GE Healthcare

White paper

Advancements in DXA body composition analysis:

Metabolic phenotyping with CoreScan*

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METABOLIC PHENOTYPING

The classical definition of obesity is the accumulation of excess adipose tissue (fat) to the point where health is negatively impacted[1]. Because it has historically been difficult to measure the amount of fat in the body, physicians have relied on indices such as body mass index (BMI). Measurement of BMI is attractive to clinicians because it is cost effective; however, BMI is not always a reliable indicator of metabolic disease. In fact, studies have shown that 30% of individuals with obese BMI are metabolically healthy, and 20% of subjects with healthy BMI have metabolic disease[2]. Better identification of metabolic risk requires that we look beyond BMI and consider metabolic phenotyping based on body composition measures.

Phenotyping is a term that describes the process of grouping individuals based on measurable traits. For example, within any given BMI category, several metabolic phenotypes can be defined based on where body fat is located. These phenotypes have different risks of developing cardiometabolic disease. A phenotyping approach allows us to move beyond the shortcomings of BMI as a cardiometabolic risk indicator.

VISCERAL FAT

Visceral adipose tissue (VAT), or the fat that accumulates deep within the abdomen, has been associated with the abdominally obese phenotype – one likely to develop cardiometabolic disease[3]. While VAT only accounts for approximately 10% of total body fat, it lies deeper in the abdomen – inside the intra-abdominal cavity. VAT is highly vascularized, contains large fat cells, and secretes disproportionate amounts of inflammation markers into the blood circulation relative to subcutaneous adipose tissue (SAT). This, combined with the location of the VAT, which provides it direct access to the liver, implicate VAT as a pathogenic fat depot[4].

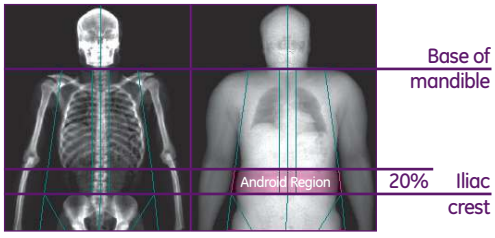
Numerous clinical studies have shown statistically significant associations between VAT and cardiometabolic disease including the Framingham Heart Study[5], the Dallas Heart Study[6], Health Aging and Body Composition (Health ABC)[7], and the Japanese American Community Diabetes Study[8]. These studies, which span a wide variety of gender, age, and ethnic background all show associations between VAT and cardiometabolic disease.

CORESCAN MEASUREMENT

While the weight of the evidence suggests that VAT is an important measurement to make in assessing obesity, routine use has been limited by cost and access to CT or MRI, which have been the research tools for measuring VAT[9]. Recently, a dual-energy x-ray absorptiometry (DXA) based VAT measurement approach, CoreScan*, has been developed. This automated tool can be conducted on standard DXA equipment and is derived from a total body scan where x-ray exposure is less than the equivalent of one day's natural background radiation[10]. CoreScan has the potential to greatly increase the reach of VAT as a metabolic phenotyping tool.

The patented CoreScan algorithm[11] computes VAT within the Android region of a total body DXA scan. The Android region, located over the abdomen, is roughly 10 cm in height, extending from iliac crest towards the head a distance that is 20% of the distance from the iliac crest to the base of the mandible *(Figure 1)*.

Figure 1: The Android region over the abdomen of a total body DXA scan is highlighted.



The CoreScan algorithm works through detection of two key parameters: the width of the SAT layer on the lateral aspects of the abdomen *(Fig 2a)*, and the anterior-posterior thickness of the abdomen *(Fig 2b)*, which can be attained using the DXA tissue attenuation image. A simple geometric model using these measures is used to estimate the android SAT. VAT is computed by subtracting the android SAT from the total android fat.

The CoreScan algorithm was developed using paired DXA and volumetric CT images from close to 350 subjects from three clinical sites. This sample contains men and women over a wide range of age and BMI.

