures of mesenteric fat. Waist circumference measures and the DXA (android % body fat, subscore) demonstrated no significant change over time. See Table 3.1. Pearson's correlation coefficients showed mostly moderate to high correlation between the DXA (android % body fat, subscore), and visceral fat measures, subcutaneous fat measures and mesenteric fat thickness measures for all three visits. Additionally, BMI and WC showed high correlations to subcutaneous fat and mesenteric fat thickness measures. See Table 3.2. The visceral minimum measures did not show a high correlation to the DXA (android % body fat, subscore).

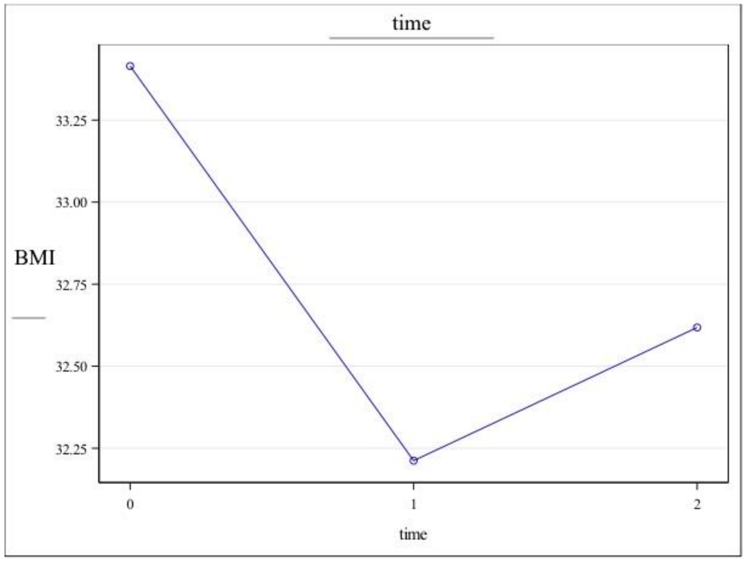

Figure 3.1 Trend graph representing BMI over time

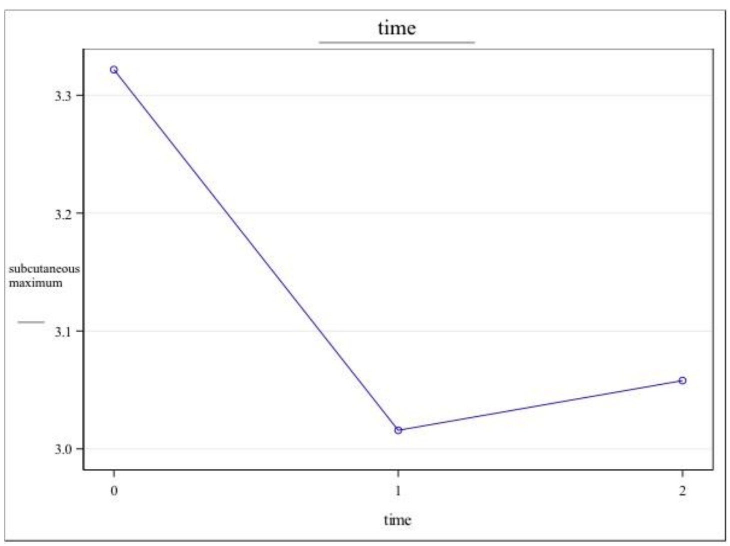

Figure 3.2 Trend graph representing subcutaneous fat

measures over time

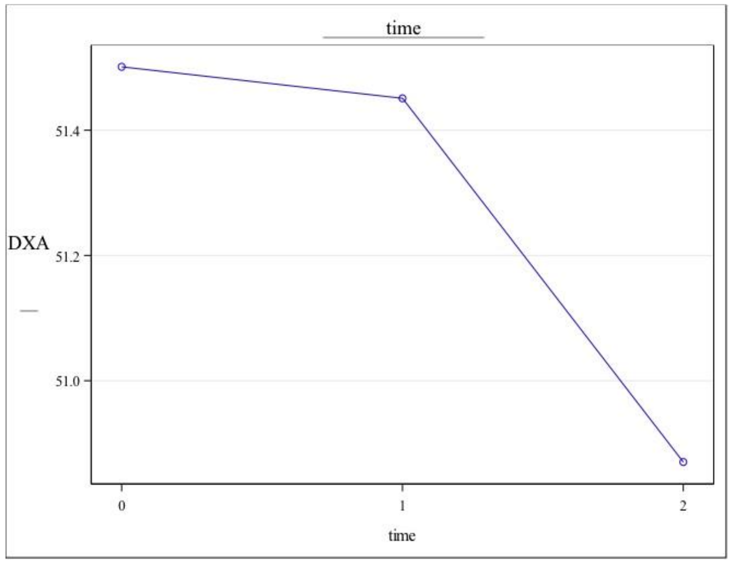

Figure 3.3 Trend graph representing DXA (android % body fat, subscore), measures over time

