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Open Surgical and Needle Biopsy to Study Abdominal Subcutaneous Adipose Tissue in Obesity

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Abstract

The importance and the role of adipose tissues are now largely expanded not only because the very high occurrence of obesity but also because the emerging view that adipose tissue could be a reservoir of therapeutic cells. Adipose tissue biopsies offer tissue samples that, upon analysis, may provide interesting and useful information about mechanisms relating to metabolism and disease. A critical examination of the adipose tissue features according to their location shows that sampling is not as easy as previously thought and needs special attention to heterogeneity and differences. We discussed here these different points and give precise protocols to sample the different adipose tissues. Adipose tissue biopsies offer tissue samples that, upon analysis, may provide insightful overviews of mechanisms relating to metabolism and disease.

Keywords: Adipose tissue biopsy; Severe obesity; Bergström side-cutting needle; Aspiration; Adipose samples.

Introduction

Adipose tissue (AT) is no longer considered to be simply a passive lipid reservoir but rather an endocrine organ capable of secreting factors that profoundly influence processes such as feeding behavior, energy flux, and immunoinflammation [1]. Moreover, adipose tissue displays enormous plasticity and is capable of changing its size, phenotype and metabolic functions [2].

The classical abdominal adipose tissue (AT) compartmentalization into subcutaneous adipose tissue (SCAT) and visceral adipose tissue (VAT) has been widely studied in relation to obesity-related complications. The anatomical distinction of SCAT compartments into superficial subcutaneous adipose tissue (sSCAT) and deep subcutaneous adipose tissue (dSCAT), divided by Scarpa's fascia, is well documented in literature. A few studies have shown that dSCAT is strongly related to insuline resistance (IR) in a manner nearly identical to that of VAT [3].

The main white adipose tissues (WATs) are abdominal subcutaneous adipose tissue (SCAT) and visceral adipose tissue (VAT). VAT surrounds the inner organs and can be divided in omental, mesenteric, retroperitoneal (surrounding the kidney), gonadal (attached to the uterus and ovaries in females and epididymis and testis in men), and pericardial. The gluteofemoral adipose tissue (g) is the SCAT located to the lower-body parts and is measured by hip, thigh, and leg circumference. WAT can also be found intramuscularly. The adipose tissue depots that have been linked to risk of developing obesity-related diseases are the omental and mesenteric [4].

Commonly obesity is characterized by adipocyte hypertrophy, followed by increased angiogenesis. There is a chronic state of low-grade inflammation with progressive immune cell infiltration, extracellular matrix overproduction into obese adipose tissue. Production of proinflammatory adipocytokines is increased during the progression of chronic inflammation [5].

The subcutaneous fat is readily accessible to study and has been shown to be metabolically correlated to indices of insulin resistance. Obtaining adipose tissue samples is paramount to the understanding of the pathophysiology of human obesity and its analysis may provide insightful overviews of mechanisms relating to metabolism and disease [1].

Abdominal subcutaneous adipose tissue (SCAT) biopsy procedures

Open (surgical) SCAT biopsies: Surgical subcutaneous fat biopsies can offer tissue samples that may provide a more comprehensive overview of the complexities of biological indices in white adipose tissue. Subcutaneous superficial AT samples are obtained by surgical biopsy from the periumbilical area, under local anesthesia (1% xylocaine) [1,6,7]. First, the skin is cleaned and covered with special surgical drapes. An incision of <5 mm is made with a plain scalpel to access the subcutaneous AT. The surgeon held the tissue with atraumatic forceps and cut the tissue pieces with scissors. About 2-3 cm^3 (corresponding to about 3-5 g) AT could be removed. The skin incision is then closed with absorbable suture material [8].

Side effects includes local discomfort, infections, bleeding or skin lesions in the tissue after diathermy.

Punch biopsy: The biopsy site is prepared with three betadine scrubs and covered with a fenestrated sterile drape [9]. The dermis at the biopsy site (at the right anterior axillary line at the level of the umbilicus) is infiltrated with 0.5 ml of 1% lidocaine followed by injection of 4 mL in the very superficial layers of adipose tissue immediately below the skin (no more than 1 cm deep). Punch biopsy is performed using a circular blade (3.0 mm in diameter) attached to a pencil-like handle. The instrument is rotated down through the epidermis and dermis and into the s.c. fat. Punch biopsy yields a cylindrical core of tissue that requires gentle handling (usually with a needle) to prevent a crush artefactat the pathological evaluation. The biopsy site is closed with a single absorbable suture. The procedure yield about 150 mg of intact SCAT.