Fig 2a: DXA planar image†

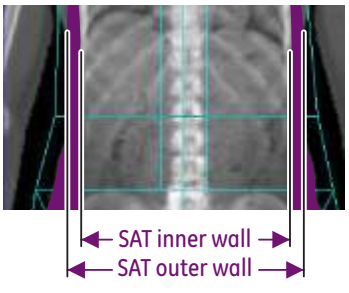
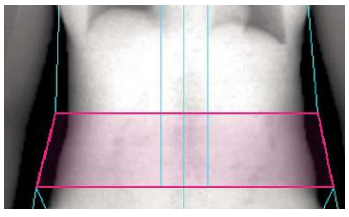


Fig 2b: Tissue attenuation image



Android region

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CORESCAN VALIDATION AND ACCURACY

CoreScan was validated using an independent data set acquired at Oregon Health & Sciences University (OHSU) in Portland, OR[12]. The validation study was performed on 109 adult men and women, ages 18–90 years, representing a wide range of BMI values (18.5–40 kg/m^2) that were assessed with both DXA and CT within a one hour fasting state. The descriptive statistics of the study population are shown in *Table 1*.

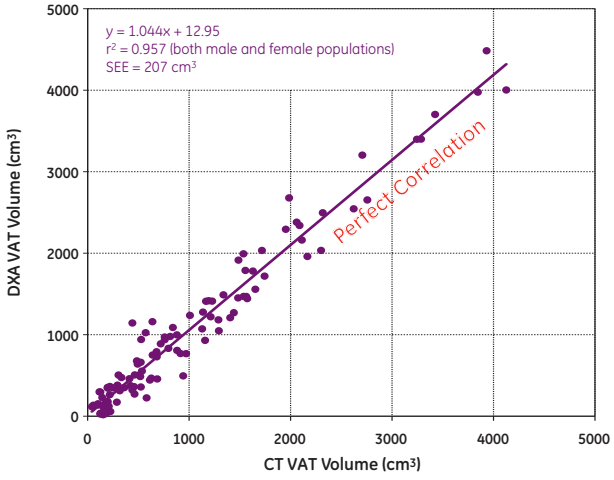
Variable	Female (n = 61)	Male (n = 48)
Age (yrs)	48.5 ± 14.3	50.8 ± 13.4
Height (cm)	164.5 ± 6.7	177.9 ± 6.7
Weight (kg)	72.5 ± 14.4	84.8 ± 14.5
BMI (kg/m^2)	26.7 ± 4.7	26.7 ± 3.5
DXA Android Fat (cm^3)	2310 ± 1450	2334 ± 1130
DXA SAT (cm^3)	1650 ± 810	1010 ± 469
DXA VAT (cm^3)	800 ± 960	1382 ± 946
CT VAT (cm^3)	730 ± 870	1337 ± 900

Table 1: Descriptive statistics of the OHSU validation study.

DXA images were acquired using a Lunar iDXA* running enCORE software using a standard total body (TB) scan. Placement of the Android region along with calculation of VAT was performed automatically by the software. Volumetric CT images over 15 cm of the abdomen were acquired on the same subjects. VAT was quantified based on subject-specific VAT threshold, set as 2SD from the mean Hounsfield units of a representative VAT sample. VAT was reported as the sum of all slices across a region equivalent to the DXA Android region.

Figure 3 shows the correlation between DXA measure of VAT volume and CT. The coefficient of determination (r^2) for regression of CT on DXA values was 0.957 for the combination men and women. The average Bland–Altman bias was +57 cm^3 for males, with 95% of subjects within -355 to +468 cm^3 difference between CT and DXA.

Figure 3: Correlation between CoreScan and CT.



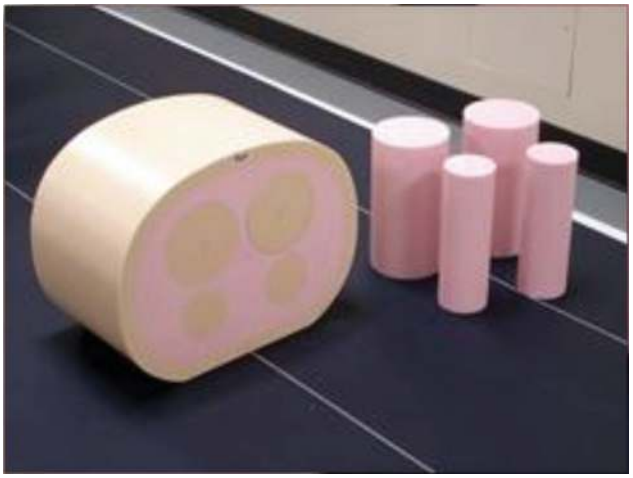
CORESCAN PRECISION

Previous studies have shown that VAT is responsive to both dietary and physical activity interventions and that cardiometabolic health can improve in individuals who do not meet overall weight loss goals, but who lose a large proportion of their VAT[13, 14,15]. Using CoreScan to monitor VAT changes over time may be useful to clinicians and interventionists who are trying to track progress towards metabolic health goals beyond weight loss.