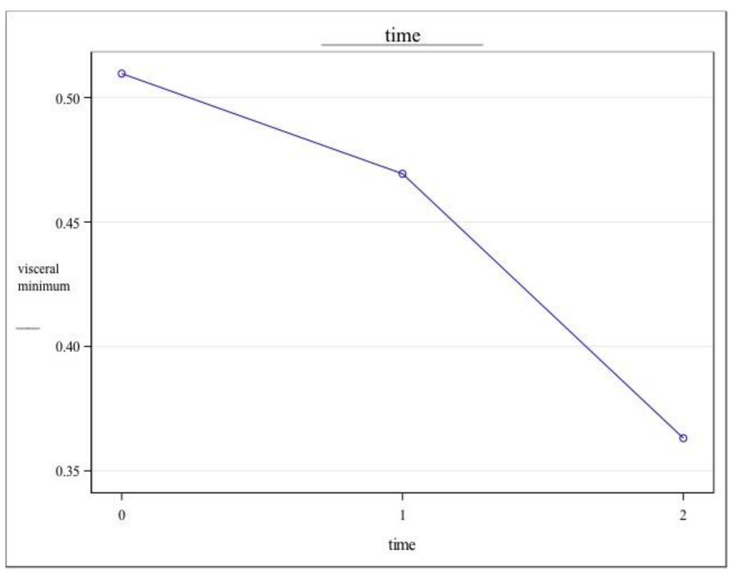

Figure 3.4 Trend graph representing visceral fat measures over time

Type III Test of Fixed Effects	
	Pr>F
BMI	<.0001
DXA (android % body fat, subscore),	.2442
Subcutaneous Min	.0007
Subcutaneous Max	.0005
Visceral Min	.0012
Visceral Max	.0001
Mesenteric	.0022

Table 3.1 Type III test of fixed effects where effect is time. $p < .05$ is considered significant

		Visceral Min	Visceral Max	Subcutaneous Min	Subcutaneous Max	Mesenteric Fat Thickness
Visit 1:	**DXA (android % BF, subscore)**	.1028	.0262	<.0001	<.0001	<.0001
	BMI	.8270	.8335	<.0001	<.0001	<.0001
	WC	.1257	.1669	<.0001	<.0001	<.0001
Visit 2:	**DXA (android % BF, subscore)**	.0102	.0022	<.0001	<.0001	<.0001
	BMI	.1303	.0916	<.0001	<.0001	<.0001
	WC	.0213	.0830	<.0001	<.0001	<.0001
Visit 3:	**DXA (android % BF, subscore)**	.1164	.001	.0015	.0002	<.0001
	BMI	.1022	.0054	<.0001	<.0001	<.0001
	WC	.0683	.0007	.0002	<.0001	<.0001

Table 3.2 Pearson correlations comparing visceral, subcutaneous and mesenteric fat measures to DXA (android % BF, subscore), BMI and WC, where $p<.05$ is considered significant

3.5 Discussion

Although DMS is not a method that is commonly utilized for quantifying abdominal adipose tissue, this study suggests that DMS may be a useful tool for assessing abdominal adipose tissue in overweight and obese cancer survivors. In this group of participants, the data suggest that all of the measures of BMI and the sonographic measures used are more sensitive to detecting changes over time than the DXA (android % body fat, subscore) or the WC measures. By following these participants over the course of a year, we were able to assess their abdominal adiposity over time. Assessment of visceral fat accumulation has been investigated. The most common and simplest measures consist of BMI and waist circumference measures. These methods provide a noninvasive technique to assess abdominal adiposity.[12] However, these methods, neither BMI nor WC can quantify variations in visceral or subcutaneous fat and therefore create pitfalls in the use of BMI and WC measures. Unfortunately, BMI assesses the total body fat distribution and therefore does not have the ability to estimate abdominal adiposity measures. Although insulin resistance and metabolic conditions have been associated with obesity or higher BMI, even lean subjects can be at risk for these conditions due to increased visceral fat accumulation.[35] The intra-abdominal fat measures by DXA and anthropometric measures compared to the visceral adipose tissues measures of single slice CT have been explored previously by researchers.[12] When measuring a cohort of obese women, DXA and the anthropometric data showed to be inaccurate compared to

