Optimization of Surgical Technique by Objective Quantification and Reconstruction of Adipose Tissue Volume

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1.1-ABSTRACT

Background/hypothesis/objectives: Plastic and Reconstructive surgeons commonly manipulate adipose tissue for reconstructive and cosmetic purposes. Common procedures that involve adipose tissue include free flap reconstruction, liposuction, and fat grafting. Adipocutaneous free flaps are commonly harvested for reconstructive purposes, notably for autologous breast reconstruction post mastectomy (e.g. Deep Inferior Epigastric Perforator flaps). Liposuction is commonly used for cosmetic purposes or as an adjunct to breast reduction and reconstruction, lipoma removal, flap defatting in reconstructive surgery and gynecomastia, to name a few applications. When harvesting adipose tissue, there is no practical way of measuring fat volume. Surgeons currently estimate the required volume by tactile sensation (i.e. pinch test). Computed tomography scans and magnetic resonance imaging can potentially be used to measure adipose tissue volume; however, these modalities are both resource and time-consuming. Moreover, they cannot be used intra-operatively. We would like to develop a quick and inexpensive tool to measure patients' fat volume in order to improve procedures that manipulate adipose tissue. Using ultrasound, a readily available and inexpensive modality, the goal is to develop a software that facilitates pre-operative planning with three-dimensional graphic representation. Our main objective is to improve results and decrease complications by implementing intra-operative real-time guidance and immediate feedback. We hypothesize that objective measurement of adipose tissue will result in improved surgical outcomes, decreased donor-site morbidities, and higher patient satisfaction.

Methods: The first phase of our project (current thesis) constitutes three extensive literature searches aimed at collecting data for the development of a software that accurately measures abdominal fat volume using ultrasound. The information presented in this thesis was essential for the technological development of the current and future prototypes. The first literature search aims to report techniques of subcutaneous adipose tissue measurement using ultrasound. The second systematic review aims to summarize the available techniques used to objectively measure flap volume in reconstructive surgery. Finally, the third systematic review aims to summarize the available techniques used to objectively measure adipose tissue during liposuction. In the second phase of our project (ongoing pilot project), a prototype was developed for validation of ultrasound quantification in both flap reconstruction and liposuction using the software Rhinocerus 5.0 spatial

reconstruction software (McNeel North America, Seattle, WA).

Results: To establish a standardized approach, the most consistent and reliable techniques are summarized in the first review. Literature findings related to the following parameters are summarized: type of measurement, ultrasound make/model, transducer frequency, external and internal landmarks, pressure applied on probe, special techniques and inter/intra-observer reliability. Reported methods of objective adipocutaneous flap quantification are summarized in the second review. Flap volume was calculated using the following techniques: magnetic resonance imaging, computed tomography, three-dimensional imaging and modeling, material templates, ultrasound, and weighing scales. Techniques and results of the included studies are summarized. Finally, the third review summarizes reported methods of fat quantification following liposuction. The details of the above reviews were crucial for the development and validation of a prototype for volumetric measurement of adipose tissue designed by our laboratory.

Conclusion: The preliminary results are promising, and we believe that three-dimensional representation and objective quantification is the future of reconstructive and cosmetic surgery. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility. Using the information gathered in the first phase of our project, we hope to contribute to our specialty by validating the first tool that objectively quantifies fat volume using ultrasound along with computer-assisted three-dimensional and volumetric representation.

1.2-RÉSUMÉ

Introduction/hypothèse: Les spécialistes en chirurgie plastique et esthétique manipulent souvent le tissu adipeux. Les reconstructions par lambeaux libres, les greffes adipeuses ainsi que la liposuccion sont parmi les procédures les plus fréquentes. Les lambeaux libres, contenant du tissu adipeux, sont fréquemment utilisés par les micro-chirurgiens, notamment pour la reconstruction mammaire suite à une mastectomie (e.g. artère épigastrique inférieure profonde). La liposuccion est largement utilisée pour des raisons esthétiques. De plus, cet outil est un complément pour plusieurs procédures, telles que les réductions/reconstructions mammaires, la gynécomastie, traitement de lipome etc. Il n'y a présentement aucun moyen objectif de mesurer le volume de tissu adipeux de la zone donneuse. Les chirurgiens se fient aux moyens subjectifs pour estimer le volume de tissu adipeux adéquat (e.g. test du pincement). L'imagerie par résonance magnétique et la tomodensitométrie peuvent mesurer le volume de tissu adipeux, cependant les limites d'accès (temps d'attentes) et les coûts associés à ces techniques d'imageries limitent leur applicabilité. De plus, ils ne peuvent pas mesurer le volume adipeux en temps réel durant la chirurgie. En utilisant l'échographie, nous aimerions développer un outil qui permet de mesurer le tissu graisseux en temps réel et le représenter en utilisant un modèle trois-dimensionnel. Notre objectif principal est d'améliorer les résultats des procédures reliées aux tissus graisseux, diminuer les complications, ainsi qu'améliorer la satisfaction des patients.

Méthodes: La première partie de notre projet (thèse actuelle) est composée de trois revues de littérature. Les données ramassées étaient essentielles au développement du logiciel protoype qui servira à mesurer le volume du tissu adipeux par échographie. La première revue de littérature a comme but de standardiser la mesure du tissue adipeux abdominal par échographie. Le but de la deuxième revue de littérature est de comparer les différentes méthodes décrites pour mesurer le tissu adipeux dans le domaine de la chirurgie reconstructive. Finalement, le but de la troisième revue de littérature est de comparer les différentes méthodes décrites pour mesurer le tissu adipeux durant la liposuccion. Dans la deuxième partie de notre projet (projet pilote en cours), notre laboratoire a développé un prototype pour la mesure du tissu adipeux avec le logiciel "Rhinocerus 5.0 spatial reconstruction software (McNeel North America, Seattle, WA) ".

Résultats: Afin de développer une approche standardisée, les techniques d'échographie les plus

fiables et communes ont été analysées dans la première revue de littérature. Les paramètres suivants ont été analysés : le type de mesure, la marque et le modèle de la machine, la fréquence du transducteur, les repères anatomiques externes et internes, la pression transmise par la sonde, les techniques spéciales (inspiration, position etc.) et la reproductibilité. Les diverses méthodes de quantification objective de lambeaux libres ont été analysées et résumées dans la deuxième revue de littérature. Le volume des lambeaux libres a été calculé à l'aide des méthodes suivantes : imagerie par résonance magnétique, tomodensitométrie, modélisation tridimensionnelle, modèles physiques, échographie, et diverses échelles. Les diverses méthodes de quantification objective de tissu graisseux suite à la liposuccion ont été analysées et résumées dans la troisième revue de littérature. L'information ci-haut a été essentielle pour le développement et la validation du prototype ayant comme but de quantifier le tissu adipeux de la liposuccion et des lambeaux libres.

Conclusion : Les résultats préliminaires confirment que la modélisation tridimensionnelle et la quantification objective sont le futur de la chirurgie reconstructive et esthétique. Plus d'études sont nécessaires pour confirmer la pertinence clinique de la quantification objective et des mesures volumétriques automatisées. Les résultats de cette première phase de notre projet serviront comme point de référence afin de développer le premier outil pour mesurer le tissu adipeux par échographie et modélisation tridimensionnelle.

1.3-LIST OF ABBREVIATIONS

3D	Three-dimensional
CT	Computed Tomography
CTA	Computed Tomography Angiography
DIEP	Deep Inferior Epigastric Perforator
DXA	Dual-Energy X-ray Absorptiometry
MRI	Magnetic Resonance Imaging
MRA	Magnetic Resonance Angiography
SAT	Subcutaneous Adipose Tissue
TRAM	Transverse Rectus Abdominis Myocutaneous
US	Ultrasound
VAT	Visceral Adipose Tissue

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1.5 - CONTRIBUTION TO ORIGINAL KNOWLEDGE

There has been recent interest in the quantification of soft tissues in the field of plastic and reconstructive surgery. A consistent and reproducible technique for subcutaneous adipose tissue measurement using ultrasound was lacking in the literature. The information gathered in this thesis was crucial to define the current limitations in soft tissue volumetric analysis and to guide the decision-making for the ongoing pilot project in our laboratory. The first phase of the project, presented in this thesis, was essential for the technological development of the current and future prototypes. A prototype for volumetric measurement of soft tissue was designed by our laboratory. We hope to contribute to our specialty by developing the first tool that objectively quantifies fat volume using ultrasound along with computer-assisted three-dimensional and volumetric representation.

1.6 - CONTRIBUTION OF AUTHORS

Alain J. Azzi - Concept of design, acquisition and analysis of data, development of prototype, drafting of the thesis, revision of the thesis

Ann-Sophie Lafrenière – Acquisition and analysis of data (section 2.1)

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Alex Viezel-Mathieu – Acquisition and analysis of data, acquisition and revision of the manuscript (section 3.1)

Thomas Hemmerling – Concept of design, drafting of thesis, revision of the thesis

Mirko Gilardino - Concept of design, drafting of the thesis, revision of the thesis

2.1-Ultrasonography Technique in Abdominal Subcutaneous Adipose Tissue Measurement

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2.2-Abstract

There are currently several reported techniques of sonographic subcutaneous adipose tissue (SAT) measurement described in the literature. This systematic review aims to report techniques of SAT measurement using ultrasound. A systematic literature search was performed to identify relevant articles using ultrasound to quantify abdominal SAT. The following parameters were collected: type of measurement, ultrasound make/model, transducer frequency, external/internal landmarks, pressure applied on probe, special techniques and inter/intra-observer reliability. A total of 30 studies were included. Literature findings related to the above parameters were summarized. When compared with other modalities (computed tomography and magnetic resonance imaging), ultrasound proves to be an accurate and efficient tool in measuring SAT. This systematic review highlights the broad role of ultrasound in abdominal SAT measurement. A summary of the most common techniques and parameters is provided, serving as a reference for a necessary standardized approach.

2.3-Introduction

Since the discovery of adipose-derived stem cells in 2001, adipose tissue has been gaining popularity (Zuk et al. 2002). Adipose tissue is no longer perceived as static and has become the target of many surgical procedures in plastic surgery and regenerative medicine. Visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) differ in their profile of endocrine and paracrine secretions of hormones and cytokines (Bazzocchi et al. 2011). VAT has been associated with metabolic syndrome and an increased risk of cardiovascular risk factors, insulin resistance, increased intima-media thickness at the common carotid artery, high CRP, hypertriglyceridemia and low HDL, to name a few (Kim et al. 2004). SAT is independently associated with high blood pressure, high alanine aminotransferase (ALT) and metabolic syndrome (Bertoli et al. 2016; Suzuki et al. 1993).

Procedures involving subcutaneous adipose tissue include fat grafting, liposuction and autologous breast reconstruction post-mastectomy, amongst others. Subcutaneous adipose tissue, notably abdominal adipose tissue, is also measured as a marker for various research purposes. For example, it has been used to predict serum HDL levels (Abe and Fukunaga 1994) and to detect associations with metabolic or cardiovascular risk factors. Moreover, the measurement of subcutaneous adipose tissue has become common in various surgical procedures to quantify and monitor outcomes, particularly following bariatric surgery (Djuric-Stefanovic et al. 2013) and liposuction (Bilgili et al. 2004). SAT is composed of two distinct layers, the deep and the superficial layers. The deep and the superficial SAT, separated by Scarpa's fascia, may have different metabolic properties (Gradmark et al. 2010).

There is currently no readily available modality to objectively measure subcutaneous adipose tissue volume. Computed tomography (CT) scans and Magnetic Resonance Imaging (MRI) can be used to measure adipose tissue volume, however MRI is resource and time-consuming, while CT is limited by radiation exposure (Hu et al. 2011; Kvist et al. 1986). Ultrasound is gaining momentum as a readily available, simple, inexpensive and radiation-free modality. There are currently several techniques of sonographic SAT measurement described in the literature. However, there is significant heterogeneity in technique, such as the amount of pressure applied on the probe, timing of measurements (inspiration/expiration), patient posture, ultrasound make/model, transducer frequency, external and internal landmarks, etc. This systematic review aims to report and compare techniques of subcutaneous adipose tissue measurement using ultrasound.