The precision of a measurement determines how frequently measurements should be made, and the magnitude of the changes that can be detected with a given instrument. CoreScan precision is demonstrated with a series of experiments where both imaging phantoms and clinical subjects undergo repeated DXA measures with repositioning between scans[16].

Imaging phantoms enable large numbers of replicate measures to be collected using materials with known DXA composition values. A custom anthropomorphic imaging phantom (Figure 4) was developed to characterize VAT precision (CIRS, Norfolk, VA USA). The phantom is made of two materials: a simulated SAT layer (tan), and a lean core (pink), which has four holes. When rods simulating either lean or adipose tissue are inserted into the holes, a variety of VAT masses, ranging from 0 – 1800g, can be achieved.

Figure 4: Photograph of VAT phantom. This corresponds to a configuration with all adipose rods inserted (1800g).



The phantom was used to characterize intra-scanner precision, which is an indication of how precise the CoreScan measurement is on a single scanner, and inter-scanner precision, where different DXA systems are compared. Both of these are important measures in establishing clinical utility. The intra-scanner precision for the VAT phantom across nine quantities of VAT mass (0 – 1800g) ranged from 28.4 – 38.0g. The inter-scanner precision ranged from 24.7 – 38.4g. Combining inter- and intra-scanner precision yielded a total phantom precision estimate of 47.6g for VAT mass, which corresponds to a 4.8% coefficient of variance (CV) for a 1kg VAT mass.

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The precision of CoreScan was also measured on clinical population consisting of young obese women (n=32), each completing replicate total body scans with repositioning between scans (Table 2).

Variable	Mean (SD)	Range
Age (years)	35.3 (5.2)	25.2 – 45.2
Height (cm)	162.6 (7.1)	150.0 – 178.5
Weight (kg)	92.9 (11.0)	73.8 – 112.5
BMI(kg/m2)	35.1 (3.1)	30.0 – 40.0
VAT (g)	1110.4 (435.0)	404.2 – 2296.8

Table 2: Descriptive statistics of CoreScan precision study.

The average VAT mass on these subjects was 1110.4g and the precision was 56.8g or 5.1% CV. Both the phantom and clinical study demonstrate that CoreScan has a precision of approximately 60g on a VAT mass of 1kg. CoreScan precision is consistent with use in longitudinal and interventional trials where VAT loss is a desired outcome.

CORESCAN AND CARDIOMETABOLIC PROFILE

The cross-sectional associations between VAT and cardiometabolic disease have been well documented using CT and MRI for VAT measurement[7,17,18]. An essential step in demonstrating the clinical utility of the CoreScan VAT measurement is to replicate the disease associations that have been observed in CT and MRI with the novel CoreScan technology.

An analysis of cross-sectional relationships between CoreScan VAT and cardiometabolic disease was performed on a subset of the baseline population of the Progression of Carotid Intimal Lesions (PLIC) population-based study conducted at the University of Milan[19] (Table 3). These subjects (n=939) had both total body iDXA scans and measures of cardiometabolic risk factors including, height, weight, BMI, waist circumference (WC), triglycerides (TG), high density lipoprotein cholesterol (HDL), total cholesterol (TC), systolic and diastolic blood pressure (SPB, DPB), and fasting plasma glucose. CoreScan was retrospectively applied to the iDXA total body images.