CT.[12] DXA has the ability to identify whole-body fat composition and regional analysis, but lacks a way to distinguish and quantify visceral adiposity.[12]

DMS, provides comparable measures of abdominal adipose tissues without the use of ionizing radiation. Arguably, obesity must be kept ‘in check’, maintained and prevented through weight monitoring and weight loss therapy.[36] Mohan and Anburajan conducted a study to justify the use of anthropometric empirical indicator (AEI), by chest and pelvic radiograph for quantifying obesity.[36] These researchers found that the use of AEI by pelvic and chest radiographs, could precisely gauge obesity. The authors suggest that this method could replace the expensive more commonly used method of DXA. Interestingly, in another study conducted by Mauad, et al.[37], theytested the accuracy and reproducibility of measuring abdominal adiposity by DMS and CT and identified an increased intra-observer reliability. However, both methods, DMS and CT showed high accuracy and good reproducibility when measuring abdominal adiposity.[37] Although, these researchers found an alternative to DXA, by using CT, and AEI X-ray, these methods still required low doses of radiation. Whereas, DMS demonstrates high accuracy and reproducibility without the ionizing radiation.

It is important to note that sonographic measures perform in a similar manner compared to those measures considered ‘gold standard’, when determining an individual’s risk for disease. Stolk et al.,[38] suggests that DMS measures of intra-abdominal fat are more reliable than WC measures. DMS measures were performed on 600 participants. Participants with high abdominal fat measures, correlated with higher plasma glucose, total cholesterol, and triglycerides.[38] The associations observed were independent of weight and contrasted with the waist circumference, suggesting that DMS measures correlate more with the association of abdominal adiposity and increase risk for metabolic disease, versus the traditional anthropometrics measures.[38]

DMS provides a tool that can measure visceral fat accumulation that BMI could not detect. In the current study, BMI was highly correlated with subcutaneous fat during all three visits. This is likely due to the increased amount of subcutaneous fat distribution in individuals. The subcutaneous fat measurements showed higher correlations to the DXA (android % body fat, subscore) over the correlations of visceral fat. This is likely due to the limitations of measuring the visceral fat minimum. This low correlation could be due to the amount of visceral fat at the umbilicus region. This measurement is the smallest measurement of all the abdominal adiposity measurements. Therefore, this measurement can be challenging to correlate with the DXA (android % body fat, subscore) since DXA measures takes into account the entire abdominal adiposity and is unable to differentiate between the different fat layers. Most participants demonstrated larger measures of subcutaneous fat versus visceral fat overall. The android % BF subscore of DXA calculates the total fat distribution within the abdomen, therefore, it is suspected that it would correlate higher with the increased amount of fat layers.

This particular cohort consisted of overweight and obese cancer survivors. The use of DMS as a screening tool could help to determine their risk for metabolic conditions, disease reoccurrence, and prevent the use of added radiation to the patient. This provides prospective for this method to be used to screen pediatric abdominal adiposity in the future.

Chapter 4:
Measuring abdominal adiposity in children

4.1 Introduction

According to the CDC, the percentage of obesity in children and adolescents has more than tripled since the 1970's.[41] Children with obesity are more at risk for chronic health conditions and diseases.[41] The increasing rate of childhood obesity will also increase the likelihood of adult obesity and associated comorbidities, including but not limited to type 2 diabetes, fatty liver, glucose intolerance and increased incidence of metabolic conditions, in youth.[39] Obesity is a major determinant for cardiovascular disease and a risk factor for type 2 diabetes. The progression of type 2 diabetes, typically begins with the accumulation of abdominal adiposity.[40] Additionally, childhood obesity is associated with increased risk for atherosclerosis and mortality due to adult cardiovascular disease, regardless of an adult's weight.[42]

In order to define obesity in children, the CDC uses age and sex specific BMI percentiles. Size and growth patterns of children and adolescents are used to categorize BMI percentiles (Figure 4.1)[41]. These BMI percentiles are referenced versus the standard adult calculations, this is mainly due to the varied body compositions of male and female children at different ages.[41] BMI percentiles have become the standard for determining overweight and obese children, although BMI is an incomplete assessment due to the complex behaviors of obesity.[43]

Weight Status Category	Percentile Range
Underweight	Less than the 5th percentile
Normal or Healthy Weight	5th percentile to less than the 85th percentile
Overweight	85th to less than the 95th percentile
Obese	Equal to or greater than the 95th percentile

Table 4.1 BMI for age weight status categories with corresponding percentiles.