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Precautions must be taken in patients who have a history of bleeding disorders and those that are on medications that aect hemostasis. The punch biopsy itself takes roughly 15 minutes and does not require any hospitalization. A patient may return to normal daily life immediately following a punch biopsy (Tables I and II).

Needle SCAT biopsies

Needle muscle biopsy sampling offers a less invasive, more rapid alternative to conventional open SCAT biopsies for for research purposes. The cellular material could be obtained through needle puncture, either relying on the forward motion and the intrinsic capillary action of an FNA or by using spring-loaded physical cutting action of a tissue core by CNB [10]. The external diameter of the needle is described by the respective needle gauge, with a higher gauge corresponding to a smaller needle outer diameter. The needle gauge and thickness of the needle wall dictates the maximal diameter of any tissue fragments obtained by FNA or CNB, although appreciable microscopic tissue architecture can be obtained even with high gauge needles.

Fine needle aspiration (FNA): FNA biopsy is a reliable, cost-effective procedure that may be performed anywhere (bedside, outpatient clinic, remote setting). The risk of a significant complication is minimal, and although such incidents have been reported, the chances of such an occurrence may be equated to the risk incurred when undergoing simple venipuncture. As with venipuncture, local anesthetic is generally not required [11].

The technique involves application of negative pressure during the procedure, typically with the use of a syringe (10-20 mL) placed in a syringe holder (aspiration gun/handle). When using an aspiration gun or handle, one must remember to pull the plunger back only after the needle has been placed into the lesion; the plunger should remain pulled while rapid, short strokes are made. More important,

Table I. Techniques to study Subcutaneous Adipose Tissue (SCAT)

Procedure	Open SCAT biopsy	CNB	FNA
Preparation:	8 h fast	8 h fast	8 h fast
Setting	Bedside procedure	Bedside procedure	Can be performed anywhere
Anesthesia	Local anesthesia	Local anesthesia	No anesthesia
Location	Abdominal region: periumbilicus (5 cm from the umbilicus)		
Procedure	Incision: Open biopsy: 5-mm skin incision. The tissue is held with atraumatic forceps and cut the tissue pieces with scissors. The procedures last about 40 min. Punch biopsy: circular blade (3.0 mm in diameter). The procedure last about 15 min. The skin incision is then closed with absorbable suture material.	Incision: 5-mm skin incision. The needle biopsy is performed using a 20-50-mL plastic syringe (filled with saline) attached to a 14-gauge aspiration needle (or modified Bergström 6 mm). The needle is passed through the sc fat several times while applying negative pressure. The procedure last about 20 min.	No incision. The needle biopsy is performed using a 20-50-mL plastic syringe (filled with saline) attached to a 16-gauge aspiration needle. The aspiration procedure takes only 5-8 min.
Safety	Local discomfort, infection, blood collection under the skin	Well tolerated, low incidence of painful hematomas	Cause little pain or after effects.
Tests	Adipocyte size and number Immunohistochemistry Tissue culture RNA extraction FISH studies	Tissue culture RNA extraction Flow cytometer FISH studies	RNA extraction Flow cytometer FISH studies
Tissue yield	3-5 g (open biopsy)	1-2 g	100 - 500 mg

Table II: Advantages and disadvantages of different biopsy techniques used to study SubCutaneous Adipose Tissue (SCAT)

	Advantages	Disadvantages
Open SCAT Biopsy	Succes rate close to 100% Yield: adequate sample for any analysis accessible for sampling quick (40 min), larger samples.	Surgical procedure, most invasive than needle biopsy, Performed under local anesthesia in a hospital or outpatient clinic Scarring Additional risk of conscious sedation Expensive side effects such as infection or blood collection under the skin
CNB	Provides larger intact tissue fragments than FNA with preserved architecture Validated tissue for ancillary studies or immunohistochemistry Higher diagnostic yield for fibrotic tissue lesions For most lesions, has higher sensitivity, specificity, and diagnostic accuracy measures	Success rate 95% Requires the presence/expertise of an interventionalist. More expensive (equipment, requires image guidance) Higher complication rate (i.e. hemorrhage) Requires use of anesthesia or local anesthetic
FNA	Can be performed by a trained physician Rapid procedure (few minutes) Usually does not require anesthetic or anesthesia (not painful) Less traumatic (low risk of bleeding) Can be performed anywhere (bedside, outpatient clinic, remote setting) Lower complication rate Less expensive (needle and other processing equipment) Collection of fresh, intact, viable cells Entire nucleus present for FISH studies Excellent collection method for flow cytometry.	Success rate 95% Limited tissue architecture Lower yield for fibrotic lesions Cytologic specimen processing may pose validation challenges for downstream testing (immunohistochemistry, molecular testing) For most lesions, has lower sensitivity, specificity, and diagnostic accuracy measures.

it is imperative that suction be released before the needle is removed, because continued negative pressure results in suction of the material back into the syringe preventing preparation of direct smears.

