Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–13, 2016

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2016.06.016

● *Original Contribution*

ADIPOSCAN: A NOVEL TRANSIENT ELASTOGRAPHY-BASED TOOL USED TO NON-INVASIVELY ASSESS SUBCUTANEOUS ADIPOSE TISSUE SHEAR WAVE SPEED IN OBESITY

Magali Sasso,* Yuejun Liu,*† Judith Aron-Wisnewsky,† Jean-Luc Bouillot,‡ Mériem Abdennour,*† Michel Clet,* Laurent Sandrin,* Gilles le Naour,§ Pierre Bedossa,¶ Joan Tordjman,† Karine Clément,† and Véronique Miette*

*R&D Department, Echosens, Paris, France; †Institute of Cardiometabolism and Nutrition, ICAN, UMR INSERM/UPMC 1166, Nutrition Department, Pitié-Salpêtrière Hospital, Paris, France; ‡Department of General, Digestive and Metabolic Surgery, Assistance Publique-Hôpitaux de Paris, Ambroise Paré Teaching Hospital, Boulogne, France; §Department of Anatomic Pathology, Assistance Publique-Hôpitaux de Paris, Pitié-Salpêtrière Hospital, Paris, France; and ¶Department of Anatomic Pathology, Assistance Publique-Hôpitaux de Paris, Beaujon Hospital, Clichy, France

(*Received* 8 *December* 2015; *revised* 3 *June* 2016; *in final form* 8 *June* 2016)

Abstract—We describe a novel device called the AdipoScan that was adapted from the FibroScan to specifically assess shear wave speed (SWS) in human abdominal subcutaneous adipose tissue (scAT). Measurement reproducibility was assessed on tissue-mimicking phantoms with and without repositioning, with resultant coefficients of variation of 1% and 0%, respectively, as well as *in vivo* (14% and 7%, respectively). The applicability of the AdipoScan was tested on 19 non-obese volunteers, and a scAT thickness >2 cm was found to be mandatory to perform a valid measurement. Abdominal scAT SWS was assessed in 73 severely obese subjects, all candidates for bariatric surgery. Subcutaneous AT SWS was positively associated with scAT fibrosis and obesity-related co-morbidities such as hypertension, glycemic status, dyslipidemia and liver dysfunction. These results suggest that the AdipoScan could be a useful non-invasive tool to evaluate scAT fibrosis and metabolic complications in obesity. Further investigation is required to evaluate the relevance of using the AdipoScan to predict patient weight trajectories and metabolic outcomes after bariatric surgery. (E-mail: magali.sasso@echosens.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Abdominal subcutaneous adipose tissue, Transient elastography, Shear wave speed, AdipoScan, Obesity, Bariatric surgery.**

INTRODUCTION

Obesity (*i.e.*, body mass index [BMI] ≥30 kg/m^2) and its related complications, such as type 2 diabetes, dyslipidemia, non-alcoholic fatty liver and cardiovascular diseases, as well as some cancers (Bray 2004; Ogden et al. 2007), are major public health concerns (Campos et al. 2006; Ng et al. 2014). According to the World Health Organization (WHO), obesity causes 2.8 million deaths each year, and the worldwide prevalence of obesity has more than doubled since 1980. In 2014, more than 13% of the world's population was obese, and in wealthy countries, obesity affects as many as one in four people (WHO 2015). By 2030, predictions suggest that 65 million adults in the United States, and 11 million in the United Kingdom, will be obese (Kelly et al. 2008). Severe obesity (*i.e.*, BMI ≥35 kg/m^2) has also rapidly progressed in both developed and emerging countries (Finkelstein et al. 2012).

Obesity is clinically defined as an increased accumulation of adipose tissue with health consequences. It is a complex and heterogeneous disease in which a range of different organ dysfunctions exist. Adipose tissue, initially considered as a "passive" reservoir for energy storage, is actually recognized as an active endocrine organ that secretes a myriad of hormones (Kershaw and Flier 2004). The secretion of these hormones is

Address correspondence to: Magali Sasso, 30 place d'Italie, 75013 Paris, France. E-mail: magali.sasso@echosens.com

Conflict of interest disclosure: M.S., L.S. and V.M. are Echosens employees. Y.L. and M.A. received support from Echosens for the duration of their Ph.D. programs. All other authors declare no conflicts of interest.

dysregulated in obesity. Morphologic anomalies are also observed in obese adipose tissue, which becomes pathologic during obesity development (Bluher 2013). Subcutaneous adipose tissue (scAT) in obese people undergoes major pathologic alterations such as adipocyte hypertrophy, inflammation and fibrosis, which may affect tissue hardness (Sun et al. 2013).