The rising trend in childhood obesity, would suggest a need to advocate for screening and early diagnosis of disease and metabolic conditions, in children and adolecents.[40] Screening children and adolescents for early diagnosis could promote preventative measures and early treatment to help avoid future chronic disease implications in adulthood. An accumulation of abdominal adiposity in adolescents has been shown to be associated with disorders such as cardiovascular disease and metabolic syndrome.[44] An accurate and reliable tool that measures visceral adiposity to screen children and adolescents' for disease risk should be readily available. BMI, waist circumference (WC), and waist-to-hip ratio have shown to be better correlated with total body fat distribution compared to direct measures of visceral fat.[44] The use of CT and MRI is often not readily available and is an expensive screening tool. Previous research has used DXA to estimate visceral fat accumulation. Lee et al.,[44] used an algorithm that estimates the mass and volume of visceral fat in the android region to both evaluate and estimate visceral fat in girls aged 9-13 years.[44] Lee et al.,[44] suggested that DXA estimated visceral fat measures almost as well as MRI in this particular cohort of participants. DXA (android % body fat, subscore) in addition to WC improved the estimate of the visceral fat measurements.[44]

Although DXA could be used as an alternative to MRI or CT, it still does not have the capability of definitively differentiating visceral and subcutaneous fat layers within the abdomen. Additionally, DXA is not readily available and requires low-doses of ionizing radiation to make an indirect quantitative assessment. DMS has been shown to accurately measure visceral adiposity compared to CT.[22] Previously, DMS has been a screening tool researched to measure subcutaneous and visceral fat in adults.[32,33] The use of DMS to measure abdominal adiposity in children has not been extensively researched previously. However, DMS may be an accurate and reproducible tool that could be utilized in measuring visceral fat in children and adolescents.

4.2 Subject Population and Methods

Fifty-eight third grade children, aged 8-10 years were recruited for a ten-week study (31 males and 27 females). This study and all data collection and intervention materials were permitted through the appropriate approval board. Participants were asked to attend a day of data collection at a research center prior to intervention. Prior to data collection, a verbal and written consent process was conducted for participants and their parents/guardians. During their initial visit these participants underwent multiple anthropometric measures and imaging, as part of the data collection. These specific measures recorded were height, weight, bioelectrical impedance, blood pressure, skin carotenoids and DMS measures.

Anthropometric Measures

Height and weight were measured to calculate participants' BMI percentiles. Percentiles were calculated utilizing the CDC growth charts.[41] A registered dietitian performed bioelectrical impedance and blood pressure measures. DMS measures were conducted on a GE Logiq i ultrasound machine with a 9.0 (6-8 MHz) linear transducer. An optimized protocol referenced by Woldemariam, et al.[15] and Stigall, et al.[33] was utilized to measure the visceral and subcutaneous adiposity of each participant. Trained and credentialed sonographers performed all the imaging and data analysis. Cine clips and static images were taken from the xiphoid down to the umbilicus in the sagittal plane.

An additional transverse image was taken at the middle of both iliac crests (the level at which waist circumference measures are performed). These images were then analyzed by a trained sonographer and measurements of visceral fat (minimum and maximum), subcutaneous fat (minimum and maximum) and mesenteric fat thickness were measured at the appropriate levels (Figure 4.1, 4.2 and 4.3).

Figure 4.1 Sagittal image taken at the level of the xiphoid. Subcutaneous minimum measurement (1), visceral maximum measurement (2)