2.4-Methods

Literature Search

A search of Ovid MEDLINE, EMBASE, and PubMed was performed from database inception to August 1st 2017. Variations of the following key words were searched: [("fat" or "adipose tissue" or "subcutaneous") and ("ultrasound" or "ultrasonography" or "sonography") and ("volume" or "distribution" or "measure" or "quantification" or "map" or "model" or "representation")]. Citations were limited to human studies published in the English language. Studies were included if subcutaneous adipose tissue was measured using ultrasound and a description of the technique was provided. Cadaver studies, case reports, and review articles were excluded. Studies using A-mode ultrasound were excluded as they produce an amplitude pattern and not a two-dimensional image. Studies solely assessing visceral adipose tissue were also excluded as the focus of this systematic review was subcutaneous fat. Two independent reviewers assessed the eligibility of the studies using the same systematic inclusion/exclusion criteria.

Studies were selected based on the relevance of the title and/or abstract of retrieved records (Figure 1). If content was unclear in the initial screen based on abstract review, a formal article review was undertaken. Relevant studies from the reference list of included articles were also manually searched and included. All cited studies have gotten informed consent from each study participant and protocol approval by an ethics committee or institutional review board. The systematic review followed the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher 2010).

Data extraction

The main purpose of this systematic review was to report and compare techniques of abdominal SAT measurement. Studies were first analyzed to identify the following variables regarding adipose tissue measurement technique:

1) Ultrasound machine: Make/model, transducer frequency
2) External landmarks: The external location of the ultrasound probe (e.g. 5cm below the umbilicus)
3) Internal landmarks: Definition of total subcutaneous adipose tissue (e.g. distance between posterior line of dermis to rectus abdominis muscle)
4) Pressure on the subcutaneous tissues
5) Type of measurement: Depth, area, or volume
6) Reproducibility: Inter/intra-observer reliability
7) Special Techniques: Inspiration/expiration, supine/prone, arm positioning etc.

Studies were then divided into different categories based on similarity of application (e.g. metabolic, visceral fat, cosmetic and miscellaneous) (Tables 1-4). Finally, studies were analyzed to identify those with a focus on comparing ultrasound with other imaging modalities for SAT measurement (Table 5).

2.5-Results

Technique

Out of 6065 studies, a total of 30 were included in this review. Researchers have studied ultrasound measurement of abdominal SAT thickness using a wide range of techniques and parameters. To establish a standardized approach, the most consistent and reliable techniques are summarized below. Literature findings related to the following parameters are summarized: type of measurement, ultrasound make/model, transducer frequency, external and internal landmarks, pressure applied on probe, special techniques and inter/intra-observer reliability. Tables 1-4 report various techniques of subcutaneous adipose tissue measurement using ultrasound.

Ultrasound make/model

Using different makes/models of ultrasound invariably leads to variation in image quality. Bazzocchi et al. (2013) studied the impact of a technological gap between ultrasound machines but found no significant difference. In the recent literature, the most common ultrasound makes used for abdominal SAT thickness measurement are the Technos MPX (Esaote S.p.A., Genova, Italy) (Bartha et al. 2007; Bazzocchi et al. 2013; Bazzocchi et al. 2011; Bazzocchi et al. 2014b), GE Logiq (Bertoli et al. 2016; De Lucia Rolfe et al. 2010; Emmons et al. 2011; Haymes et al. 1976; Leahy et al. 2012; Muller et al. 2013; Philipsen et al. 2013; Philipsen et al. 2015; Toomey et al. 2011), GE Voluson 730 Expert (Barros et al. 2016; Battaglia et al. 2011), Aloka 500 SSD (Tokyo) (Abe and Fukunaga 1994; Eston et al. 1994; Koda et al. 2007; Kuchenbecker et al. 2014) and the Acuson Sequoia 512 (Siemens, Mountain Woods, California) (Brei et al. 2015; Gradmark et al. 2010; Muller et al. 2013).

Transducer frequency

Because SAT is a very superficial layer, most studies were performed with high frequency probes. However, there was significant heterogeneity in the literature, ranging from 5 to 12.5 MHz, mostly linear. Authors used probes with frequencies of 5 MHz (Abe and Fukunaga 1994; Armellini et al. 1991; Bellisari et al. 1993; Eston et al. 1994; Haymes et al. 1976), 7.5MHz (Armellini et al. 1997; Armellini et al. 1993; Bazzocchi et al. 2013; Bazzocchi et al. 2014b; Bertoli et al. 2016; Bilgili et al. 2004; Boey and Wasilenchuk 2014; Coleman et al. 2009; Fanelli and Kuczmarski 1984; Milanese et al. 2014) or 12-12.5MHz (Barton et al. 2016; Bazzocchi et al. 2011; Leahy et al. 2012; Muller et al. 2013; Toomey et al. 2011). Others used probes with multi-frequency probes, ranging from 5-8MHz (Gradmark et al. 2010), 5-12MHz (Gishti et al. 2015),12-15MHz (Barros et al. 2016). One study used a probe with a frequency of 20MHz (Sasaki et al. 2014).

External landmarks

Most authors described the ideal location to measure abdominal SAT thickness as 2 cm above or below the umbilicus along the xipho-umbilical line (Figure 2) (Armellini et al. 1994; Armellini et al. 1991; Bartha et al. 2007; Barton et al. 2016; Battaglia et al. 2011; Bazzocchi et al. 2016; Bazzocchi et al. 2013; Bazzocchi et al. 2011; Bellisari et al. 1993; Bertoli et al. 2016; Boisnic et al. 2014; Brei et al. 2015; Eston et al. 1994; Gishti et al. 2015; Gradmark et al. 2010; Haymes et al. 1976; Koda et al. 2007; Philipsen et al. 2015; Suzuki et al. 1993; Toomey et al. 2011). One study measured SAT lateral to the umbilicus (Abe and Fukunaga 1994).

Internal landmarks

The most commonly described landmark for SAT thickness measurement is the distance between the internal skin layer and the linea alba of the rectus abdominis muscle, commonly referred to as the distance between the skin-fat and fat-muscle interface, corresponding to the total SAT thickness (Figure 3) (Abe and Fukunaga 1994; Armellini et al. 1997; Armellini et al. 1993; Bartha et al. 2007; Battaglia et al. 2011; Bazzocchi et al. 2013; Bazzocchi et al. 2011; Bellisari et al. 1993; Bertoli et al. 2016; Brei et al. 2015; De Lucia Rolfe et al. 2010; Djuric-Stefanovic et al. 2013; Emmons et al. 2011; Fanelli and Kuczmarski 1984; Gradmark et al. 2010; Kuchenbecker et al. 2014; Leahy et al. 2012; Philipsen et al. 2013; Philipsen et al. 2015; Toomey et al. 2011).

Pressure applied on probe

The higher the pressure applied on the probe, the higher the compression of tissues - a potential scenario to underestimate the SAT thickness. Toomey et al. (2011) observed that the use of maximal transducer force (defined as: *force applied through the transducer at which no further change in SAT thickness occurred on-screen*) reduced the abdominal SAT thickness by 37%, whereas the use of half maximal force reduced it by 36%. To optimize the results, the probe must *just* be in contact with the skin, as if it were brushing it (Barton et al. 2016; De Lucia Rolfe et al. 2010). The application of water-soluble gel favors acoustic transmissions and has been described to decrease tissue compression. To avoid transmission parallax error, the probe needs to be held at 90 degrees with the skin surface (Abe and Fukunaga 1994). Some authors used a basic force gauge to standardize the amount of pressure applied on the probe throughout measurements and by keeping it below 1N (Barton et al. 2016; Toomey et al. 2011).

Type of measurement

Ultrasound is mainly used to measure thickness of subcutaneous adipose tissue, not volume nor area. With regards to terminology, most articles use the term “thickness”, but some authors use terms “thickness” and “area” interchangeably (Bazzocchi et al. 2013). To ensure consistency in the literature, we recommend “thickness” as the term representing the measurement.

Inter and intra-observer reliability

Studies have confirmed the intra- and inter-observer reliability of ultrasound for abdominal SAT thickness measurement (Abe and Fukunaga 1994; Bazzocchi et al. 2013). Consistent results were obtained by novices and experts when measurements were repeated by the same operator (intra-observer reliability) and when repeated by different operators (inter-observer reliability). The inter-observer and intra-observer reliability coefficients of variation were approximately 5% and 9.5%, respectively (Philipsen et al. 2013). In a study by Philipsen et al. (2013), three junior medical doctors with no prior ultrasound training followed a three-day course about general ultrasound techniques and one-day course on the particular ultrasound technique developed by De Lucia et al. (2010). The authors report that, after a short training session, accurate abdominal SAT measurement is possible. Toomey et al. (2011) also obtained similar results, with an intraclass correlation coefficient of >0.99 and an interclass correlation coefficient of >0.99.

Sp*ecial techniques*

Ultrasonic measurements of abdominal SAT thickness are not significantly affected by post-prandial abdominal distention (Bazzocchi et al. 2013; Philipsen et al. 2013). Therefore, fasting is not necessary. Patient position appears to vary in the literature. A few studies measured patients in the upright position, but most studies measured SAT in the supine position, for comfort and stability. To the best of our knowledge, the impact of patient positioning on ultrasonographic abdominal SAT thickness measurements has not been studied. There exists a great deal of heterogeneity in the literature regarding measurements taken after inspiration or expiration. Bazzocchi et al. (2013) suggested that SAT thickness was not significantly affected by these two different states.

Comparison between ultrasound and other imaging modalities

Ultrasonographic measurements of abdominal SAT thickness have been compared with different modalities (CT and MRI), described below. Studies in Table 5 compared ultrasound with other modalities.

Computed Tomography

There is a strong correlation between ultrasound and CT measurements of subcutaneous adipose tissue thickness ($P<0.0001$, $\rho=0.93$), as opposed to area and volume measurements, where a weaker correlation exists, albeit statistically significant. Gradmark et al. (2010) reported a moderate correlation between U/S and CT for superficial SAT ($r=0.56$; $P<0.05$) and deep SAT ($r=0.87$; $P<0.0001$). However, when estimating total subcutaneous adipose area (estimated by the number of pixels from both deep and superficial SAT, separated by Scarpa's fascia), they reported a strong correlation between CT and ultrasound ($r=0.93$; $P<0.0001$). A separate study by Bazzocchi et al. (2011) also reported promising results where the authors demonstrated excellent correlations between abdominal SAT thickness measurements with ultrasound and CT (mean $\rho = 0.94$-0.96).

However, measuring small variations in SAT thickness with U/S may not be as accurate as CT. Ultrasound measurements were not reliable in obese and infertile women undergoing a 6-month lifestyle program, especially in patients with a BMI >36.5 ($r = 0.54$, $P <0.0001$). A possible explanation is the heterogeneous deposits of abdominal SAT, poorly represented by solely measuring the peri-umbilical region (Kuchenbecker et al. 2014). Likewise, Armellini et al. (1991) studied ultrasonographic SAT thickness variations in obese women undergoing a 15-day low calorie diet and reported no significant changes in abdominal SAT, likely related to the short duration of the observation.

Overall, U/S appears to be a reliable tool for measuring SAT thickness when compared to

CT, however, its use for small variations in SAT may be limited due to the heterogeneous variation of adipose thickness in the abdominal region.

Magnetic Resonance Imaging

Comparisons of ultrasound SAT measurements with MRI have been more promising in the recent past, yielding stronger correlations. Although both MRI and CT share similar problems with respect to segmentation and signal quantification, these findings may be secondary to improved precision of MRI and ultrasound in the recent years, overcoming differences in SAT measurement.

A correlation coefficient of 0.73 was found between U/S and MRI for abdominal SAT thickness measurements, with a slight overestimation of SAT using ultrasound(De Lucia Rolfe et al. 2010). The differences in measurements were 0.25 ± 0.56 cm ($P = 0.007$) in men and 0.69 ± 0.65 cm ($P < 0.0001$) in women.