Superficial subcutaneous AT samples of about 1-2 cm^3 (corresponding to bout 1-2 g) are obtained from the periumbilical area [1]. A region 5 cm lateral from the umbilicus (either to the left or right side of the abdomen) is sterilized. A needle 16 G, 40 mm, regular bevel is adapted to a 20 mL syringe and the piston compressed. Approximately one-third of the length of the needle is inserted into the subcutaneous fat, and the needle piston is released maximally until it is locked by a stopper, thereby creating a vacuum. Tissue resistance is created by the physician gripping the abdominal wall with one hand while the other hand rotated the needle throughout the tissue in an up-down motion. Once the tissue is aspirated by the syringe, the needle is withdrawn, and the piston is removed. The aspiration procedure takes only 5-8 min, causes little pain or after effects, and does not require sutures or entail a return visit by the patient [12-14].

Core-Needle Biobsy (CBN): CNB is generally performed with a larger-gauge needle, ranging from 13-gauge to 14-gauge (an outer diameter of 2.4 to 2.1 mm) [15]. The other two common needle biopsy instruments used are the Bergstrom needle [16] and the modified Bergstrom needle also known as the UCH biopsy needle. The most important modification of the UCH is the addition of a Luer lock attachment to the inner cannula to allow the application of suction during the procedure [17]. Suction applied during the procedure results in consistently larger samples. Superficial subcutaneous AT samples obtained are of about 1.5 grams, which ranged from 5-10 times greater than thosed obtained using a punch biopsy method [15,16,18,19,20].

The biopsy site is prepared with three betadine scrubs and covered with a fenestrated sterile drape. The dermis at the biopsy site (at the right anterior axillary line at the level of the umbilicus) is infiltrated with 0.5 cc of 1% lidocaine followed by injection of 4 cc in the very superficial layers of adipose tissue immediately below the skin (no more than ½- inch deep). A 6-7 mm incision is made in the skin and a 6-mm Bergström side-cutting needle is introduced approximately 1-1.5 inches through the incision into the deeper SCAT. After the needle is angled obliquely, an assistant applied brief suction from a 60 cc irrigation syringe attached to the Bergström needle with gastrointestinal irrigation tubing (Kendall; no. 1; 16 Fr/Ch × 48 inches). Four cuts are made with the cutting trochar as the needle was further advanced and rotated 90 degrees. The procedure is repeated with a second pass to generate eight total cuts. Ultrasound (US) guidance could be used to ensure sampling from deep SCAT below the Scarpa's fascia, which is often 2-3 inches below the skin in obese participants. Some patients could experienced minor discomfort when the needle was advanced through Scarpa's fascia. To rectify the discomfort, 1% lidocaine is administrated through a spinal needle guided by US into the superficial layer of Scarpa's fascia.

The time period from prepping the biopsy site to tissue processing averaged about 20 minutes.

After the biopsy procedure, manual compression is applied for 10 minutes to prevent bleeding. Following compression, a single nylon suture is used to close the wound. Bacitracin ointment is applied to the wound, which is then covered with dressing. The suture will be removed 5-7 days following the biopsy (Tables I and II).

Conclusions

The abdominal fat biopsy procedure using a Bergström side-cutting biopsy needle and yielding an average of 1.5 grams of intact SCAT, could be a safely and consitenetly method to obtain sample adipose tissue from the dSAT compartment by a percutaneous bedside approach. This is in contrast to other procedures whereby SCAT samples are obtained by forceful extraction with tissue forceps, punch biopsy instrument or continued manual suction using smaller gauge cutting needles.

Subcutaneous adipose tissue biopsies from normal weight or overweight individuals provide adequate tissue morfometry, immunohistochemistry, flow cytometry, tissue culture, RNA extraction, gene expression analysis, FISH studies, and other possible uses.

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Conflict of interets

Authors have no conflict of interest to disclose.

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