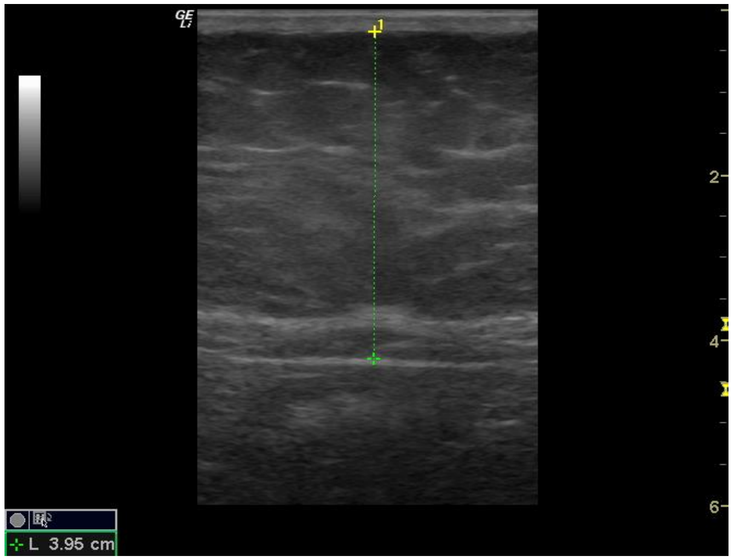

Figure 4.2 Sagittal image taken at the umbilicus. Subcutaneous maximum measurement (green dotted line), visceral minimum measurement (yellow dotted line)

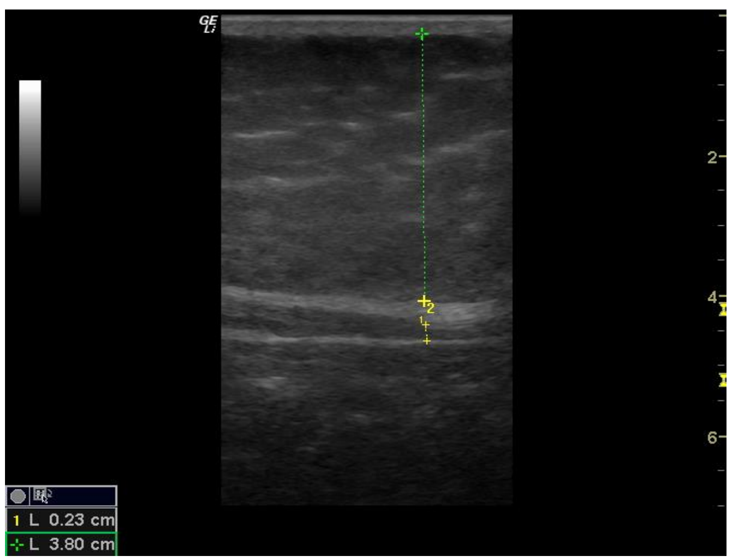

Figure 4.3 Transverse image taken at level of iliac crests. Mesenteric fat thickness measurement (green dotted line).

4.3 Results

Demographics of the participants are located in table 4.2. This cohort consisted of a fairly equal ratio of male participants to female participants with the minimum age being 8 years old and the maximum age being 10 years old. The average BMI percentile was 71.4 (SD± 30). On average, participants were classified at the upper limits of the normal or healthy weight category. The breakdown of BMI percentiles is shown in table 4.3. Descriptive statistics of adiposity measurements of the participants prior to intervention are provided in table 4.4. These measurements were acquired from the sonographic images taken as previously described.

	Age (years)	Height (m)	Mass (kg)
Females (n = 27)	8.70±0.47	1.38 ± 0.09	37.3 ± 13.8
Males (n = 31)	8.74±0.51	1.38 ± 0.07	38.3 ± 10.9
Total (n = 58)	8.72±0.49	1.38 ± 0.07	37.8 ± 12.2

Table 4.2 Descriptive statistics of participants by sex

	BMI Percentile	Weight Category
Females (n = 27)	64 ± 31.7	Normal or Healthy Weight
Males (n = 31)	77.8 ± 27.4	Normal or Healthy Weight
Total (n = 58)	71.4 ± 30	Normal or Healthy Weight

Table 4.3 Mean BMI percentiles of participants

	Females (n = 27)	Males (n = 31)	Total (n = 58)
BMI Percentile	64 ± 31.7	77.8 ± 27.4	71.4 ± 30
Subcutaneous Minimum	0.63 ± 0.61	0.59 ± 0.49	0.60 ± 0.54
Subcutaneous Maximum	1.2 ± 1.2	1.1 ± 0.93	1.10 ± 1.00
Visceral Minimum	0.12 ± 0.11	0.11 ± 0.13	0.12 ± 0.12
Visceral Maximum	0.69 ± 0.30	0.61± 0.32	0.64 ± 0.31
Mesenteric	1.5 ± 1.1	1.30 ± 1.10	1.40 ± 1.1

Table 4.4 Descriptive statistics of the participants prior to intervention comparing BMI percentiles and adiposity measures