Abe et al. (1996) demonstrated that SAT volume can be reliably estimated by measuring SAT thickness with ultrasound. By multiplying the average SAT thickness with the total body surface area, an estimate of the subcutaneous adipose tissue volume was obtained. MRI-measured volume was compared with the ultrasound volume estimate and a moderate correlation was observed between the two, particularly in the abdominal region (correlation coefficient r=0.81). Koda et al. (2007) further confirmed the validity of fat volume estimates using ultrasound compared to MRI, as demonstrated by previous studies (Fanelli and Kuczmarski 1984; Kuczmarski et al. 1987). The sonographic SAT thickness correlated with the MRI serial-slice measurements of SAT volume ($r = 0.816$; $P<0.0001$) (Koda et al. 2007). They also compared the sonographic SAT index (SAT thickness standardized by height) and reported a correlation with standardized MRI serial-slice measurements of SAT volume ($r = 0.825$; $P<0.0001$). These results demonstrate the safety and accuracy of U/S in measuring SAT volume, while obviating the need for more costly investigations like CT or MR.

2.6-Discussion

The technique used to measure SAT with ultrasound was relatively homogeneous throughout the various studies. Most of the variability originated from the ultrasound make/model as well as the transducer frequencies. Despite heterogeneous terminology, the internal landmarks were similar in most studies. However, external landmarks varied, with different abdominal locations being used for measurements, mostly within 2cm of the umbilicus along the xipho-umbilical line. Moreover, authors reported different special techniques with no significant effect on SAT measurement (e.g. fasting and measuring at end of expiration)(Bazzocchi et al. 2013).

As presented in Tables 1-4, ultrasound SAT measurements were frequently used for clinical and research purposes. New significant associations between SAT and metabolic markers have been reported, resulting in a recent interest in SAT as a useful clinical index of metabolic syndrome. (Abe and Fukunaga 1994; Bartha et al. 2007; Battaglia et al. 2011; Bertoli et al. 2016; Gishti et al. 2015; Philipsen et al. 2015). Moreover, there has been recent interest in ultrasound to quantify adipose tissue in reconstructive and cosmetic surgery. Examples include flap volume measurement for breast reconstruction (Minn et al. 2010), liposuction/lipoplasty (Bilgili et al. 2004), and to monitor outcomes of bariatric surgery (Djuric-Stefanovic et al. 2013).

Comparisons between ultrasound and MRI/CT showed promising results . Ultrasound is a cost-effective and portable alternative, with the added advantage of obviating exposure to ionizing radiation. Correlation between ultrasound and CT (the current gold-standard) were high in two separate studies (r value between 0.93 and 0.96, $P<0.0001$) (Bazzocchi et al. 2011; Gradmark et al. 2010). The main limitation was ultrasound's inaccuracy in detecting small variations in SAT over time, a discrepancy unanimously found by the authors and attributed to heterogeneous SAT deposits not detected by ultrasound (Armellini et al. 1991; Kuchenbecker et al. 2014). On the other hand, correlations between MRI and ultrasound measurements of SAT have improved in recent years, but remain relatively moderate (r value between 0.73 and 0.82) (Abe et al. 1996; De Lucia Rolfe et al. 2010; Koda et al. 2007). Emerging trends in dual-energy x-ray absorptiometry (DXA) are promising, allowing precise differentiation between SAT and VAT, resulting in measurements comparable to those of CT (Bazzocchi et al. 2014a). Moreover, the SAT ultrasound measurements correlate with those obtained with DXA ($r = 0.659$, $P<0.0001$). More research is needed to compare ultrasound to this low-radiation technology as it evolves.

We are still limited in the use of ultrasound for volumetric measurement of adipose tissue. Three-dimensional reconstruction of ultrasound images is the logical next step for this technology. As technology is constantly changing, future research should also focus on head-to-head comparisons between new ultrasound and CT/MRI machines.

2.7-Conclusion

This systematic review highlights the broad role of ultrasound in abdominal SAT measurement. A summary of the most common techniques and parameters is provided, serving as a reference for a necessary standardized approach. When compared with other modalities, ultrasound proves to be an accurate and efficacious tool in measuring SAT.

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2.9-LIST OF FIGURES

Figure 1. Flow diagram of systematic review study selection and eligibility

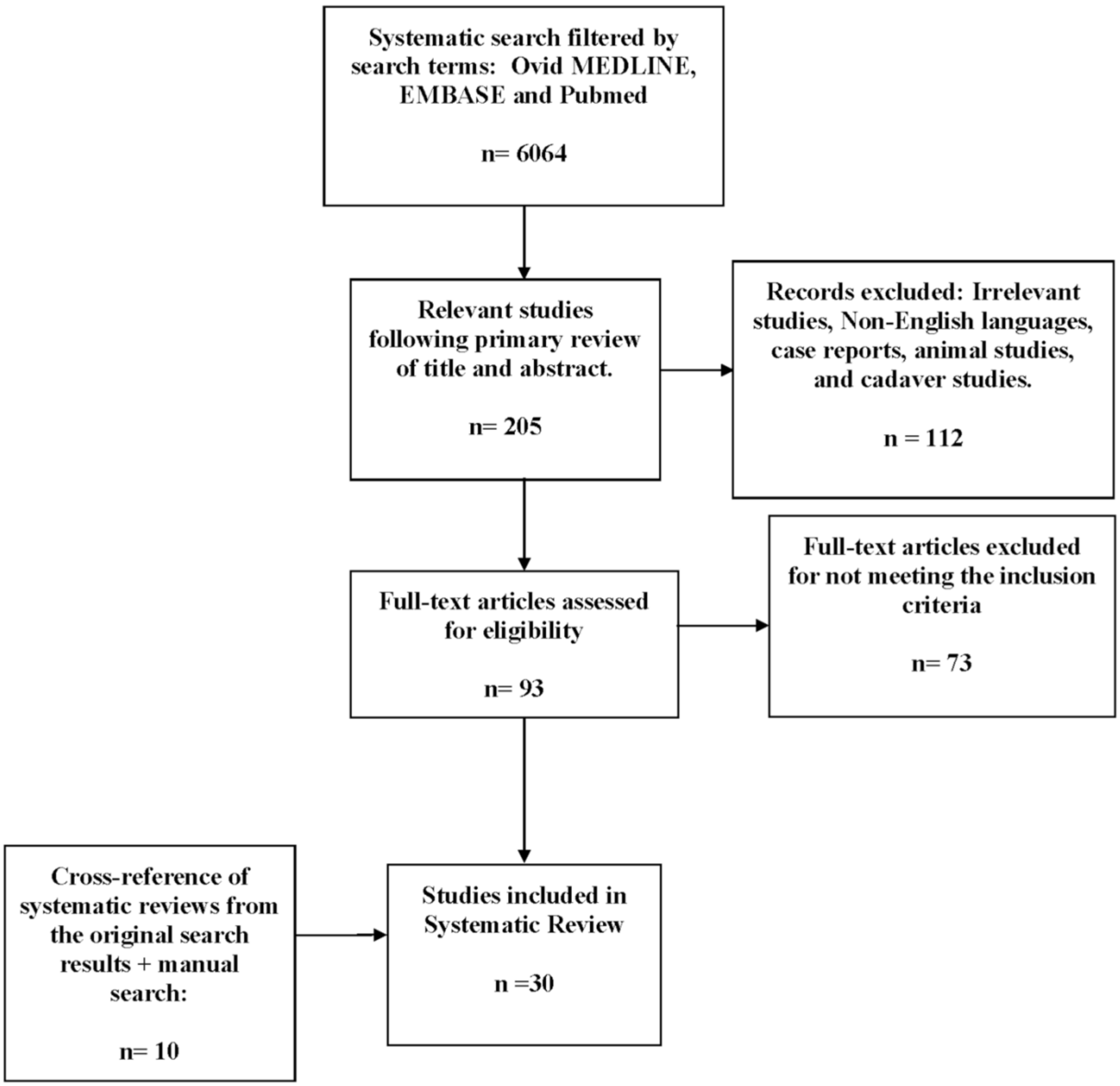


Figure 2: Xipho-umbilical line represented by the "X". The ideal location to measure abdominal SAT thickness is within 2cm of the umbilicus, along the xipho-umbilical line.

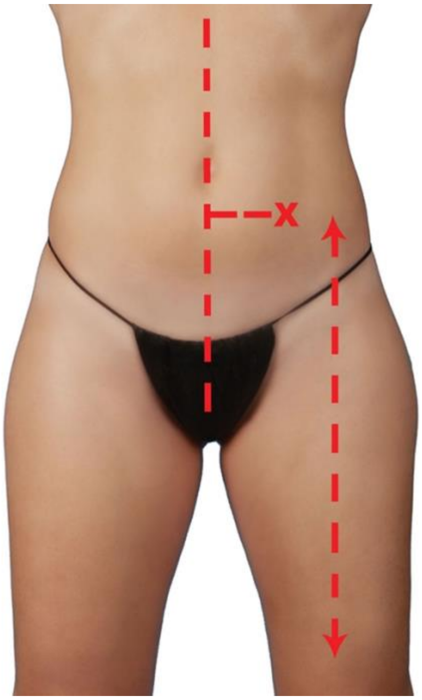
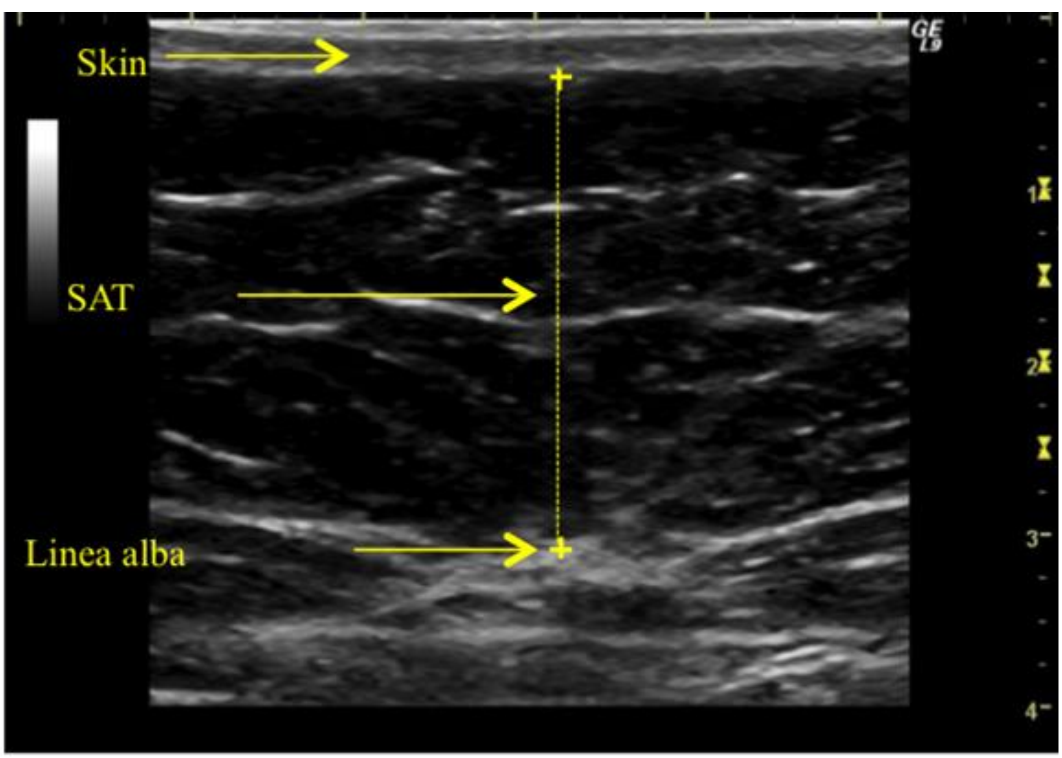


Figure 3: Skin-fat and fat-muscle interface, corresponding to the total SAT thickness



2.10-LIST OF TABLES

Table 1. Summary of ultrasound technique of subcutaneous adipose tissue measurement. The studies in this table measured subcutaneous adipose tissue for prediction of metabolic markers.