Today, the only treatment leading to a major and sustained long-term weight loss and improvements in comorbidities, is bariatric surgery, which is currently indicated only for severe obesity (Fruhbeck 2015; Sjostrom 2013; Sjostrom et al. 1999). Patient eligibility for bariatric surgery is currently determined by their BMI (BMI $\geq$40 kg/m^2 or BMI $\geq$35 kg/m^2 with at least one obesity-related comorbidity). However, it is now understood that candidacy for bariatric surgery based solely on patient BMI is inappropriate; moreover, there is huge inter-individual variability in bariatric surgery outcomes (Fruhbeck 2015). Thus, to improve patient selection for surgery based on clinical outcomes, obese patients absolutely require refined stratification with alternate parameters, that is, a "beyond BMI" concept (Fruhbeck 2015).

Subcutaneous AT fibrosis is a hallmark of pathological alteration that occurs during the development of obesity. It has been found that this fibrosis is related to severe metabolic impairment and impaired weight loss after bariatric surgery (Abdennour et al. 2014; Divoux et al. 2010). Subcutaneous AT morphology and fibrosis can be assessed in clinical practice via surgical biopsies (Mutch et al. 2009), scAT volume can be assessed by CT scan and thickness can be assessed with ultrasound (US) (Wajchenberg 2000). These procedures are not routinely used in the clinic because they are radioactive, invasive and painful and/or can cause bleeding, hematoma and scarring. Thus, these procedures cannot easily be repeated. Currently, there are no non-invasive techniques in use that simply characterize scAT properties. Thus, elastography techniques could be used in this context.

Ultrasound-based shear wave elastography has become a common method for non-invasive characterization of the properties of soft biological tissues (Shiina et al. 2015), either for research purposes in heterogeneous organs such as intervertebral discs (Vergari et al. 2014) and breast (Feldmann et al. 2015) or in clinical routine for evaluating the thyroid gland (Cosgrove et al. 2013), breast (Barr et al. 2015) or liver (Ferraioli et al. 2015). Transient elastography (TE) with the FibroScan (Sandrin et al. 2003) is the technique most commonly used to assess liver fibrosis in clinical practice (Cosgrove et al. 2013; Ferraioli et al. 2015).

Here, we describe the development of a novel device called the AdipoScan to non-invasively characterize scAT properties based on TE principles, and more specifically, we examine its ability to quantify scAT fibrosis. To date, the characteristics of this new device, such as the adaptation of TE technology to adipose tissue, reproducibility and *in vivo* applicability, have never been described in detail.

Our objectives were to (i) describe this new AdipoScan device and assess its repeatability on tissue-mimicking phantoms and reproducibility *in vivo*, (ii) illustrate its *in vivo* applicability and, (iii) search for potential relationships between adipose tissue fibrosis and bioclinical parameters in severe obesity as a first step toward patient stratification.

METHODS

AdipoScan: A new tool for characterization of abdominal subcutaneous adipose tissue

Transient elastography has been successfully used in the FibroScan device to assess liver tissue fibrosis (Sandrin et al. 2003). FibroScan technology is also referred to as vibration-controlled transient elastography. Briefly, a single-element US transducer is mounted on the axis of an electrodynamic actuator (vibrator). Low-frequency impulses (50-Hz center frequency for FibroScan) are generated by the vibrator and transmitted to the tissue *via* the ultrasound transducer, thereby inducing an elastic shear wave that propagates through the tissues. In parallel, pulse-echo US acquisitions are made to measure tissue displacement induced during propagation of the shear wave. Shear wave speed (SWS) is then deduced from the shear wave propagation map.

The AdipoScan was developed by Echosens (Paris, France) using the same principle as the FibroScan, but specifically adapted for evaluating scAT SWSs. A dedicated probe was specifically designed to be light enough to minimize initial static forces, which might compress tissues and modify scAT viscoelastic properties. The probe also had to be small enough to enable easy attachment to patient skin, without needing to be held in place by the operator (see Fig. 1) and without significantly compressing the tissues.

The probe is composed of a flat electrodynamic actuator joined together with a 9-mm-diameter flat US transducer with a 3.5-MHz center frequency. Figure 2 is a schematic drawing of the device. The system is embedded in a shell composed of a durable component surrounding the electrodynamic actuator (see Fig. 2) and three soft strips that allow the probe to be adapted and adhere to the patient's morphology via surgical adhesive tape, as illustrated in Figure 1. The surgical tape ensures that the device can stand on its own on the patient's abdomen.

The mechanical vibration center frequency is set to 70 Hz, which is suitable for abdominal scAT evaluation