4.4 Discussion

The accumulation of visceral adiposity has been closely correlated with HDL-cholesterol, triacylglycerol, high-sensitivity C-reaction protein concentrations, and the intima thickness at the common carotid artery.[45] The relationship between these variables has been explored in an adult population, by other researchers.[15,33,23] Kim et al.,[45] conducted a study containing 240 men and 106 diabetic patients who had DMS measurements of visceral fat taken and compared to the prevalence of cardiovascular disease, dyslipidemia, and metabolic syndrome. Men whose visceral fat measured in the middle to high quartile were found to have greater prevalence of cardiovascular disease, hypertriacylglycerolemia, low-HDL cholesterolemia, and metabolic syndrome than those in a lower quartile.[45] Additionally, women were shown to have a prevalence of metabolic syndrome and dyslipidemia in the middle to higher quartile.[45] Regardless of gender, visceral adiposity accumulation relates to increased risk for chronic conditions and severe illnesses. In another study, Silveira evaluated the correlation of body fat composition and components of metabolic syndrome in the pediatric population.[46] In that study, 182 obese pediatric subjects, 6 years to 16 years, had body composition and trunk fat measures obtained with DXA.[46] Participants with higher intra-abdominal adipose tissues were positively associated with increased dyslipidemia, non-alcoholic fatty liver disease, and components of metabolic syndrome.[46] All of these components in the pediatric population could lead to chronic conditions into adulthood.

It has been suggested that specific abdominal fat measures may be stronger associated with risk factors in childhood, than standard BMI percentiles in children.[47] Gishti et al.[47] examined abdominal fat distributions associated with cardiovascular disease in 6,523 children. Participants received a series of measures that included, BMI, DXA, and DMS measures. Gishti et al.[47] suggested that higher fat distribution measures were correlated with increased risk of hypertension, hypercholesterolemia, and clustering of cardiovascular risk factors. Additionally, higher abdominal fat mass, was associated with increased risk of cardiovascular disease factors, independent of BMI.[47] The close association of visceral adiposity accumulation and metabolic conditions as well as other disease risk, perpetuates the want for a screening tool that is reliable, reproducible, and safe for children and adolescents. Cross sectional images were collected from 122 African American adolescents and 129 Caucasian adolescents, aged 8-19 years to analyze metabolic syndrome and its relationship to abdominal adipose tissue.[48] Researchers concluded that increased prevalence of metabolic syndrome was seen in overweight youth, versus non-overweight as predicted by previous studies. Additionally, the participants with higher prevalence of metabolic syndrome had higher visceral fat measurements as well.[48]

Although the use of DMS as tool for measuring pediatric abdominal adiposity has not been widely studied, previous research and the present study would suggest that with an optimized protocol, DMS could be a reliable tool to evaluate visceral and subcutaneous fat in children and adolescents. Philipsen et al.,[49] explored the reproducibility of DMS assessment of abdominal fat distribution in 86 participants. Visceral and subcutaneous fat were estimated with adequate intra- and inter-observer reproducibility.[49] They concluded that DMS could be used as a feasible method for determining subcutaneous and visceral fat measures.[49] Mook-Kanamori, et al.,[50] investigated whether visceral fat measures in children could be determined by DMS compared to CT. DMS measures of abdominal fat correlated with CT measurements ranging from 0.75-0.97 (all $p<0.001$)[50]. DMS of abdominal adiposity in children highly correlated with CT measures of abdominal adiposity in children. It is suggested that sonographic measures of abdominal fat in children, is a valid method for epidemiological and clinical studies.[50] DMS offers a possible method that is reliable, non-invasive, and easily accessible for means of screening children for metabolic conditions, cardiovascular disease risk and other risk factors. Moreover, DMS could provide a reliable screening tool that has the added benefit of not utilizing ionizing radiation.

Chapter 5:
Discussion

5.1 Pitfalls of Body Mass Index

As there is an increase of obese populations, there is an increase of metabolic syndrome prevalence within the patient population. Assessing the total amount of body fat has become increasingly important when predicting complications and disease risk.[51] Studies have continuously exhibited how an increased BMI is linked to comorbidities/mortality risk and many organizations use body-mass index (BMI) categories to establish classes of obesity.[51] However, the limitations of BMI create complex issues for the overweight and obese populations. Obesity has been shown with an increased prevalence of metabolic syndrome and other disease risks, but not all obese patients develop these complications. BMI uses assumptions to determine adipose distributions. BMI relies on the idea that body fat is distributed evenly throughout the body.[51] BMI may be flawed due to the assumption that body fat is distributed similarly across the population. There are many different body types and fat distribution is different for each individual. BMI does not take into the account of how abdominal adipose tissue fluctuates. Previous studies have taken two groups of obese participants with the same total fat distribution but varying abdominal visceral adiposity.[51] In both men and women, it was found that those participants with lower levels of visceral adiposity had normal glucose levels compared to lean controls.[51] Additionally, when obese individuals were matched with the same total fat distribution, but different subcutaneous and visceral fat measures, participants with higher levels of visceral adiposity were found to have higher glucose values and insulin resistance.[53] Moreover, increased visceral fat has been associated with metabolic markers, including antherogenic dyslipidema, proinflammatory and prothrombotic states.[54]