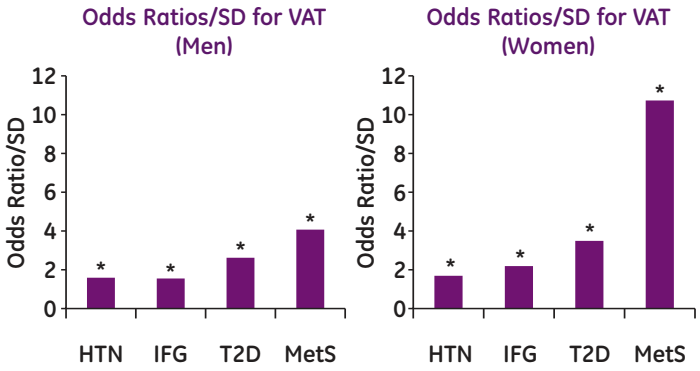
Variable	Women (n=541)	Men (n=398)
Age (yrs)	56 ± 12	55 ± 13
BMI (kg/m2)	25 ± 4	27 ± 3
WC (cm)	86 ± 11	97 ± 9
TG (mg/dl)	85 (62, 115)	101 (72, 143)
HDL (mg/dl)	61 ± 15	51 ± 12
TC (mg/dl)	230 ± 47	218 ± 42
SBC (mmHg)	124 ± 18	130 ± 16
DBC (mmHg)	75 ± 9	79 ± 8
HTN (%)	23	36
FPG (%)	96 ± 15	102 ± 19
IFG (%)	27	46
T2D (%)	4	8
MetS (%)	22	23
VAT (cm3)	839 ± 622	1614 ± 857

Table 3: Descriptive Statistics of PLIC cohort, including cardiometabolic disease states.

Hypertension (HTN) was defined as systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mmHg. Impaired fasting glucose (IFG) was defined as fasting plasma glucose (FPG) = 100-125 mg/dl. Type 2 diabetes (T2D) was defined as FPG > 125 mg/dl. Finally, metabolic syndrome (MetS) was defined using the Adult Treatment Panel (ATP) criteria.

Figure 5 shows multi-variable regression analysis for both women (top) men (below) to determine odds ratio for cardiometabolic disease states. The odds ratio is a statistical method that describes the increase in likelihood of having disease for a one standard deviation increase in VAT. For both men and women, VAT was significantly associated with increase odds of hypertension, impaired fasting glucose, metabolic syndrome, and type 2 diabetes ($p<0.05$). The largest odds ratio observed for both genders was for metabolic syndrome with an odds ratio of 10.73 in women and 4.07 in men. These associations are consistent with previously reported literature where volumetric CT was used to measure VAT[5].

Figure 5: Age-adjusted odds ratio (OR) for VAT and cardio-metabolic disease states for men and women. *p<0.05 (probability of OR equal to one is less than 0.05).



In order for a new measurement of obesity to have value in clinical practice, it must add new information about disease, above and beyond BMI and WC. Statistical adjustment techniques allow us to remove the effects of BMI and WC on disease association and look at the independent association between VAT and disease (Table 4). After adjustment, the odds ratio for type 2 diabetes remained high at 2.07 for women and 2.25 for men. Similarly, the odds ratio for metabolic syndrome was 3.46 for women and 1.75 for men. This analysis shows that VAT association with cardiometabolic disease remains strong even after adjusting for common obesity metrics (BMI, WC) suggesting an independent role of CoreScan VAT on cardiometabolic disease status.

	Women		Men	
	Adjusted CoreScan Odds Ratio	p	Adjusted CoreScan Odds Ratio	p
HTN	1.09	0.76	1.69	0.011
IFG	1.31	<0.33	1.67	<0.0094
T2D	2.07	<0.17	2.25	<0.011
MetS	3.46	<0.0006	1.75	<0.023

Table 4: Adjusted OR for VAT and cardiometabolic disease.

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SUMMARY

CoreScan is the first readily available method to quantify VAT. CoreScan accuracy has been validated across a broad population of adults, and precision has been characterized in phantoms and human subjects. In a large cross-sectional study, there was a strong association between CoreScan and clinical disease. All of these results suggest that the CoreScan application may be useful in helping physicians to manage cardiometabolic risk in patients with hypertension, type 2 diabetes, impaired fasting glucose, impaired glucose tolerance, dyslipidemia and metabolic syndrome. Because of the simplicity of implementing CoreScan, it may be especially useful to help characterize risk where standard indices fall short in both the normal and overweight population.

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¥ Current address is Exact Sciences Corp., Madison WI USA

† Figure adapted from Del Rio et al., European Congress on Obesity, 2007.

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