Study	Design	N (total)	SAT Measurement	Transducer	Ultrasound Make/Model	External Landmarks	Internal Landmarks	Probe pressure	Inter/intra-observer reliability	Special Techniques
Abe and Fukunaga (1994)	Cross-sectional	991	Thickness	5MHz	SSD-500 Aloka Co, Tokyo.	2-3cm to the right of the umbilicus	Distance from edpidermis to fat-muscle interface	No tissue compression	Intra-observer reliability r=0.94-0.99	Subjects were standing
Bertoli et al. (2016)	Cross-sectional	2414	Thickness	7.5MHz linear	Logiq 3 Pro	1 cm above the umbilicus in the midline.	Distance from epidermis to external surface of rectus abdominis muscle	N/A	N/A	Fasting. At end of expiration.
Battaglia et al. (2011)	Cohort	131	Thickness	RSP-16 multi-frequency linear	Voluson 730 Expert, GE	Along the linea alba between xiphoid process and pubic bone.	Distance from inner edge of skin and outer edge of linea alba	No tissue compression	N/A	Between days 3-5 of menstrual cycle, after overnight fasting. Supine. Breath held during scan.
Gishti et al. (2015)	Cross-sectional	6523	Thickness	12.5MHz	N/A	From the xiphoid process to the navel along the linea alba	Inner surface of subcutaneous tissue to the linea alba	N/A	N/A	N/A

Philipsen et al. (2015)	Cross-sectional	1342	Thickness	N/A	Logiq 9 machine, GE	Intersection between xiphoid line and waistline	Distance from skin to the linea alba	No tissue compression	N/A	Supine. End of expiration
Bartha et al. (2007)	Cross-sectional	30	Thickness	3.5MHz	Esaote Techno MPX	1 cm above the umbilicus the in midline	Distance from external surface of rectus abdominis muscle and internal edge of skin	No "undue pressure"	Intra and inter-observer reliability of 2.2% and 5.1%, respectively	Supine. End of expiration. Fasting.

SAT, subcutaneous adipose tissue; U/S, ultrasound; N/A, not available; MHz, megahertz; cm, centimeter; AT, adipose tissue

Table 2. Summary of ultrasound technique of subcutaneous adipose tissue measurement. The studies in this table compared subcutaneous adipose tissue with visceral adipose tissue.

Study	**Design**	**N (total)**	**SAT Measurement**	**Transducer**	**Ultrasound Make/Model**	**External Landmarks**	**Internal Landmarks**	**Probe pressure**	**Inter/intra-observer reliability**	**Special Techniques**
Alves et al. (2010)	Cross-sectional	1200	Thickness	4-7 MHz curvilinear	ATL HDI 5000	N/A	Minimal distance from subcutaneous tissue to the linea alba	No tissue compression	Intra-class correlation coefficient for SAT of 0.96	Supine
Suzuki (1993)	Cross-sectional	62	Thickness	3.75MHz convex		From the xiphoid to the navel	N/A	No tissue compression	N/A	Supine

					Toshiba SSA-250A and 270A	along the linea alba.				
Armellini et al. (1993)	Cross-sectional	137	Thickness	7.5MHz	Ansaldo AU 440	5cm from the umbilicus on the xipho-umbilical line.	Distance between skin-fat and fat-muscle interfaces	N/A	Intra- and inter-observer reliability of 1.36% and 5%, respectively	N/A
Emmons et al. (2011)	Cross-sectional	44	Thickness	2-5MHz curvilinear	Logiq Book XP, GE	1cm above umbilicus along xipho-umbilical line.	Distance from skin-fat interface and outer edge of the linea alba	No tissue compression	N/A	Supine. exhalation
Liu (2003)	Cross-sectional	37	Thickness	4-7MHz curvilinear	ATL HDI 5000	Distance from the xiphoid process and the umbilicus.	N/A	Without undue pressure	Inter-observer ICC=0.92. Intra-observer ICC=0.99.	At the end of a quiet expiration
Armellini et al. (1997)	Cross-sectional	197	Thickness	7.5MHz	Ansaldo AU 440, Esaote Biomedica	5cm from umbilicus on the xipho-umbilical line	Distance between skin-fat and fat-muscle interfaces	N/A	N/A	N/A

SAT, subcutaneous adipose tissue; U/S, ultrasound; N/A, not available; MHz, megahertz; cm, centimeter; ICC, intra-class coefficient correlation

Table 3. Summary of ultrasound technique of subcutaneous adipose tissue measurement. The studies in this table measured subcutaneous adipose tissue to monitor outcomes of cosmetic surgery.

Study	Design	N (total)	SAT Measurement	Transducer	Ultrasound Make/Model	External Landmarks	Internal Landmarks	Probe pressure	Inter/intra-observer reliability	Special Techniques
Bilgili et al. (2004)	Cross-sectional	14	Thickness	7.5MHz	GE LOGIQ MD 400	N/A	Distance from anterior surface of fat layer to deepest posterior margin	Loose contact between the U/S probe and skin surface	N/A	Supine
Boisnic et al. (2014)	Cohort	21	Thickness	N/A	Philips HD 11 XE	5cm inferior to the umbilicus	N/A	N/A	N/A	N/A
Milanese et al (2014)	Cross-sectional	28	Thickness	7.5-MHz linear	Chinson 600M	N/A	N/A	N/A	N/A	N/A
Boey and Wasilenchuk (2014)	Cohort	17	Thickness	7.5-MHz linear	SonoSite TITAN, Bothell, WA	Upper and lower abdomen	N/A	N/A	N/A	N/A
Sasaki et al. (2014)	Cross-sectional	118	Thickness	20-MHz	DermaScan C, Cortex Technology, Hadsund, Denmark	N/A	Below the fat-dermal junction	N/A	N/A	N/A
Coleman et al. (2009)	Cohort	10	Thickness	7.5-MHz linear	SonoSite 180	N/A	N/A	No tissue compression	N/A	N/A
Minn et al. (2010)	Cross-sectional	30	Thickness	N/A	N/A	N/A	N/A	N/A	N/A	N/A

SAT, subcutaneous adipose tissue; U/S, ultrasound; N/A, not available; MHz, megahertz; cm, centimeter

Table 4. Summary of ultrasound technique of subcutaneous adipose tissue measurement (miscellaneous uses)

Study	Design	N (total)	SAT Measurement	Transducer	Ultrasound Make/Model	External Landmarks	Internal Landmarks	Probe pressure	Inter/intra-observer reliability	Special Techniques
Guimaraes et al. (2007)	Cohort	160	Thickness	3.5-MHz convex	Siemens Sonoline Prima machine	5cm from umbilicus on xipho-umbilical line	Distance from skin-fat and fat-muscle interfaces	N/A	Intra-observer reliability of 4.6%	N/A
Bazzocchi et al. (2014)	Cross-sectional	250	Thickness	7.5MHz linear	Technos MPX, Esaote	2cm above and 2cm below the umbilicus along linea alba	MinSFT, MaxSFT: respectively, minimal and maximal distancse between the anterior surface of linea alba and the fat-skin barrier.	No tissue compression	N/A	Supine, arms at side, at the end of normal expiration
Barros et al. (2016)	Cohort	76	Thickness	15MHz linear	Voluson 730 Expert, GE	N/A	Distance from inner surface of subcutaneous tissue to linea alba	Without any pressure	N/A	Supine. Relaxed, showing no or little movements
Djuric-Stefanovic et al. (2013)	Cohort	30	Thickness	5-10MHz linear	Shimadzu SDU-2200	2cm above and 2cm	Distance from skin	N/A	N/A	8 hours fasting

						below the umbilicus	surface to linea alba			

SAT, subcutaneous adipose tissue; U/S, ultrasound; N/A, not available; MHz, megahertz; cm, centimeter; MaxSFT, maximum subcutaneous fat thickness; MinSFT, minimum subcutaneous fat thickness

2.11-Bridging Text

The information gathered above was essential for the technological development of the current and future prototypes. The technological design heavily relies on the details gathered above. There is significant heterogeneity in techniques of subcutaneous abdominal adipose tissue measurement using ultrasound. To establish a necessary standardized approach, the most consistent and reliable techniques were summarized. The following parameters were analyzed: type of measurement, ultrasound make/model, transducer frequency, external and internal landmarks, pressure applied on probe, special techniques and inter/intra-observer reliability. This information was also essential to the development of a standardized approach for our pilot project (see discussion, section 5). The second literature review, presented below, focused more on results of objective volumetric quantification of reconstructive flaps, a prominent aspect of plastic and reconstructive surgery. By analyzing and comparing the various described methods, we identified current limitations of widespread application. Moreover, validation of our prototype relies on adipocutaneous flap measurement. The review below was therefore essential for the development of the methodology described in section 5. We will tailor our technique, guided by the results of the first review, to minimize the described limitations and optimize ergonomic integration during reconstructive surgery. Furthermore, the following review confirmed the novelty of our project.

3.1-A Review of Objective Measurement of Flap Volume in Reconstructive Surgery

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3.2-Abstract

Background: The utility and efficacy of three-dimensional representation has been proven in bony reconstruction, however its role in soft-tissue reconstruction remains limited. There is currently no reliable gold standard to objectively measure flap volume. This systematic review aims to summarize the available techniques used to objectively measure flap volume in reconstructive surgery.

Methods: A systematic literature search was performed to identify all relevant articles describing objective techniques to quantify flap volume. The search included published articles in three electronic databases—Ovid MEDLINE, EMBASE, and PubMed.

Results: A total of 16 studies were included. Flap volume was calculated using the following techniques: magnetic resonance imaging, computed tomography, three-dimensional imaging and modeling, material templates, ultrasound, and weighing scales. Techniques and results of the included studies are summarized.

Conclusions: This systematic review provides a summary of various published techniques for objective pre- or intra-operative quantification of flap volume in reconstructive surgery. The preliminary results from this review are promising, and we believe that three-dimensional representation and objective quantification is the future of reconstructive flap surgery. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility.

3.3-Introduction

Reconstruction of soft-tissue defects with local or distant tissue transfer is an important tool for plastic surgeons. Although the volume of tissue transferred is often subjectively measured, notably in autologous breast reconstruction, breast symmetry plays an important role in patient satisfaction and in the quality of life of patients who undergo post-mastectomy reconstructive surgery. It has been demonstrated that patient-perceived breast appearance is significantly associated with quality of life psychosocial outcomes.[1] Women with pronounced breast asymmetry are more likely to experience depressive symptoms, stigmatization related to their surgery, and perceived worse health after treatment of their breast cancer.[1] Accurate volume determination is also essential in controlling donor site morbidity. Harvesting the minimally required flap volume can reduce donor site morbidity and increase postoperative patient quality of life.

Computer-assisted three-dimensional and volumetric representation has gained tremendous popularity in craniomaxillofacial surgery and has aided in mandibular reconstruction, Lefort 1 maxillary advancement, cranial defect repair, and orbital wall/floor reconstruction to name a few.[2-6] The utility and efficacy of three-dimensional representation has been proven in bony reconstruction, however its role in soft tissue reconstruction remains limited. When designing, and harvesting a flap, there is no practical way of measuring volume. Surgeons currently estimate the required volume by subjective tactile sensation and visual estimation. Objective measurement of the flap pre- and/or intra-operatively may be a useful adjunct to the artistic aspect of reconstructive surgery. Potential benefits include improving symmetry, increasing patient satisfaction, and decreasing revision rates. This systematic review aims to report described techniques used to objectively measure flap volume.

3.4-Methods

A search of the Ovid MEDLINE, EMBASE and PubMed databases was performed from database establishment to August 1st 2017. Different spellings and versions of the following key words were searched: [("quantitative" or "objective" or "measurement") and ("flaps" or "microsurgery" or "reconstruction" or "autologous") and "volume"]. Citations were limited to human studies published in the English language. Studies were included if objective flap volume measurement was described in the context of flap reconstruction. Cadaver studies and animal studies were excluded. Two independent reviewers assessed the eligibility of the studies using the same systematic inclusion/exclusion criteria. A total of 9212 studies were identified and further narrowed to 316 potentially eligible studies after primary review. Studies were selected based on the relevance of the title and/or abstract of retrieved records (Figure 1). The initial screen excluded studies with evidently irrelevant titles or abstracts. If content was unclear in the initial screen based on abstract review, a formal article review was undertaken. Potentially eligible studies were further reviewed, leading to a total of 16 eligible studies. Studies were also collected from an extensive manual Internet search and from the reference list of relevant articles, yielding an additional 4 studies. The systematic review followed the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[7]

3.5-Results

A total of 16 studies were included in this review (Table 1). Flap volume was calculated using the following techniques: magnetic resonance imaging[8], computed tomography[9-12], three-dimensional virtual modeling or material templates[13-19], ultrasound[20], and weighing scales.[21-23] The results of each study are categorized by imaging modality used and described below. Table 2 provides a summary of the advantages, disadvantages and cost.

Magnetic Resonance

The radiation sparing and high-quality images of magnetic resonance angiography (MRA) make it a valuable imaging technique, particularly for soft tissues such as the breast. Currently, only one study has reported the use of MRA for pre-operative volume estimation of various free flaps including deep inferior epigastric perforators (DIEP), posterior thigh and gluteal artery perforator flaps in 102 patients[8]. Pre-determined landmarks were used for virtually estimated flap volumes, which closely correlated to surgically harvested flap volumes (r = 0.97). Determining flap volume can be performed manually or with an automated reporting software based on standard flap territory. Moreover, the addition of gadolinium contrast has the advantage of simultaneously mapping perforator arteries. Although MRA appears to be accurate and safe for flap volume estimation, restricted access to this costly imaging modality limits its widespread applicability.

Computed Tomography

The use of computer tomography (CT) for objective free flap volume measurement is a relatively new concept. Most studies describing this technique were performed in the past decade, with the oldest study published in 2005[13]. A multitude of pre-operative volume estimation techniques have been described using enhanced CT and CT angiography (CTA), primarily in breast and craniofacial reconstruction[9-12].

CTA has been proven to be an accurate method in preoperatively estimating flap volume[9-11]. Pre-operative markings and radiopaque markers have been described in guiding virtual volume estimation[9]. Several authors have demonstrated that pre-operative CT-estimated flap volumes closely correlate to intra-operative harvested flaps (Pearson correlation coefficient= 0.88-0.99)[9-12]. Moreover, in breast reconstruction, pre-mastectomy or contralateral breast volume (in delayed reconstruction) can be measured to adjust abdominal flap volume[9-11] This becomes challenging when a concomitant balancing procedure, such as a reduction mammoplasty, is planned on the contralateral breast. Pre-operative volumetric measurement by means of virtual surgical planning, commonly practiced in craniomaxillofacial surgery[2-6], will play an important role in these patients.

In addition to simple volume calculation, CT results have been used to create virtual 3D models of desired structures. In a cohort of patients undergoing craniofacial reconstruction for hemifacial atrophy or following tumor resection, preoperative enhanced CT was performed prior to surgery and a 3D computer model of the patient's face was constructed[12]. A mirror image of the unaffected side was constructed and used as a guide for reconstruction. The preoperative evaluation of the 3D computer model allowed for the determination of the ideal size, shape and position of the desired flap. A free anterolateral thigh flap was subsequently harvested and de-epithelialized according to the 3D model dimensions and transferred to a subcutaneous pocket.

Compared to MRI, CT has the advantage of generally being more easily accessible and cost-effective. Exposure to ionizing radiation remains the main disadvantage. Like MRA, CT with contrast allows for the simultaneous mapping of perforator vessel anatomy. Pre-operative CT has been proven to reduce morbidity and time in perforator flap reconstruction[24] and its efficacy in flap volume estimation for breast reconstruction has been widely reported.

Ultrasound

Ultrasound (US) is a widely available, cost-effective, non-ionizing and portable imaging modality. Ultrasound has good penetration of soft tissues and can be used to measure adipose tissue thickness, however, its role in measuring flap volume is limited to date. One study reported its use for pre-operative transverse rectus abdominis myocutaneous (TRAM) flap volume estimation in breast reconstruction.[20] TRAM flap area was designed on the patient's abdomen, based on approximate breast volume determined by manual examination. US was used to measure tissue thickness at various zones of the proposed flap site. These depth measurements were used to estimate volume (by multiplying area and volume). To confirm the reliability of this technique, excised flap volume was measured intraoperatively by water-displacement prior to detaching it from its pedicle and was modeled to match the desired flap volume. Mastectomy volume measured by water-displacement was used to further adjust flap volume. The authors found a strong correlation between US-estimated and measured flap volumes (r=.9258).

Breast volume assessment is limited somewhat by the convex breast shape and heterogeneous density. More global limitations of ultrasound imaging is the narrow field of view in a typical ultrasonic probe making it difficult to assess the volume of large areas (ex. an abdomen or thigh). Moreover, US imaging is operator dependent, where the scanned image can vary significantly depending on tissue pressure or probe angulation. As such, there is potential for US as a modality for assessing flap volumes but significant technical advances are still required.

Three-Dimensional Modeling and Material Templates

Three-dimensional laser scanners are an accurate tool to determine a structure's dimensions and volume. The technology has been successfully used in breast and craniofacial reconstruction[13-15,17-18]. The low cost and portability of the scanner is unique compared to other imaging techniques such as MRI and CT. Although radiographs and CTs provide pertinent tissue information, their ability to analyze surface anatomy is limited compared to 3D photogrammetry. Before this technology, physical templates of craniofacial defects have been described using wax or alginate molds[16,19]. These molds can be used to guide intra-operative flap volume and design. The development of virtual planning with three-dimensional imaging has led to more practical methods of measuring defect volume[13-15,17-18] .

Due to its portability and small size, laser scanners can be used intra-operatively. One study described the use of intraoperative 3D scans for autologous breast reconstruction with TRAM flaps[13]. After mastectomy, scans of the reconstructed and contralateral breasts were performed and compared. Corrections were made by excising excess flap tissue until acceptable volume differences and a symmetrical appearance were established. Such a technique can be highly useful for less experienced surgeons.

Three-dimensional laser imaging has also been used to create a mold for determining flap volume[14,15]. In delayed breast reconstruction, the use of a cast of the unaffected breast has been described as a template for msTRAM and DIEP flap reconstruction. The excised flap was placed into the cast, which provided surgeons with the target flap volume and orientation. Excess flap volume was excised prior to flap anastomosis. Intra-operative use of the cast showed reduction in surgery time and improved symmetry.

Laser scanning has also been used to monitor tissue expansion. One study used 3D digital color scanning of a facial skin graft contracture induced defect[17]. Expanders were placed in preparation for cervicofacial and scalp flaps. The expanders were progressively inflated until the expanded area reached a similar value to that of the facial defect, confirming the availability of adequate flap area to over the defect of the excised facial scar. The contralateral side of the face can also be used as a guide to determine adequate expansion volume[18].

Scales

The weight of 1g of abdominal adipose tissue has an approximate volume of 1cm^3 [9-11,25-28]. Under this assumption, scales can be used intra-operatively to convert the weight of abdominal flaps to corresponding volumes. The size, portability, low cost and ease of use of scales are incomparable to any other volume measuring technique. The disadvantage of this technique is that over- or underestimation of flap volume can occur. Subcutaneous adipose tissue density varies from 0.925ml/g to 1.32ml/g[9-11,25-28]. Moreover, unlike previously described techniques, flap shaping and molding is not possible.

Scales have been used to estimate flap volume and improve post-operative symmetry in breast reconstruction. Excised mastectomy specimens can be weighed and raised flaps trimmed to match the mastectomy specimen's weight[21,22]. This technique has proven to be quick and can help improve postoperative breast symmetry[21,22]. Scales have also been used in conjunction with BMI measurements to construct an equation aimed at estimating the required latissimus dorsi flap weight based on a patients' BMI or body weight[23].

3.6-Limitations and Future Direction

Volumetric measurement is only one aspect of computer-assisted three-dimensional representation. For example, with more complex three-dimensional procedures such as breast reconstruction, the skin envelope, pocket, projection and breast footprint are also critical variables and must be accounted for. There is no guarantee of a symmetric outcome by simply estimating the volume in breast reconstruction, for example with a scale. Three-dimensional imaging is a promising modality for breast reconstruction due to its relatively low cost, excellent topographical surface measurements, and its proven utility in reduction mammoplasty and alloplastic breast reconstruction[29,30]. The current review focuses on adipose tissue measurement, however, practical imaging modalities must also discriminate between various tissues, such as muscle and skin. Future advancements in the field must focus on overcoming the above-mentioned limitations. Future studies must also evaluate the impact of objective quantification in reconstructive surgery on symmetry, patient satisfaction, procedure length, and cost-effectiveness.

3.7-Conclusion

This systematic review provides a summary of various published techniques for objective pre- or intra-operative quantification of flap volume in reconstructive surgery. Potential benefits include improved symmetry, increased patient satisfaction, decreased procedure length and revision rates when compared to subjective measurements. Potential risks may include exposure to ionizing radiation (e.g. CT scan) and increased cost or time. The preliminary results from this review are promising, and we believe that three-dimensional representation and objective quantification is the future of reconstructive flap surgery. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility.

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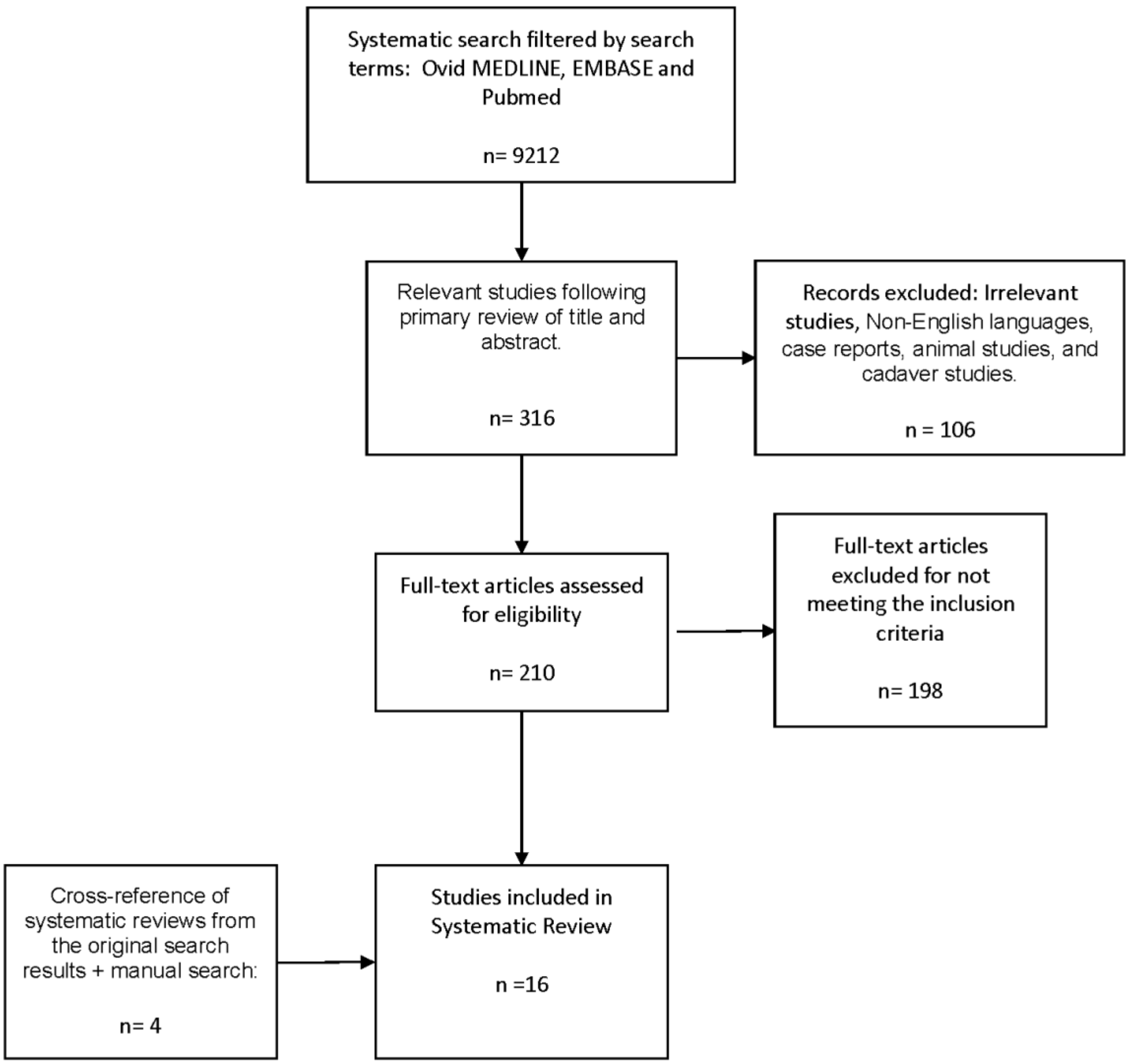
3.9-LIST OF FIGURES

Figure 1. Flow diagram of systematic review study selection and eligibility



3.10-LIST OF TABLES

Table 1. Summary of various published techniques for objective pre- or intra-operative quantification of flap volume in reconstructive surgery.

Study	Design	N (Total)	Specialty	Method of Flap Volume Quantification
Ahcan et al. 2012[14]	Cohort: prospective	12	Breast	3D imaging and modeling
Chang et al. 2001[22]	Cohort: prospective	28	Breast	Scales
Eder et al. 2014[11]	Cohort: retrospective	40	Breast	CTA
Jayaratne et al. 2010[18]	Case report	1	Craniofacial	3D imaging and modeling
Kim et al. 2012[10]	Cohort: prospective	71	Breast	CTA
Kubo et al. 2014[23]	Cohort: retrospective	21	Breast	Scales
Lange et al. 2017[8]	Cohort: retrospective	102	Breast	MRA
Minn et al. 2010[20]	Cohort: prospective	37	Breast	Ultrasound
Pribaz et al. 1994[16]	Cohort: prospective	19	Craniofacial	Material template
Rosson et al. 2011[9]	Cohort: prospective	15	Breast	CTA
Shimizu et al. 2016[12]	Cohort: prospective	3	Craniofacial	CT
Tanabe et al. 2005[13]	Case report	1	Breast	3D imaging and modeling
Tomita et al. 2015[15]	Cohort: prospective	11	Breast	3D imaging
Shamoun and Hartrampf 1996[21]	Case report	2	Breast	Scales
Ji et al. 2002[17]	Case report	1	Craniofacial	3D imaging and modeling
Kadam et al. 2013[19]	Cohort: retrospective	8	Craniofacial	Material template

MRA, Magnetic resonance angiography; CTA, computed tomography angiography; CT, computed tomography; 3D, three-dimensional

Table 2. Advantages, disadvantages and cost of various flap quantification methods

MRI	Advantages	◊ No ionizing radiation ◊ High quality images, particularly of soft tissue and bone (superior to CT and U/S) ◊ Possibility of including gadolinium for perforator artery mapping ◊ Existing software to design virtual 3D models from MRI data
	Disadvantages	◊ Restricted access ◊ Costly
	Cost*	◊ $1,400 CAD/ scan[31,32]
CT	Advantages	◊ Good quality images, allowing accurate estimation of flap volumes ◊ Allows perforator artery mapping with contrast ◊ Existing software to design virtual 3D models from CT scan data ◊ Easily accessible ◊ Cost-effective
	Disadvantages	◊ Exposure to ionizing radiation
	Cost*	◊ $550 CAD/ scan[33]
U/S	Advantages	◊ Portable ◊ Widely available

		◊ Cost-effective ◊ Good penetration of soft tissue
	Disadvantages	◊ Probes have a narrow field of view, increasing difficulty to assess volumes of large areas ◊ Operator dependent; requires skilled personnel
	Cost*	◊ $70 CAD/ scan[34]
3D Laser Scan	Advantages	◊ Accurate measurements of a structure's dimensions ◊ High quality analysis of surface anatomy ◊ Existing software to design virtual 3D models from laser scanner data ◊ Cost-effective ◊ Portable
	Disadvantages	◊ Inability to assess tissue and structures deeper than skin
	Cost*	◊ $20,000-100,000 US/ machine[35] ◊ minimal expense/ scan
Scales	Advantages	◊ Highly portable due to small size; can be brought into the operating room ◊ Cost-effective ◊ Easy to use; operator-independent
	Disadvantages	◊ Only measures tissue weight
	Cost*	◊ Minimal expense/ machine and use

∗ costs are variable between institutions and countries.

3.11-BRIDGING TEXT

The previous literature review focused on results of objective volumetric quantification of reconstructive flaps, a prominent aspect of plastic and reconstructive surgery. By analyzing and comparing the various described methods, we identified current limitations of widespread application. The information gathered above was essential for the technological development of the current and future prototypes. The preliminary results are promising, and we believe that three-dimensional representation and objective quantification is the future of reconstructive flap surgery. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility. The following literature review is similar, with a focus on liposuction, one of the most common procedures in cosmetic surgery. Surgeons also rely on subjective methods to judge liposuction results. The purpose of this final review was to analyze reported methods of monitoring liposuction results by objectively measuring subcutaneous adipose tissue. The review provides a summary of various techniques for quantification of liposuction results. Like the previous review, the following information was essential to the development of a standardized approach for our pilot project (see discussion, section 5). By analyzing and comparing the various described methods, we identified current limitations of widespread application. Moreover, validation of our prototype relies on liposuction aspirate measurement. The review below was therefore essential for the development of the methodology described in section 5. Finally, the review confirmed the novelty of our project.

4.1-Objective Quantification of Liposuction Results

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4.2-Abstract

Background: There currently exists no reliable gold standard for the objective outcome measurement following liposuction. The purpose of this systematic review was to summarize reported methods of monitoring liposuction results by objectively measuring subcutaneous adipose tissue.

Methods: A systematic literature search was performed to identify relevant articles that described techniques for objectively quantifying adipose tissue following traditional liposuction. The search included published articles in three electronic databases—Ovid MEDLINE, EMBASE, and PubMed.

Results: Subcutaneous adipose tissue was estimated using the following techniques: ultrasound, dual-energy X-ray absorptiometry, magnetic resonance imaging, computed tomography, and three-dimensional imaging volumetric analysis. Reported benefits of liposuction objective measurements included providing patients with a quantitative assessment of the liposuction results pre- and post-operatively, detecting significant changes in body fat deposits and following patterns of fat redistribution.

Conclusion: This review provides a summary of various techniques for quantification of liposuction results. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed, as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility. The preliminary results from this review are promising, and we believe that three-dimensional representation and objective quantification is the future of cosmetic surgery.

Keywords: Liposuction; adipose tissue; quantification; volume.

4.3-Introduction

Liposuction is the second most commonly performed cosmetic surgical procedure in the United States, second only to breast augmentation(1). In 2016, more than 230 000 liposuction procedures were performed in the US alone, amounting to $1.3 billion (USD)(1). This popularity is partly due to its ubiquitous application in plastic surgery and the reliability of its use(2). Despite the popularity of this procedure, very few surgeons objectively quantify liposuction results. Surgeons rely mainly on visual inspection through photographs, waist circumference (measuring tape), or through skin-pinch measurements (2-6). The aforementioned techniques may not accurately reflect surgical results as subcutaneous adipose tissue is composed of heterogeneous deposits(7). There currently exists no reliable gold standard to objectively measure changes following liposuction. The purpose of this systematic review was to summarize reported methods of monitoring liposuction results by objectively measuring subcutaneous adipose tissue.

4.4-Methods

A search of the Ovid MEDLINE, EMBASE, and PubMed databases was performed starting from database establishment to August 1st 2017. Different spellings and versions of the following key words were searched: [("volume" or "objective" or "quantification" or "measurement" or "mapping" or "representation" or "distribution") and ("adipose tissue" or "fat") and "liposuction"]. Citations were limited to human studies published in the English language. Studies were retained if they included objective measurement of adipose tissue following liposuction. Skin caliper and waist circumference measures were excluded. Cadaver studies, animal studies, case series (N<10), abstracts and review articles were excluded. Studies with combined abdominoplasty and liposuction, as well as studies that reported liposuction for non-cosmetic purposes (i.e. lipoedema, lipodystrophy, lipomatosis, lymphedema etc.) were also excluded. All non-invasive techniques for lipolysis and body contouring were also excluded. Studies were only included if the entirety of the adipose tissue treated was suctioned and available for potential measurement. Two independent reviewers assessed the eligibility of the studies using strict inclusion/exclusion criteria. Studies were selected based on the relevance of the title and/or abstract of retrieved records (Figure 1). The initial screen excluded studies with evidently irrelevant titles or abstracts. If content was unclear in the initial screen based on abstract review, a formal article review was undertaken. Additional studies were identified from an extensive manual Internet search and from the reference list of relevant articles. The systematic review followed the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement(8).

4.5-Results

A total of 1192 studies were identified and further narrowed to 82 potentially eligible studies after primary review. A total of 7 studies met the inclusion criteria and were included in this review. Objective measurement of subcutaneous adipose tissue (SAT) was measured using the following techniques: ultrasound(2, 9), dual-energy X-ray absorptiometry (DXA) (3, 10, 11), magnetic resonance imaging (MRI) (10), computed tomography(CT) (12) and three-dimensional imaging volumetric analysis(4) (Table 1).

Ultrasound

Ultrasound has been used in abundance to measure SAT. Due to its relative affordability, easy accessibility, radiation free and high-resolution studies, ultrasound is a powerful tool (2, 5, 7, 13-15). The accuracy of ultrasound-measured adipose tissue surpasses skin-fold calipers (21) and has proven to highly correlate with MRI(16-18) and CT(19, 20) . Ultrasound has been reliably used to quantify tumescent liposuction results (2,9). Fat thickness measurement using ultrasound has been described for the thighs, submental and abdominal regions. In addition to visual inspection, patients can also be provided with quantitative pre- and postoperative assessments of the liposuction results.

Although not included in the current review, *Toomey et al*.(21) and *Barton et al.*(5) studied the measurement of SAT using ultrasound. The authors observed a significant degree of SAT variation caused by pressure applied on the ultrasound probe (up to 37%) and proposed a protocol using a force gauge to maintain a fixed amount of pressure on the probe (below 1N) in order to minimize compression variability and fat distortion. The authors were able to demonstrate a higher correlation between total body fat percentage and ultrasonographic SAT using this protocol. *Barton et al.* subsequently validated the Toomey protocol and assessed its efficacy at measuring SAT reduction after non-surgical treatment. They obtained good reproducibility of SAT measurements (precision of ±0.558 mm). One of the challenges encountered was the identification of the deep fascial point (as a reference point for further measurements). This was proven to be more challenging than finding the right pressure to apply on the probe and likely accounted for a small variation in depth measurements. The authors concluded that when the transducer pressure remains below 1N, ultrasound can achieve constant and accurate results in clinically monitoring SAT reduction following non-surgical fat removal.

Overall, when transducer pressure is controlled, ultrasound can accurately quantify liposuction results in relatively small areas (e.g. submental region). When treating a large surface area (e.g. the abdomen), ultrasound carries the disadvantage of scanning multiple zones due to its relatively narrow field of view and to the heterogeneous deposits of adipose tissue.

Dual-energy X-ray absorptiometry (DXA)

DXA is tool used to measure body composition using differences in the attenuation of two X-rays as they penetrate tissue(3) and has been shown to provide accurate and objective visual improvement of body composition following liposuction (3,10,11). Pre- and post-operative DXA scans can be used to measure and compare total fat mass, total lean mass, total bone mineral mass and body weight. One advantage offered by this modality is the possibility of visualizing the entire body and body fat redistribution patterns. One study (10) demonstrated a significant reduction in body fat following liposuction at 6 weeks and at 6 months, but not at 1 year. Additionally, this imaging modality demonstrated remodeling at the hips and thighs and a preferential accumulation of fat in the abdominal region. The reduction in body fat percentage calculated by DXA correlates with skinfold caliper and circumference measurements (10). DXA is a relatively inexpensive, simple and efficient method of assessing liposuction results, using minimal radiation. More studies are needed to confirm its accuracy and reliability in measuring subcutaneous adipose tissue.

Magnetic Resonance Imaging (MRI)

The high quality and radiation-free images of soft tissues obtained using MRI make it a valuable modality to assess SAT(4, 16, 17). The cost, time requirements and limited availability of MRI may restrict its use(4, 16, 17). Currently, only one study has reported the use of MRI for objective quantification of liposuction results, more specifically to assess redistribution of subcutaneous and visceral adipose tissue following liposuction (10). By manually tracing the appropriate borders of muscle and fascia, subcutaneous adipose tissue was distinguished from visceral adipose tissue. Although MRI appears to be accurate and safe for adipose tissue monitoring, restricted access to this costly imaging modality limits its widespread applicability.

Computed Tomography (CT)

Similar to MRI, CT scans are useful for the simultaneous visualization of subcutaneous and visceral adipose tissues. Currently, only one study has reported the use of CT for objective quantification of liposuction results, more specifically to measure the effect of liposuction and physical activity on visceral fat (12). The authors found CT-calculated adipose tissue volume to be accurate when compared with aspirated fat volume during liposuction. Despite the availability and accuracy of CT in measuring subcutaneous fat volume, exposure to ionizing radiation remains the main disadvantage (4, 16, 17, 22). CT should be considered when visualization of deeper tissue is required.

Three-dimensional (3D) digital photographic imaging system

Three-dimensional imaging techniques are frequently used in body contouring to assess surface anatomy. Two or more digital cameras rotate around an object and simultaneously take pictures at different angles(4). An algorithm subsequently uses the data to create a 3D image(4). The reliability and accuracy of 3D imaging in detecting changes in 3D shape and volume have been validated(6, 23-25). The low cost and portability of the scanner is unique compared to other imaging techniques such as MRI and CT. Although radiographs and CTs provide pertinent tissue information, their ability to analyze surface anatomy is limited compared to 3D photogrammetry. Three-dimensional digital photographs have been used to follow abdominal volume reduction following liposuction, with high intra-observer reliability (intraclass correlation = 0.985-0.998)(4). One study compared the SAT volume measured by 3D imaging with the volume of aspirated fat (after gravity separation), and found no correlation between the two measurements. The discrepancies between 3D-imaging and aspirated fat volume was attributed to varying individual response. Early results of 3D digital photographs are promising. More studies are needed to assess reliability in objectively quantifying changes in abdominal volume after liposuction.

4.6-Limitations

The focus of the systematic review was traditional surgical liposuction. Non-invasive techniques were not included. The rational for the above exclusion criteria was to compare estimated SAT volume with actual aspirated volume. Only three studies(4, 10, 12) however compared estimated SAT volume with aspirated fat or with a different imaging modality. Comparison between estimated and actual SAT is crucial to validate the accuracy of the various methods described above. Moreover, many studies were missing inter- and intra-observer reliability data which are essential to support study conclusions and reproducibility.

4.7-Conclusion

This systematic review provides a summary of various techniques for adipose tissue quantification of liposuction results. Objective measurement of liposuction results has been described using a multitude of techniques. Due to paucity of studies, it is difficult to establish superiority of one technique over another. Individualized decisions should be made with consideration of the potential risks and benefits of the various imaging modalities described. More studies are needed to study the clinical relevancy and impact of the various imaging modalities reviewed as well as to develop automated volumetric measurement technology with improved accuracy, efficacy and reproducibility. The preliminary results from this review are promising, and we believe that three-dimensional representation and objective quantification is the future of cosmetic surgery.

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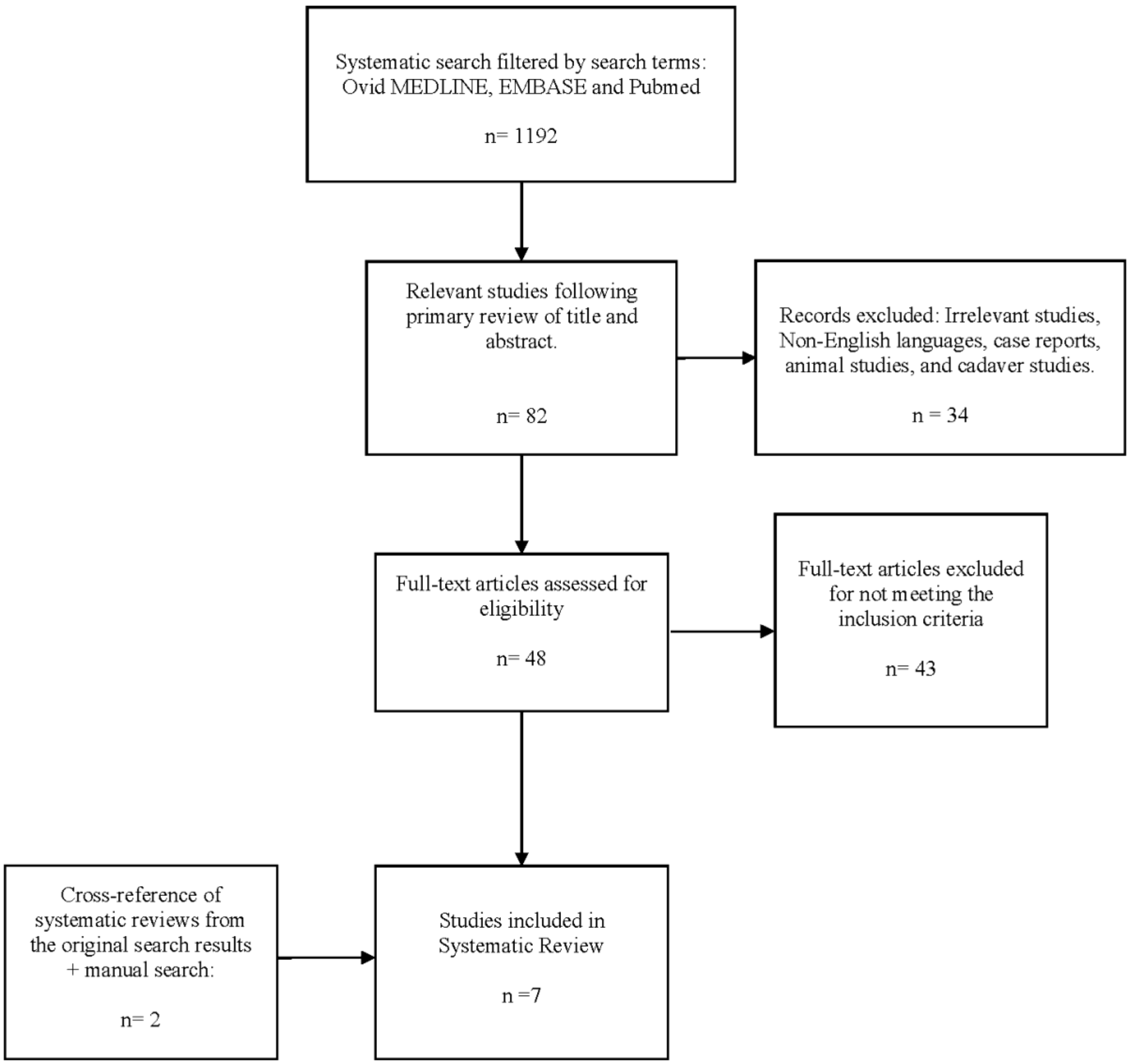
4.9-LIST OF FIGURES

Figure 1. Flow diagram of systematic review study selection and eligibility



4.10-LIST OF TABLES

Table 1. Summary of studies that performed objective measurement of adipose tissue following liposuction.

Study	Design	N (total)	Liposuction Area	Liposuction details	Method of SAT quantification
Bilgili et al. 2004	Cross-sectional study	14	submental (3), abdomen (10), and thighs (11)	Tumescent Technique	Ultrasound
Cohen et al. 2012	Cross-sectional study	23	area defined as +60 mm to −80 mm, relative to the umbilicus	Suction-assisted tumescent liposuction	3D imaging
Hernandez et al. 2011	RCT	14	thighs, hips, and lower abdomen below the umbilical line	Suction-assisted, tumescent technique (<5000ml)	DXA and MRI
Shi et al. 2009	Cross-sectional study	28	Abdomen	N/A	DXA
Valizadeh et al. 2016	RCT	20	Submental area	Tumescent technique. The procedure was	Ultrasound

				performed using a 1–3-mm cannula with a spatula-shaped tip	
Benatti et al. 2012	RCT	36	Pelvis, thigh, abdomen	Tumescent abdominal liposuction (<4L)	CT
Davis et al. 2006	Cross-sectional study	15	Abdomen	Tumescent Technique. 1-3mm cannula	DXA

N/A, not available; mm, millimeters; ml, milliliters; 3D, three-dimensional; DXA, dual-energy X-ray absorptiometry; CT, computed tomography; MRI, magnetic resonance imaging

5-DISCUSSION AND FUTURE DIRECTIONS

There has been recent interest in the quantification of soft tissues in the field of plastic and reconstructive surgery. A consistent and reproducible technique for SAT measurement using ultrasound was lacking in the literature. The objective of the first phase of the current project was to gather evidence-based information regarding ultrasound technique and its application in the field of plastic and reconstructive surgery (liposuction and flap reconstruction). The information gathered above was crucial to define the current limitations in soft tissue volumetric analysis and to guide the decision-making for the ongoing pilot project in our laboratory.

The first phase of the project, presented in this thesis, was also essential for the technological development of the current and future prototypes. The technological design heavily relies on the details gathered above. The next phase of this project (phase two or pilot project) focuses on ergonomic and efficient integration of ultrasound, minimizing the impact on operative length and operating room efficiency. The ultimate goal is to interpret and segment continuous intra-operative images produced by ultrasound. Sensors will be placed on the ultrasound probe to detect its angulation, position in space, and the pressure applied on the soft tissues. By simply scanning an area of interest, the software will virtually reconstruct the area of interest and generate volumetric measurements. By replacing subjective techniques with ultrasound, we hope to improve symmetry, increase patient satisfaction, and decrease revision rates. A prototype for volumetric measurement of soft tissue was designed by our laboratory using the software Rhinocerus 5.0 spatial reconstruction software was used (McNeel North America, Seattle, WA). The validity of the prototype has yet to be confirmed (awaiting approval from the institutional Research Ethics Board), however, using the information collected by our analysis, the following methodology will be applied for both abdominoplasty and liposuction validation.

5.1 - Abdominoplasty

General Overview

After approval from the Research Ethics Board, eligible patients will be consented in clinic. Patients to be included in this study are all adult patients planning to undergo abdominoplasty. Pre-operative estimation of the abdominoplasty tissue volume will be performed based on the surgeon's pre-operative marking (Figure 1). Intra-operatively, the discarded abdominoplasty tissue volume will be estimated again using ultrasound. The discarded tissue will also be weighed on a scale and submerged in water for volume estimation. Estimated volumes by ultrasound and by water displacement/scale will be compared by t-test analysis. Statistical significance will be set at a P value of 0.05. All analysis will be carried out using the statistical program SPSS.

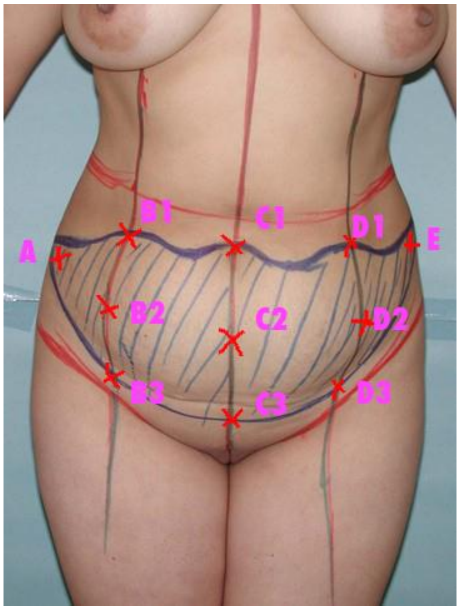


Figure 1. Eleven landmarks for SAT measurement based on the surgeon's intra-operative marking. The 11 landmarks are the following: superior midline (C1), center midline (C2), inferior midline (C3), superior midclavicular line (B1 and D1), center midclavicular line (B2 and D2), inferior midclavicular line (B3 and D3), and the lateral-most aspects of the planned abdominoplasty (A and E).

<u>Technical details</u>

SAT thickness will be measured using a Sonostar wireless mini ultrasound machine with a linear probe (Sonostar Technologies Co., Limited). Transducer frequency will be set to 12 MHz. Thickness will be defined as the distance between the internal skin layer and the fascia overlying the abdominal muscles (Figure 2). The ultrasound probe will be held at 90 degrees with the skin surface and attention will be paid not to exert undue pressure on the tissue (no visible compression). All patients will be fasting for at least 8 hours. All measurements will be taken at end-expiration in the supine position.

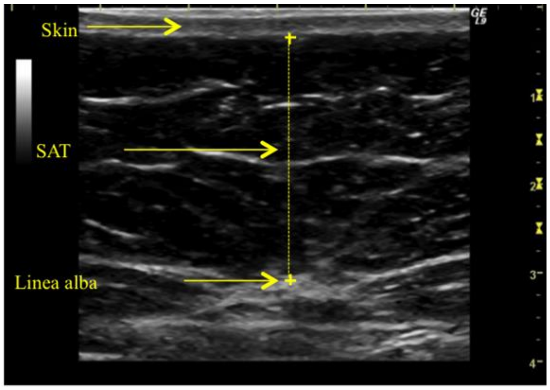


Figure 2. Example of ultrasonic thickness measurement in the midline. Thickness is measured from the internal skin layer to the linea alba of rectus abdominis muscle.

Pre-operative measurement

Abdominoplasty thickness will be measured at 11 predetermined landmarks, represented in Figure 1. Thickness will be measured along: 1) the midline (center and the superior/inferior edges), 2) midclavicular lines (the superior/inferior edges and the center), and 3) the lateral-most aspects of the planned abdominoplasty. Thickness data points will be used for three-dimensional representation of the planned abdominoplasty and volume estimation of the SAT (Figure 3). Rhinocerus 5.0 spatial reconstruction software will be used for volumetric representation and estimation (McNeel North America, Seattle, WA).

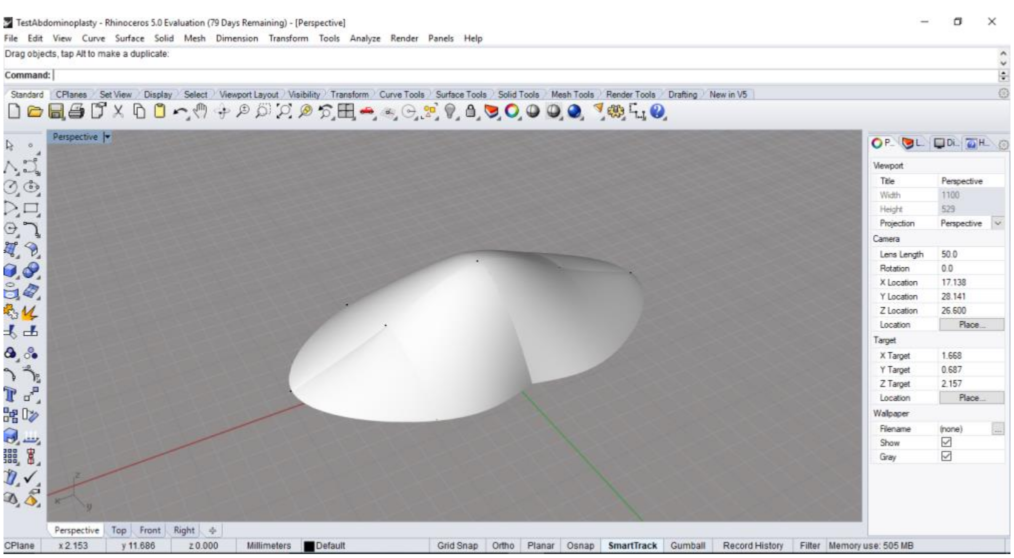


Figure 3. Example of three-dimensional representation of abdominoplasty adipocutaneous tissue using Rhino.

Intra-operative validation

After excision, the abdominoplasty tissue will be weighed on a scale and subsequently placed in a predetermined volume of normal saline. Weight of the discarded tissue (in grams) will be used to estimate volume assuming a density of $1 g/cm^3$ (adipose tissue, blood, skin). A density of $1 g/cm^3$ is commonly used in the literature (1-6).

Volume of tissue (cm^3) = Weight (g) / Density (g/cm^3)

Volume will also be estimated using the water displacement technique (Archimedes' principle). Finally, thickness of the discarded abdominoplasty tissue will be measured again at the same predetermined landmarks (Figure 1). This information will once again be used to estimate flap volume.

5.2 - Liposuction

General Overview

After approval from the Research Ethics Board, eligible patients will be consented in clinic. Patients included in this study will be adult patients planning to undergo abdominal liposuction for cosmetic purposes. An area of 8cm x 8cm will be marked in the right lower quadrant (RLQ). Pre-operative estimation of the marked volume will be performed using ultrasound. Intra-operatively, volume of aspirated adipose tissue will be measured. Estimated volumes by ultrasound and by gravity separation will be compared by t-test analysis. Statistical significance will be set at a P value of 0.05. All analysis will be carried out using the statistical program SPSS.

Technical details

SAT thickness will be measured using a Sonostar wireless mini ultrasound machine with a linear probe (Sonostar Technologies Co., Limited). Transducer frequency will be set at 12 MHz. Thickness will be defined as the distance between the internal skin layer and linea alba of rectus abdominis muscle. The ultrasound probe will be held at 90 degrees with the skin surface and attention will be paid not to exert undue pressure on the tissue (no visible compression). All patients will be fasting for at least 8 hours. All measurements will be taken in the supine position at end-expiration.

Pre-operative measurement

SAT thickness will be measured at 9 predetermined landmarks within the 8cm x 8cm marking, represented in Figure 1. Thickness will be measured at the following landmarks: 1) center of the square 2) corners 3) halfway between each corner and the midpoint. Thickness data points will be used for three-dimensional representation of the marked area and volume estimation of the SAT (Figure 2). Rhinocerus 5.0 spatial reconstruction software will be used (McNeel North America, Seattle, WA).

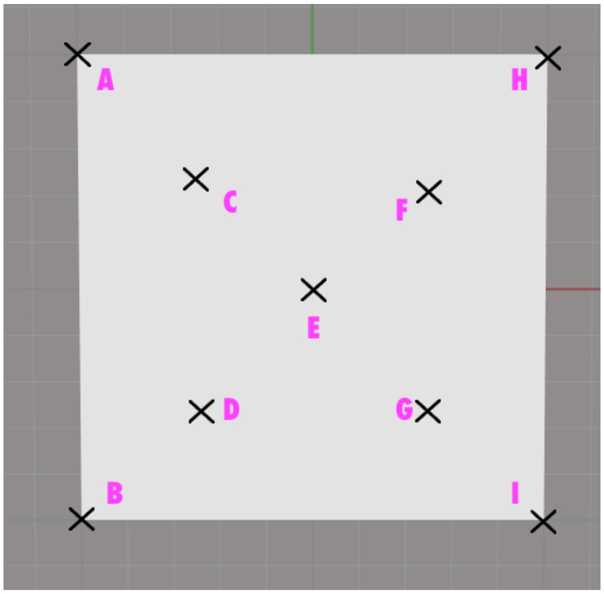


Figure 1. Landmarks of abdominal SAT thickness measurement based on an 8cmx8cm in the right lower quadrant. The 9 landmarks are the following: centre of the square (E), corners(A,B,H,I), and halfway between each corner and the center (C,D,F,G).

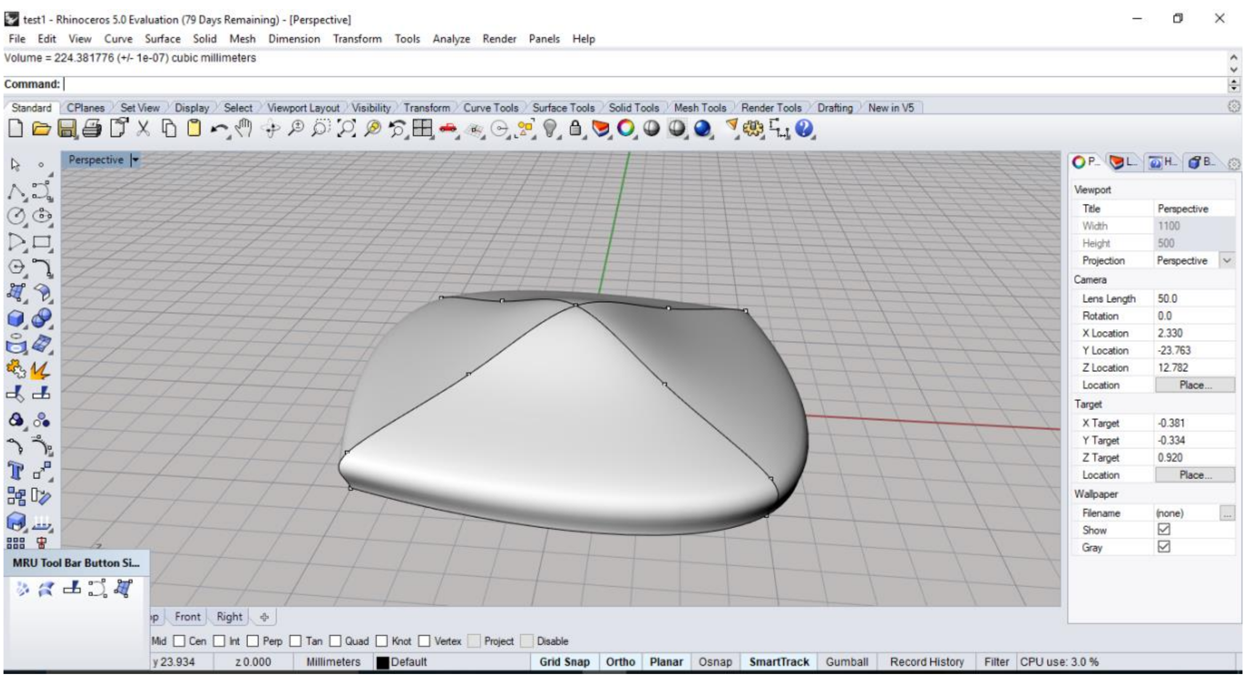


Figure 2. Example of three-dimensional representation of the 8cmx8cm square of adipose tissue using Rhino.

Intra-operative measurement

Aspiration of the marked square in the RLQ will be performed by liposuction. Attention will be payed to remain within the limits of the pre-operative marking. Aspirated adipose tissue volume will be measured in the canister after 10 mins of gravity separation. Thickness of the RLQ marking will be measured again post-liposuction at the same predetermined landmarks (Figure 1). The volume difference between pre- and post-liposuction measurements will be compared to the aspirated adipose tissue volume (validation process).

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CONCLUSION

The information gathered above was crucial to define the current limitations in soft tissue volumetric analysis and to guide the decision-making for the ongoing pilot project in our laboratory. The two areas of interest in this project were liposuction and adipocutaneous flap reconstruction. The work presented in this thesis confirms the necessity of a technique for adipose tissue quantification for both these procedures. CT and MRI are excellent imaging modalities for research purposes, however, cost and limited access prevent their widespread use for clinical purposes. Moreover, intra-operative and real-time imaging is not possible with these modalities. Ultrasound is the most promising avenue moving forward. A handheld cordless probe is inexpensive and can provide adequate images in a timely manner. The development of speedy and accurate interpretation of SAT volume is necessary for its widespread use. Using the information presented in this thesis, we hope to validate the first tool to objectively quantify fat volume using ultrasound along with computer-assisted three-dimensional and volumetric representation. Cost, accessibility, and portability of ultrasound renders this imaging modality superior to others.