The literature has focused on the regional distribution of abdominal fat and how visceral fat measures coincide with disease risk and metabolic conditions. Visceral adiposity has been shown to play a crucial role in risk for metabolic syndrome. According to Pouliot, et al.[52], in a group of 58 obese men the association of visceral adipose tissue measures positively correlated with fasting plasma triglyceride and insulin levels. Kwon, et al.,[56] performed a longitudinal study of 1,964 participants to assess the effect of visceral adipose tissue and subcutaneous adipose tissue on metabolic syndrome. During the course of five years, the researchers found that the visceral adipose tissue was significantly associated with higher incidence of metabolic syndrome.[56] Whereas, subcutaneous adiposity was not associated with incidence of metabolic syndrome.[56]

Over the years, numerous methods have been used to measure abdominal adiposity. Evaluating patients' risk for potentially serious medical conditions requires a quantitative assessment of visceral adiposity. This assessment should be easily accessible and easily reproducible to allow for quicker implementation into a clinical setting. The increasing rates of the obesity epidemic have shown the want for changes and better ways of determining disease risk in individuals. Researchers have explored the use of DMS as a tool for measuring abdominal adiposity previously. This current study looked to explore the use of sonographic images to assess visceral adiposity in different subject populations in a short-term approach as well as a long-term approach.

5.2 Study Populations and Demographics

Demographic information describes an adult population of eighty overweight and obese cancers survivors and a population of fifty-eight third grade children. The adult cohort was predominantly female with the mean age of 50 years. The maximum age was 72 years and the minimum age was 29. Initial short-term statistical analysis was conducted on the baseline measurements of this cohort. Additionally, this cohort was followed longitudinally over the course of one year. The adolescent cohort consisted of an almost even distribution of males and females with a mean age of 8 years. The maximum age in this cohort was 10 years and the minimum age was 8 years. This cohort was seen for all DMS and anthropometric measures prior to any intervention.

5.3 Utilization of Diagnostic Medical Sonography

Each cohort of participants received the same fundamentals of image acquiring. The adopted scanning protocol form Hamagawa et al.[5], and Suzuki et al.[6], that was optimized by Woldemariam, et al.[15], was used for both adults and children. Sonographic measures of both subcutaneous and visceral adiposity were shown to detect significant changes over time and moderately to highly correlate with BMI, WC, and DXA (android % body fat, subscore), as previously described in the adult population. Multiple studies have shown DMS as an optional tool for assessment of abdominal adiposity.[5,6,15,22,33,45] DMS provides a portable method of gauging an individual's risk for metabolic conditions and other risk factors. It can be brought bedside or transferred among multiple exam rooms. As previously discussed, DMS is readily available, reproducible, and accurate. The use of DMS to quantify abdominal adiposity has been shown to not only be possible, but preferred in adults. Furthermore, DMS has shown to be a positive option of evaluating visceral adiposity in youth.

5.4 Clinical Implications

Understanding the importance of preventative medicine and early diagnosis of chronic conditions has become more evident in obese populations. As the epidemic of obesity continues to rise in the United States, researchers, health care professionals and the media are constantly discussing, debating and reporting on the pervasiveness. The multiple Healthy People initiatives, have underscored the importance of improving the health of the nation. Due to the complexity of obesity and metabolic conditions, reliable screening tools, and methods are necessary to help accurately describe disease risk and provide proper treatment.

According to the US preventative service task force (USPSTF), all adults who are obese should have proper screening.[57] They recommend that clinicians refer patients with a BMI of 30kg/m^2 or higher to an intensive, multicomponent behavioral interventions.[57] Currently primary screening tools are BMI and WC when determining intervention for obese individuals. However, these two methods have pitfalls and shortcomings for screening patients for chronic conditions and disease risk. Historically, providers have faced complications with effective obesity counseling and treatment.[58] Physicians and healthcare professionals may be able to overcome obstacles with proper use of tools, continuation of medical education and education of care delivery models.[58] Adopting new medical practices and methods will require patience and advocacy.

The key aspect before a method can be adopted in research or clinical practice is to ensure reproducibility.[49] Implementing new methods or tools into routine care is a slow and unpredictable process.[59] Carlfjord, et al.,[59] conducted a qualitative study to determine the key factors of how the adoption of an innovation in a primary health care setting is influenced. Overall, adoption was positively influenced by positive expectations within the department. Positive opinions were seen when the change or innovation was compatible with routine exams.[59] The adoption of DMS as a tool for screening patient's for metabolic syndrome, is not only affordable, but fits into general sonography departments, private physicians' practices, and outpatient centers.

Implementing DMS into a department to measure abdominal adiposity would take proper training and a provided optimized protocol. Research has shown that DMS can be used to measure visceral and subcutaneous fat. Therefore, training could be provided to sonographers, physicians, and registered dietitians on how to properly acquire the needed imagery. Additionally, abdominal limited exams are currently being used as the charge code for many sonography departments. This type of exam could easily fit into the abdominal limited sonography billing category. Physicians and registered dietitians could use this method at patient wellness checks and during the screening and treatment process for underlying health concerns. DMS provides a non-invasive, non-ionizing method of describing patient's abdominal adiposity while assisting in determining and individual's risk for metabolic syndrome. With further research, this method could easily be adopted in the pediatric population as well.

5.5 Conclusion

The use of DMS has proven to be a reliable, practical, and cost-effective method of measuring visceral and subcutaneous adipose tissue. Researchers have found that in recent years, understanding the underlying implications of visceral fat accumulation has become extremely important when treating overweight and obese patients.[4] The use of DMS in sonography departments and physicians' offices is a realistic and sensible tool that could be easily executed within the screening process. Limited research has been done regarding this method being used in children and adolescents, however, this current research found that DMS may be an effective screening tool in youth as well.

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Appendix A: Example Data Collection Sheet

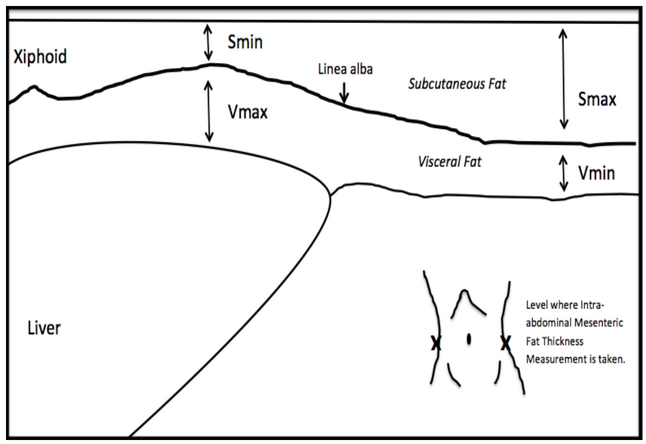
Date:

Subject # __________________ Sex (please circle): M or F Age: ____________
Height: _______________ (inches/cm) Weight: _________________ (lbs/kg)
Waist circumference: ________________ (inches/cm) DXA % body fat: _______________
Sonographer: ________________________

Sonography Study Measures: GE LOGIQ I LAPTOP
Transducer used: _________________MHz Typology (ie linear, curvilinear, etc):__________________

Frequency used: __________________MHz

**** Instructions to subject, "Try to stay as relaxed as possible and hold your breathe."***
**** Comment on each image in the bottom right corner: e.g., VF_000_T1 ("VF_000" = the subject id, T = transverse, 1 = image #; use L for longitudinal images).***



Use the following diagram to obtain the following measurements from the sagittal (longitudinal) images. Do not include the skin. Measurements should be made inside to inside. Probe marker toward the head or right side of the subject.
Both transverse and sagittal images should be saved for ALL subjects who are scanned for the study.
All images and a linea alba cine clip should be saved to the GE Logiq I for downloading and further image analysis.
Take 5 measurements and drop the high & low and average the middle three –those 3 and average are recorded here

Images	**Subcutaneous Minimum (S min)**	**Visceral Maximum (P max)**	**Subcutaneous Maximum (S max)**	**Visceral Minimum (P min)**	**Mesenteric Fat Thickness (MFT)**
Measurement 1:					
Measurement 2:					
Measurement 3:					
Average of the 3					

MFT image taken in the midline at the level of the iliac crest –marked for waist circumference (transverse image)

Comments: