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Shear wave sonoelastography of skeletal muscle: basic principles, biomechanical concepts, clinical applications, and future perspectives

Maud Creze^{1,2,3,4} · Antoine Nordez⁵ · Marc Soubeyrand⁶ · Laurence Rocher^{1,3} · Xavier Maître³ · Marie-France Bellin^{1,3}

Abstract

Imaging plays an important role in the diagnosis and therapeutic response evaluation of muscular diseases. However, one important limitation is its incapacity to assess the *in vivo* biomechanical properties of the muscles. The emerging shear wave sonoelastography technique offers a quantifiable spatial representation of the viscoelastic characteristics of skeletal muscle. Elastography is a non-invasive tool used to analyze the physiologic and biomechanical properties of muscles in healthy and pathologic conditions. However, radiologists need to familiarize themselves with the muscular biomechanical concepts and technical challenges of shear wave elastography. This review introduces the basic principles of muscle shear wave elastography, analyzes the factors that can influence measurements and provides an overview of its potential clinical applications in the field of muscular diseases.

Keywords Elastic modulus · Elasticity imaging techniques · Review · Skeletal muscle

Introduction

Imaging allows clinicians to assess the qualitative, morphologic and metabolic status of skeletal muscle by showing edema, cross-sectional areas, masses and fat infiltration [1, 2]. Despite the contributions of conventional imaging, it remains limited for the diagnosis of muscular diseases, one important

limitation being its incapacity to assess the *in vivo* contractile properties of the muscles. This is concerning, given that the function of the muscles relies precisely on their capacity to contract, which in turn modifies their tissular elasticity.

Recently, ultrasound elastography has provided a quantifiable spatial representation of “elasticity” (or “hardness” or “stiffness”) in the form of an elastogram [3–6]. The basic principle of elastography is (1) to create a shear or compression wave through a stress, (2) to map the distortion induced by the wave in the tissue using sonography and (3) to trace the wave back to the mechanical properties of the tissue by using inversion algorithms [7]. The two most frequently used elastography techniques are strain (or compressive) elastography and shear wave elastography (SWE). In strain elastography, stress is applied by repeated manual compression of the transducer. The amount of lesion deformation relative to the surrounding normal tissue is measured and displayed in an elastogram. Unfortunately, with this technique, data acquisition and interpretation are largely operator dependent, especially in muscle, which has complex biomechanical properties. SWE uses an acoustic radiation force impulse, which does not require specific experience of the examiner. SWE is less operator-dependent than strain elastography and represents a reproducible tool for quantifying stiffness. Elastography has gained an important role in the diagnostics, staging and follow-up of numerous diseases and

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is now part of routine examination for soft tissues imaging, such as breast [8] or thyroid [9] imaging, or evaluation of fibrosis in liver pathology [10].

SWE of skeletal muscle has also attracted broad research interest. Elasticity is a critical determinant of muscle performance and force; hence, its assessment *in vivo* can help to improve the understanding of muscle functions [11]. Numerous studies have been conducted that use SWE for different muscles in healthy and diseased muscle as well as in different muscular states, the findings of which are heterogeneous but informative [12–16]. This review introduces the basic principles of muscle shear wave elastography and muscle biomechanics and presents the main results obtained in healthy and pathologic muscle. Ultimately, we speculate on the limitations, clinical applications and potential future applications of SWE to skeletal muscle.

Basic principle of SWE

In clinical practice, the stiffness of a tissue is subjectively assessed by manual palpation. In biomechanics, stiffness is defined by the proportional relationship between the stress (the external force or compression) and strain (deformation) applied to it. SWE is based on Hooke's law, which establishes—only in isotropic and purely elastic media—a relationship among strain, stress and elasticity: $s = E \cdot d$, where E , the elastic or Young's modulus, is measured in kPa; s is the stress or external force; d is the strain or deformation. The applied strain is generally responsible for two kinds of waves: the shear and compression waves, which are used to quantify stiffness with SWE and strain elastography, respectively. SWE encompasses a group of techniques that act differently to create shear waves by using either an ultrasound push beam or external mechanical vibration [7, 16–18]. Transmission of a longitudinal pulse leads to tissue displacement, which is detected by pulse echo ultrasound. As a first step, SWE techniques measure the shear wave velocity [swv, also named shear wave speed (sws) or v in $\text{m} \cdot \text{s}^{-1}$] in the tissue. V is proportional to the shear modulus (also named μ or G in kPa) using the formula: $\mu = 3 \rho \cdot v^2$ (where ρ is the tissue density, equal to $1000 \text{ kg} \cdot \text{m}^3$ in the human body). E and μ are related by the formula: $E = 3 \cdot \mu$. Finally, SWE does not directly measure the E , but measures v , which in turn is used to estimate μ and then E . Hard tissues have a higher E , μ and v than soft ones. In most studies, the shear modulus is the biomechanical parameter used to characterize stiffness.

Stiffness is displayed on a B-mode scan with an overlaid elastogram in color. Warm colors correspond to hard tissues, cold colors to soft ones. The stiffness value is then measured within a region of interest (ROI) on the elastogram.

Regarding the constructor, stiffness is expressed by the shear wave speed in $\text{m} \cdot \text{s}^{-1}$, Young's modulus or shear modulus. Authors most commonly used the shear modulus obtained

(1) from the Young's modulus divided by 3 or (2) from SWV with the formula $\mu = 3\rho v^2$. Note that, regarding the rheologic fit model used, ρ was from 980 to $1100 \text{ kg} \cdot \text{m}^3$.

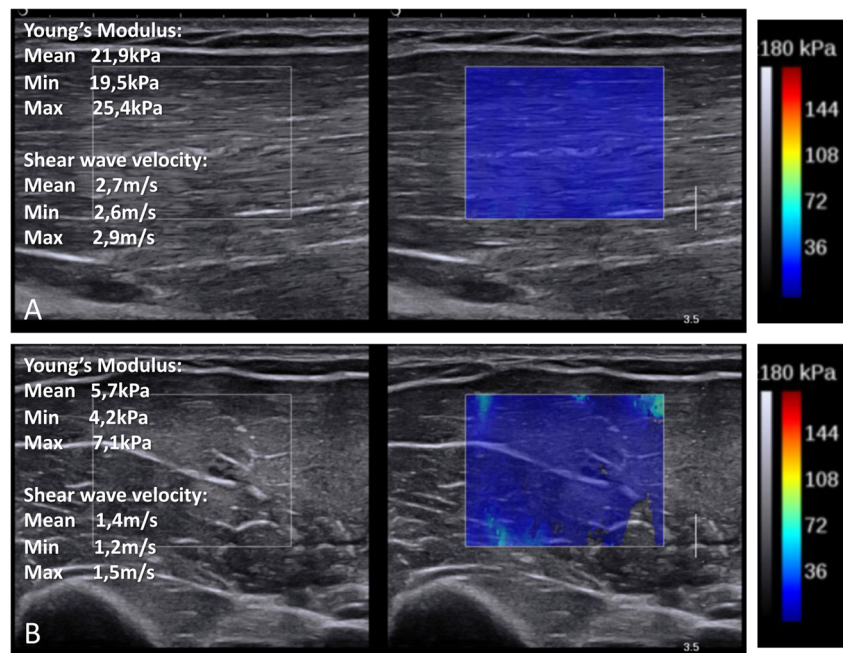
Technical considerations

A comparative study between SWE and traditional material testing techniques has shown proportional changes of the shear modulus and Young's modulus, respectively, with increasing tensile load and validated stiffness measurement using SWE [19]. Although SWE provides reliable stiffness measurements under proper conditions and using the same method, several technical parameters are known to influence the measurements and need to be taken in account [18, 20–22].

All commercially available SWE systems are based on the prerequisite that soft tissues are purely elastic, incompressible and isotropic. First, the major technical parameter that influences stiffness measurement is the anisotropic physical properties of the skeletal muscle. The tissular organization of skeletal muscle, which comprises a parallel arrangement of myofibrils, muscular fibers, collagen and elastic fibers, and fascicles, confers anisotropic, in particular orthotropic properties (which are a subset of anisotropic properties that differ along the three orthogonal axes) to the skeletal muscle. These orthotropic physical properties are responsible for the fact that shear waves travel faster along the direction of the fibers than they do when perpendicular to them [19, 21] (Fig. 1). This has a number of consequences. First, stiffness measurements are sensitive to the angle between the probe axis and the orientation of the muscular fibers. Shear modulus measurements using SWE are correlated with Young's modulus only if the probe is oriented parallel to the muscle fibers. Another consequence is the difficulty assessing meaningful results in muscles with complex anatomy. Multipennate, conic, triangular or fusiform anatomy, which yields “multi-orientation” fibers, introduces a technical difficulty in visualizing the orientation of fibers. This technical difficulty requires careful consideration of the muscle anatomy before using SWE. Finally, the stiffness value depends on the position of the probe in relation to the muscle fiber direction; therefore, SWE is partly operator dependent especially in complex and large muscles. However, intra- and inter-observer reliabilities remain good to excellent if performed by a skilled senior and if the angle between the probe axis and the orientation of the muscular fibers is inferior to 20° [21, 22].

The second parameter concerns the viscoelastic properties of skeletal muscles. Rheologic fit models (formulas) used to measure stiffness from shear wave propagation assume that muscle is purely elastic, which it is not [7, 14]. Muscle behaves as a combination of viscous and elastic properties, which together correspond to the “complex shear modulus” (G). The complex shear modulus (G) is composed of storage

Fig. 1 Stiffness differences between the longitudinal (a) and transversal (b) planes to the muscle fibers in the biceps brachii (37-year-old male volunteer). Stiffness increases by a factor of four between the longitudinal and the transversal planes. Mean, minimum (min) and maximum (max) values of both Young's modulus and shear wave velocity are measured within a circular ROI of 10 mm diameter



shear modulus (μ elastic SM or G') and loss shear modulus (or η or viscous shear modulus or G''). Also, the viscoelastic properties are non-linear, i.e., stiffness changes are relative to the characteristics of the applied stress such as the frequency of the shear wave. Moreover, given the contractile and stretching properties of muscle, muscle viscoelasticity is active [23].

Third, skeletal muscle is a deformable tissue; thus, SWE is sensitive to transducer pressure. Indeed, muscle is anisotropic (orthotropic), non-linearly viscoelastic, compressive/deformable and active tissue. Because the rheologic fit model used in SWE ignores the viscous and anisotropic properties of the muscle (which is valid for isotropic tissues such as the liver or the thyroid gland), constructors state that the most appropriate stiffness unit for muscle should be the shear wave velocity. A generous amount of coupling gel needs to be applied onto the surface of the skin so the probe does not compress the muscles.

Absolutely, SWE is less robust in deeper muscles as the propagation of the shear waves, and hence the outcomes, depends on the surrounding tissues. Greater acquisition depth, thick superficial fat layers and greater BMI are responsible for an attenuation effect that disturbs shear wave collection and creates artifacts as "holes" or areas of very high/low stiffness in the elastogram [24–27]. Interferences due to reflections (fascia, bone) might also induce changes in wave patterns and corrupt reconstruction (Fig. 2). A consequence of this is that the stiffness value might depend on the ROI size and position.

Stiffness values also depend on the transducers and machines from the different vendors [24], presets, acoustic methods and calculation formulas used [28, 29].

Functional assessment of muscle

SWE clearly emphasizes stiffness changes related to muscle contraction, stretching, manual therapy procedures and muscle manipulation (Fig. 3). Muscle response to a load creates an active and a passive force, which are both responsible for increased stiffness [18, 30, 31].

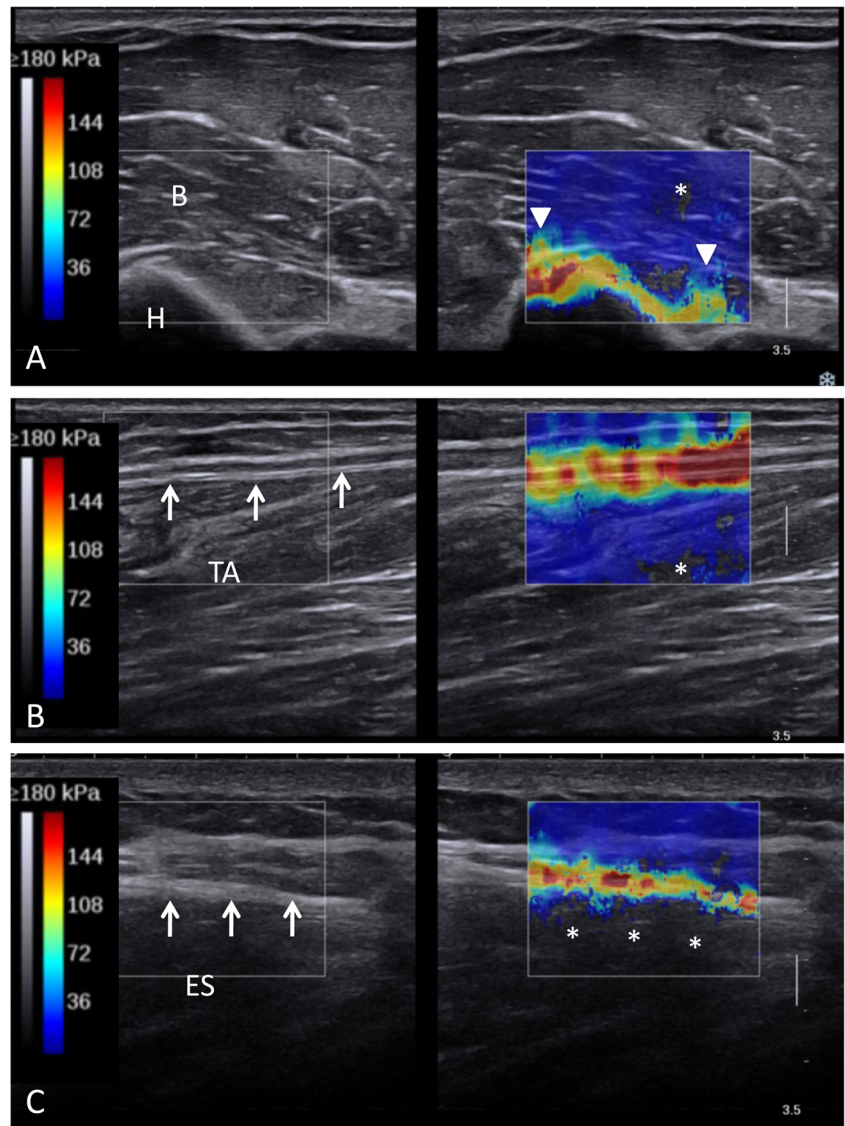
Rest

Muscle stiffness in resting condition is where the muscle has the lowest stiffness value. The resting condition is obtained in case of absence of load and torque and confirmed by the absence of neuromuscular activity on the electromyogram. More specifically, muscular stiffness reaches the lowest value when the muscle is at rest in slack length (defined as the length beyond which the muscle begins to develop passive elastic force) [32, 33]. Because of the attenuation effect in deep muscles, most studies have been conducted on appendicular and superficial muscles, in particular the gastrocnemius, quadriceps and biceps brachii. Significant stiffness differences are observed between various muscles [34, 35]. In humans, reported shear modulus values at rest range between 3.1 kPa in the biceps brachii and 42.8 kPa in the masseter in vivo (Table 1).

Muscle contraction

SWE detects subtle stiffness variations since the beginning of contraction [31, 101]. The magnitude of the biomechanical changes with contraction is positively and linearly correlated with the muscle force and myoelectrical activity level [28, 31,

Fig. 2 Examples of artifacts (37-year-old male volunteer). **a** Artifacts related to bones within the brachialis (arrowheads). *B*, brachialis; *H*, humerus. **b** and **c** Attenuation effect (*) of the fascia (arrows) (crural fascia, **b**; thoracolumbar fascia, **c**). *TA*, tibialis anterior; *ES*, erector spinae



65, 82, 83, 91, 102]. The yield curve of increased stiffness during contraction differs between muscles and depends on the intensity of the force [i.e., the vector quantity, which is a straight-line push or pull, usually expressed in pounds (lbs) or Newtons (N)] and torque [i.e., the corresponding angular variable to force is a torque (or moment of force)] as well as on

fascicle length [14, 28, 47–50, 53, 61, 71, 80, 82, 86, 103, 104].

Unfortunately, the increase in stiffness with higher contraction levels cannot always be measured as shear waves in more rigid tissues and may propagate too fast for some ultrasound systems to be properly tracked [31]. Above a certain stiffness

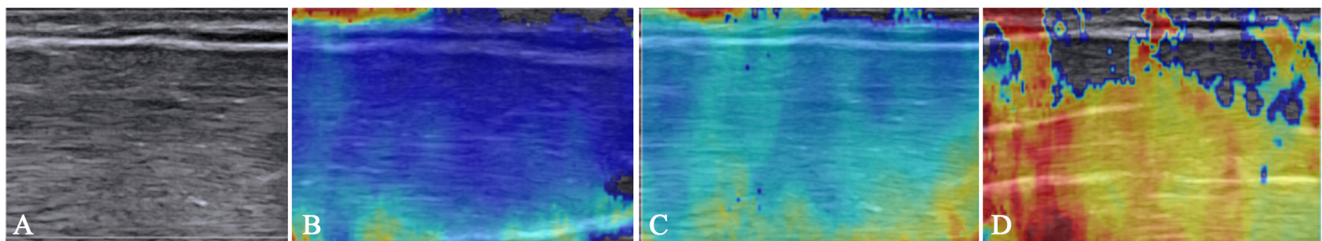


Fig. 3 Examples of elasticity images of a biceps brachii elasticity map obtained with SWE (35-year-old male volunteer). **a** B-mode ultrasound image used to find the longitudinal axis of muscle fibers. **b** Elastogram at

rest. **c** Elastogram during stretching. **d** Elastogram during contraction. Warm colors correspond to hard tissues and cold ones correspond to soft tissues

Table 1 Study characteristics using SWE in healthy individuals

Author year	Study design	Muscle	Population number (M/F) Age	Stiffness value and unit in relaxed muscle (longitudinal axis)	Functional assessment of muscle	Biomechanical parameter studied
Akagi 2013 [36]	Cohort	GM, GL	20/0 25.0 ± 3.4 years	GM: 27.6 ± 7.3 kPa GL: 33.5 ± 6.3 kPa (<i>Transverse axis only</i>)	Stretching	SM
Akagi 2014 [37]	Cohort	GM, GL	19/0 23.7 ± 2.3 years	GM: 27.0 ± 5.9 kPa GL: 32.0 ± 6.3 kPa (<i>Transverse axis only</i>)		YM
Akagi 2015 [38]	Cohort	TB	18/0 22.4 ± 2.6 years	NC	Contraction	SM
Akagi 2015 [39]	Cohort	RF, G, Sol	42/38 22-78 years	RF: 3.4 ± 0.7 kPa GL: 3.1 ± 1.1 kPa SOL: 3.6 ± 0.9 kPa		SM
Akagi 2015 [40]	Cohort	T, SpC, LvS	12/12 21 ± 1 years	T: 5.86 ± 1.6 kPa SpC: 5.10 ± 1.1 kPa LvS: 4.58 ± 1.3 kPa		SM
Akagi 2016 [41]	Cohort	TB	23/0 22.1 ± 1.1 years	6.5 ± 2.3 kPa		SM
Akiyama 2016 [42]	Cohort	GM, GL, Sol, PL, TA	20/0 19.4 ± 2.9 years <i>Control Athlete</i>	GM: 2.4 ± 0.3 m/s GL: 2.4 ± 0.3 m/s Sol: 2.6 ± 0.3 m/s PL: 2.7 ± 0.2 m/s TA: 3.2 ± 0.4 m/s	Stretching	SWV
Andonian 2016 [43]	Cohort	VM VI RF	46/4 43 ± 9.1 years <i>Athlete</i>	VM: 3 ± 0.5 kPa RF: 3.8 ± 0.5 kPa VL: 3.9 ± 0.5 kPa	Contraction	SWV SM
Andrade 2015 [44]	Cohort	GM	9/0 25 ± 3 years	NC	Stretching	SM
Arda 2011 [6]	Cohort	GM Ma	28/89 37.7 ± 9.1 years	GM: 11.4 ± 4.1 kPa Ma: 10.4 ± 3.7 kPa		YM
Ariji 2016 [45]	Cohort	Ma	21/9 31.5 years	42.8 ± 5.6 kPa		YM
Ates 2015 [28]	Cohort	ADM	10/0 27.8 ± 5.9 years	NC	Contraction	SM
Botanlioglu 2013 [46]	Cohort	VL VM	11/11 28 ± 4 years	VL: 16.2 ± 3.7 kPa VM: 14.8 ± 5.3 kPa	Contraction	YM
Bouillard 2011 [47]	Cohort	ADM First DIO	7/0 25 ± 2.7 years <i>Controls</i>	NC	Contraction	SM
Bouillard 2012 [48]	Cohort	BB, BA, BR, TB	7/3 24.9 ± 3.6 years	NC	Contraction	SM
Bouillard 2012 [49]	Cohort	ADM, VL, VM, RF	18/4 23.1 ± 2.2 years	NC	Contraction	SM
Bouillard 2014 [50]	Cohort	VL, VM, RF	15/1 24.6 ± 2.6 years	VL: 6.7 kPa VM: 5.5 kPa RF: 3.4 kPa	Contraction	SM
Brandenbourg 2015 [51]	Cohort	GL	8/12 2-12 years	8.6 ± 3 kPa	Stretching	SM
Carpenter 2015 [52]	Cohort	RF VL G	2/3 27-33 years	RF: 3.7 ± 1.4 m/s VL: 4.5 ± 1.5 m/s G: 4.3 ± 1.6 m/s	Controls	SWV
Chemak 2013 [53]	Cohort	GM	10 NC	2.1 ± 0.3 m/s	Contraction Stretching	SWV SM
Chino 2016 [54]	Cohort	GM	26/26 24.4 ± 5.9 years	NC	Stretching	SM
Chino 2015 [55]	Cohort	GM	13/12 22 ± 4.3 years	31 kPa	Stretching	YM
Cortez 2015 [21]	Cohort	TA GM	7/9 19-61 years	1.9-2.8 m/s		SWV
Creze 2017 [56]	Cohort	Mu Lg Ic	7/923 years	M: 5.4 ± 1.6 kPa Lg: 6.9 ± 2.7 kPa Ic: 4.9 ± 1.4 kPa		SM
Du 2016 [57]	Cohort	BB	18/13 46.7 ± 3.2 years <i>Control</i>	24.4 ± 5.1 kPa		YM
Dubois 2015 [20]	Cohort		10 NC	BF: 5.6 ± 1.4 kPa	Stretching	SM

Table 1 (continued)

Author year	Study design	Muscle	Population number (M/F) Age	Stiffness value and unit in relaxed muscle (longitudinal axis)	Functional assessment of muscle	Biomechanical parameter studied
		BF, Gr, RF, Sar, SM, ST, VL, VM, GM, GL, Sol	25.5 ± 2.8 years	Gr: 6.0 ± 1.7 kPa RF: 4.1 ± 0.6 kPa Sar: 5.3 ± 1.1 kPa SM: 5.3 ± 1.5 kPa ST: 4.2 ± 1.0 kPa VL: 5.5 ± 1.0 kPa VM: 3.9 ± 0.6 kPa GM: 4.5 ± 0.9 kPa GL: 4.7 ± 0.7 kPa Sol: 6.6 ± 1.4 kPa		
Eby 2015 [58]	Cohort	BB	47/86 44.3 years	4.9 ± 1.3 kPa	Stretching	SM
Eby 2016 [59]	Cohort	BB	2/256 years <i>Controls</i>	NC	Stretching	SM
Eriksson Crommert 2014 [60]	Cohort	GM	12/6 28.0 ± 6.4 years	11.0 ± 3.1 kPa		SM
Erwertesen 2016 [34]	Cohort	BB, Q, G	5/5 32.5y	BB: 14.8 ± 1.3 kPa G: 9.4 ± 1.9 kPa Q: 16.7 ± 1.3 kPa		SWV
Genisson 2010 [14]	Cohort	BA	5 NC	BA: 5.9 ± 0.2 kPa	Contraction Stretching	G (G'G'')
Guilhem 2016 [61]	Cohort	GM	9/8 25.0 ± 3.7 years	27.9 ± 9.9 kPa	Contraction	SWV SM
Hirata 2016 [62]	Cohort	GM, GL, Sol	8/4 20.4 ± 2.9 years	NC	Stretching	SM
Hirata 2015 [63]	Cohort	GM, GL, Sol	5/4 21.1 ± 2 years	NC	Stretching	SM
Hirayama 2015 [27]	Cohort	TrA	10/0 24 ± 4 years	2.1 ± 0.6 m/s		SWV
Hug 2013 [33]	Cohort	GM	9/0 22.6 ± 1.8 years	5.1 ± 1.2 kPa	Stretching	SM
Hug 2014 [64]	Cohort	RF	7/6 34 ± 6 years	3.7 ± 1 kPa	Contraction Stretching	SM
Deffieux 2008 [65]	Cohort	BB	4 NC	NC	Contraction	SWV
Ichihashi 2016 [66]	Cohort	ST, SM, BF	30/0 22.7 ± 2.2 years	NC		SM
Itoigawa 2014 [67]	Cohort	SSp	3 NC 37 years	32.7 ± 12.7 kPa - > 40 ± 12.4 kPa		SM
Koo 2014 [26]	Cohort	TA	9/11 28.7 ± 8.8 years	5.8 ± 1.9 kPa	Stretching	SM
Koo 2015 [32]	Cohort	TA GL	16 NC	TA: 25.5 kPa GL: 24.2 kPa	Stretching	SM
Kot 2012 [29]	Cohort	RF	14/6 26.4 ± 3.5 years	12.7 ± 3.4 kPa		SM
Lacourpaille 2014 [68]	Cohort	BB BA	11/5 23.6 ± 3.2 years	BB: 3.9 ± 1.2 kPa BA: 7.2 ± 1.2 kPa	Contraction Stretching	SM
Lacourpaille 2012 [69]	Cohort	GM, TA, VL, RF, TB, BR, APO, ADM	25/5 25 ± 7	GM: 3 ± 0.6 kPa TA: 4.5 ± 0.5 kPa VL: 3.3 ± 0.4 kPa RF: 3.2 ± 0.4 kPa TB: 3.1 ± 0.2 kPa BB: 3.1 ± 0.4 kPa BR: 3.5 ± 0.4 kPa APO: 3.8 ± 0.7 kPa ADM: 4.5 ± 0.6 kPa		SM
Lacourpaille 2013 [70]	Cohort	BB	12/0 21.8 ± 2.3 years	NC	Stretching Contraction	SM
Lapole 2014 [71]	Cohort	BB	7/5 38 ± 10 years	NC	Contraction	SM
Leong 2016 [72]	Cohort	T	17/0 21.7 ± 3.5 <i>Athletes</i> <i>Controls</i>	10.2 ± 1.8 kPa	Contraction Stretching	SM
Le Sant 2015 [73]	Cohort	ST, BF,	18 NC	NC	Stretching	SM

Table 1 (continued)

Author year	Study design	Muscle	Population number (M/F) Age	Stiffness value and unit in relaxed muscle (longitudinal axis)	Functional assessment of muscle	Biomechanical parameter studied
Levinson 1995 [15]	Cohort	SM Q	23.5 ± 2.3 years 10/0	4 ± 0.5 m/s	Contraction	SWV YM
MacDonald 2015 [25]	Cohort	OEA OIA TrA RA	16/14 20 ± 3 years	OEA: 6.9 ± 2.1 kPa OIA: 3.5 ± 0.9 kPa TA: 4.0 ± 0.8 kPa RA: 5.4 ± 1.8 kPa	Contraction	SM
Maisetti 2012 [74]	Cohort	GM	7/0 27 ± 6	NC	Stretching	SM
Miyamoto 2015 [22]	Cohort	BB GM	11/0 22 ± 1.1 years	NC	Stretching	SM
Miyamoto 2015 [75]	Cohort	BF, ST, SM	12/0 22 ± 3 years	NC	Stretching	SM
Moreau 2016 [76]	Cohort	Mu	6/4 25.5 ± 2.2 years	L4: 6.8 ± 1.2 kPa L2: 8.5 ± 1.0 kPa	Stretching	SM
Nakamura 2014 [77]	Cohort	GM	17/0 23.5 ± 2.6 years	8 ± 2 kPa	Stretching	SM
Nakamura 2016 [35]	Cohort	SM BF ST	15/0 22.2 ± 2.4 years	ST: 25.5 ± 4.6 kPa SM: 44 ± 11.5 kPa BF: 31.3 ± 15.6 kPa	Stretching	SM
Nakamura 2016 [78]	Cohort	GM	10/0 23.3 ± 1.1 years	8.1 ± 0.6 kPa	Stretching	SM
Nordez 2010 [31]	Cohort	BB	5/1 32.3 ± 8.9 years	11.3 ± 3.8 kPa	Contraction	SM
Poumot 2016 [79]	Cohort	BB	6/5 38 ± 9 years	17.5 ± 5.1 kPa	Contraction	SM
Raiteri 2016 [80]	Cohort	LG	7/0 28 ± 5 years	NC	Contraction Stretching	SM
Roskopf 2016 [81]	Cohort	SS	11/11 53.8 ± 15.3 years	3 ± 0.5 m/s	Controls	SWV
Sasaki 2014 [82]	Cohort	TA	2/7 28.4 ± 3.9 years	NC	Contraction	SM
Shinohara 2010 [83]	Cohort	TA, GM, Sol	1/046 years	TA: 40.6 ± 1 kPa GM: 16.5 ± 1 kPa S: 14.5 ± 2.0 kPa	Contraction	YM
Souron 2016 [84]	Cohort	TA	21/25 19 ± 2 years	NC	Contraction	SM
Tanigushi 2015 [85]	Cohort	GM GL	5/5 21.8 ± 1.2 years	GM: 9.2 ± 2 kPa GL: 7.4 ± 1.5 kPa	Stretching	SM
Tran 2016 [86]	Cohort	RA OEA, OIA, TrA	11 NC 40-62 years	RA: 5.2 kPa OE: 22 kPa OI: 10.3 kPa TrA: 8.1 kPa	Contraction Valsalva	SM
Umegaki 2015 [87]	Cohort	ST BF	23/0 23.0 ± 2.1 years	BF: 20.1 ± 7.9 kPa ST: 13.9 ± 4.4 kPa	Stretching	SM
Umegaki 2015 [88]	Cohort	ST SM BF	20/0 23.4 ± 2.3 years	ST: 12.3 ± 3.5 kPa SM: 18.0 ± 7.1 kPa BF: 23.1 ± 8.9 kPa		SM
Umehara 2015 [89]	Cohort	TFL	20 M 23.3 ± 1.6 years	24.6 ± 8 kPa	Stretching	SM
Yoshida 2016 [90]	Cohort	GM	22/11 31.7 years	4.8 ± 1.6 m/s		SWV
Yoshitake 2014 [91]	Cohort	BB	10 NC 20.9 ± 1 years	5.1 ± 0.6 kPa	Contraction	SM
Zhang 2016 [92]	Cohort	VL RF	330 NC <i>Controls Athlete</i>	VL: 3.6 ± 0.5 kPa RF: 3.90 ± 0.9 kPa		SM
Eby 2013 [19]	Animals	BA	4 Swines	NC	Stretching	SM YM
Koo 2013 [93]	Animals	TA GL	32 Chickens	TA: 25.3 ± 2.2 kPa GL: 25.8 ± 5.9 kPa	Stretching	SM
Lv 2012 [94]	Animals Animals	Legs NC	28 Rabbits 14 Bovines	10.5 ± 2.4 kPa 78 kPa		YM SM

Table 1 (continued)

Author year	Study design	Muscle	Population number (M/F) Age	Stiffness value and unit in relaxed muscle (longitudinal axis)	Functional assessment of muscle	Biomechanical parameter studied
Sapin-de-Brosses 2010 [95]						
Hatta 2015 [96]	Cadavers	SSp	30 NC 50-92 years	NC	Stretching	SM
Hatta 2016 [97]	Cadavers	D	8 NC 72-90 years	39.1 ± 11.9 -> 72.4 ± 9.1 kPa	Stretching	SM
Joy 2015 [98]	Cadavers	G Ma	3/3 81.7 ± 13.2 years	G: 31.5 kPa M: 15.5 kPa		YM
Yoshitake 2016 [99]	Cadavers	GM	3/1 89.3 ± 7.5 years	22 kPa		SM
Brandenbourg 2014 [16]	Review					
Hoyt 2008 [100]	Review					
Hug 2015 [18]	Review					
Klauser 2014 [12]	Review					

ADM, abductor digiti minimi; *APO*, adductor pollicis obliquus; *BB*, biceps brachii; *BF*, biceps femoris; *BR*, brachioradialis; *D*, deltoid; *DIO*, dorsal interosseus; *F*, female; *FDP*, flexor digitorum profundus; *G*, gastrocnemius; *GM*, gastrocnemius medialis; *GL*, gastrocnemius lateralis; *Gr*, gracilis; *Ic*, iliocostalis; *Lg*, Longissimus; *LvS*, levator scapulae; *M*, male; *Mu*, multifidus; *Ma*, masseter; *OEA*, obliquus externus abdominis; *OIA*, obliquus internus abdominis; *PL*, peroneus longus; *Q*, quadriceps; *RA*, rectus abdominis; *RF*, rectus femori; *Sar*, sartorius; *ScA*, scalenus anterior; *SCM*, sternocleidomastoid; *SM*, semimembranosus; *Sol*, Soleus; *SoP*, soft palate; *SpC*, Splenius capitis; *SSp*, supraspinatus; *ST*, semitendinosus; *T*, trapezius; *TA*, tibialis anterior; *TB*, triceps brachii; *TFL*, tensor fascia latae; *TrA*, transverse abdominis; *VI*, vastus intermedius; *VL*, vastus lateralis; *VM*, vastus medialis

threshold, which depends on performances of the equipment (maximal value v : 16 m/s or $G = 266$ kPa or $E = 800$ kPa), the measurement quality deteriorates and SWE cannot properly measure tissue stiffness. The elasticity is thereafter underestimated [31]. With the first equipment, muscle contraction was analyzed only up to 30% of the maximal voluntary contraction. Stiffness values could be measured for almost maximal contraction with more recent ultrasound systems [18].

During contraction, a heterogeneous pattern of stiffness appears within the muscular tissue probably reflecting the non-synchronization of motor units [82].

After an intense eccentric contraction, stiffness continues to increase for several days [68, 79] as a consequence of series of events leading to muscle damage [102].

Stretching

Elastography provides an individual index of passive muscle force by investigating stiffness during stretching/lengthening and torque (here, a torsion or twisting moment). Stretching was responsible for a linear increase in muscle stiffness, the magnitude of which depended on the type of muscle, joint stiffness and positioning [11, 26, 32, 42, 51, 54, 63, 64, 73–77, 87, 89, 93, 99, 105, 106].

Manual therapy procedures and muscle manipulation

Static stretching [36, 37, 66, 77, 85, 88], massage [60] and deloading tape [64] induce acute and transient decreased

stiffness in the underlying muscle region. Cryotherapy increases stiffness in the underlying muscle region [107].

Note that muscle torque, stretching and contraction affect the reliability of stiffness measurement [14, 20, 29, 48, 52].

Individual, spatial and temporal stiffness variability

Inter-individual variability

Regardless of muscle activity, large inter-individual and inter-sample stiffness differences exist that reflect a large inter-individual variability. Regarding the inter-individual stiffness, the mean shear modulus usually varies by a factor of two or even three between individuals [25, 36]. Regarding the inter-sample stiffness differences, the mean shear modulus values of a same muscle may increase by a factor of three to five between studies. In an attempt to understand the origins of such inter-individual variability, some works studied the influence of gender, age, physical activity and training or anatomical characteristics of muscles on stiffness. However, no obvious stiffness dimorphism emerges that was related to sexual, aging or physical activity. Most investigators did not observed gender differences [39, 46, 84] and the rare significant results that were reported were contradictory and dependent on the joint position and age [6, 39, 58]. With aging also, no reproductive and controversy age-related stiffness changes have been observed [6, 39, 58]. For example, aging has been associated with increased stiffness in the biceps brachii [58], whereas the opposite was observed in the legs [39]. Stiffness in childhood has not been studied with SWE. Magnetic

resonance elastography reported significantly higher stiffness in adults than in children in thigh muscles [108]. Similar trends should be expected with SWE. Concerning the influence of physical activity and training, a study reported no significant muscle stiffness change after a 6-week resistance training program, whereas muscle thickness changes were significant [41]. No reproducible and significant relationship was described between stiffness and anatomical characteristics such as cross-sectional area or muscle thickness [32, 38, 109]. Similarly, most studies did not find a side-to-side stiffness difference [92].

As shown in a previous paragraph, numerous methodologic differences such as the measurement unit used and rheologic fit modeling, probe position, variation in body and joint position, and set-up and difficulty in achieving a fully relaxed state (slack length) affect the reliability of measurement, making it difficult to precisely compare findings, and might be responsible for these differences [20, 29, 48, 52].

Spatial and temporal variability

Within a given muscle, stiffness is not uniform and displays regional differences regardless of the muscular status. Investigators reported diffuse heterogeneities—especially during contraction [31, 97]—as well as stiffness differences along the longitudinal axis of muscles [52, 56, 58, 69, 106]. Heterogeneity in the transversal axis of muscle have also been observed but showed some inconsistencies: both higher [52] and lower [34] stiffness was found in the deep part of the muscle than in the superficial. Spatial variability probably reflects the underlying histologic differences observed with a similar distribution pattern [110]. As described above, muscle geometry also influences stiffness, in particular through the technical difficulty induced by such complex anatomy.

Interestingly, SWEs have shown that a superficial to deep stiffness pattern might also result from a compressive effect of surrounding tissue (fascia, muscle, skin) on the superficial part of the muscle. By comparing muscular stiffness with the skin and after removal of the skin and fascia in human cadavers, some authors showed that the skin and fascia contributed to increasing muscular stiffness in legs [26, 99]. Conversely, in the shoulder, the skin, fat and fascia did not influence rotator cuff muscle stiffness [96].

Most of the inter-day experiments demonstrated good temporal reliability of shear modulus measurements [106]. However, studies on thin, deep or large muscles found fair to poor reliability of the shear modulus measurements with significant inter-days differences [25, 86]. In these muscles, poor temporal reliability constitutes a limitation of the SWE technique induced by an attenuation effect and complex muscle anatomy, but might also reflect daily changes related to load and muscle fatigue, in particular in trunk muscles.

SWE of pathologies of the skeletal muscle

Pathologic and dysfunctional muscles have abnormal mechanical properties, and SWE highlights therapeutic effects in muscular diseases (Table 2).

Increased stiffness has been observed in congenital myopathies such as Duchenne muscular dystrophy [112, 117] and cerebral palsy [113]. Decreased stiffness has been reported in congenital myopathies such as GNE [52] and cuff tendinopathy [72, 81, 97]. The magnitude and dynamics of stiffness changes are linked to the severity of the disorder and the efficiency of the treatment. SWE revealed abnormal stiffness in “idiopathic” muscular pain syndrome with no other radiologic features [40] or pain syndrome related to delayed onset muscle soreness (DOMS) caused by unaccustomed eccentric contraction [68, 79].

SWE is interesting for the evaluation of the biomechanical outcomes of various musculoskeletal surgical repair techniques in the shoulder [97, 115, 116]. The effectiveness of the rehabilitation technique could also be quantified using SWE [25, 114].

Structure- and function-related muscle stiffness changes

As observed with manual palpation, SWE reveals stiffness changes related to muscle activity, load and torque. Stiffness is linearly related to both active and passive muscle forces induced by actomyosin cross bridges, hyperemia and changes in the extracellular matrix during contraction [118, 119] and induced by changes in the extracellular matrix and myofibril elasticity during stretching [11]. Interestingly, SWE also objectively highlights the muscular relaxation induced by manual procedures.

Within muscle stiffness variability, inter-individual stiffness variability and stiffness changes in diseased muscles raise questions related to the nature of the relationship between muscle histology and stiffness. Within a muscle, the spatial arrangements of fascicles, number and type of fibers, isoforms of actin-myosin, amount of fat, architecture of the capillary supply network and connective tissue vary depending on the use and function of the muscle [110, 120, 121]. The spatial histologic pattern often matches with the stiffness variations observed between and within muscles: both stiffness and histology vary between the depth and surface of the muscle as well as between the proximal and distal parts of the muscle. Thus, many investigators have suggested that inter-muscular differences should correlate with the muscle histology, in particular with fiber type. Following the same reasoning, we can guess that pathologic muscles, which present pronounced biologic changes such as inflammation, denervation and edema, can be differentiated from normal muscle using SWE analysis. Despite this seeming biologic-stiffness relationship, stiffness

Table 2 Study characteristics using SWE in muscle diseases

Author year	Study design	Muscle	Population (patients) Number Age	Pathology	Stiffness (patients vs. controls)	Biomechanical parameter
Akagi 2015 [40]	Cohort	T, SpC, LvS	13 M 21 ± 1 years	Subjective symptom of neck and shoulder stiffness	No difference	SM
Akiyama 2016 [42]	Cohort	GM, GL, SoL, PL, TA	24 M 21.9 ± 6.4 years	Medial tibial stress syndrome	Increase	SWV
Botanlioglu 2013 [46]	Cohort	VL, VM	11 F 30.8 ± 8.2 years	Patellofemoral pain syndrome	Decrease (VM)	YM
Brandenbourg 2016 [111]	Cohort	GL	12 (6F-7M) 5 ± 1 years	Cerebral palsy	Increase	SM
Carpenter 2015 [52]	Cohort	RF, GL, GM, LV	8 (4F-4M) 27-33 years	GNE-related myopathy	Decrease	SWV
Du 2016 [57]	Cohort	BB	46(27 M-19F) 47.9 ± 2.8 years	Parkinson disease	Increase	YM
Eby 2016 [59]	Cohort	BB	9 (7 M-2F) 58.3 years	Chronic stroke	Increase with torque and passive extension on contralateral limb of patient	SM
Lacourpaille 2014 [68]	Cohort	BB BA	16 (11 M-5F) 23.6 ± 3.2 years	Delayed onset muscular soreness	Increase	SM
Lacoupaille 2015 [112]	Cohort	GM, TA, VL, BB, TB, ADM	14 (NC) 13.3 ± 5.9 years	Duchenne muscular dystrophy	Increase	SM
Lee 2016 [113]	Cohort	GM, TA	8 (3F-5M) 9.4 ± 3.7 years	Cerebral palsy	Increase	SWV
Leong 2016 [72]	Cohort	T	26 M 23.6 ± 3.3 years	Tendinopathy	Increase	SM
Roskopf 2016 [81]	Cohort	SSp	44(22F-22M) 20-60 years	Tendinopathy	Decrease	SWV
Yamauchi 2016 [114]	Cohort	ISP TM D	23 M 21.4 ± 1.2 years	Evaluation of physical therapy (muscle stretching) in shoulder tightness	Decrease	SM
Zhang 2016 [92]	Cohort	VL RF	36 M 22.8 ± 4.2	Tendinopathy	Increase (VL)	SM
Hatta 2015 [96]	Cadavers	SSp	30 (NC)	Tendinous tear	Smaller variation of stiffness with adduction	SM
Hatta 2016 [115]	Cadavers	SSp	8 (NC)	Evaluation of surgical repair	NC	SM
Hatta 2016 [116]	Cadavers	SSp	12 (NC)	Evaluation of surgical repair	Increase after surgical repair	SM
Hatta 2016 [97]	Cadavers	D	8 (NC)	Biomechanical effect of reverse shoulder arthroplasty	Increase with elongation	SM
Lv 2012 [94]	Animals	Hind leg	28 Rabbits	Crush	Increase	YM

ADM, abductor digiti minimi; *BB*, biceps brachii; *BA*, brachialis; *D*, deltoid; *GM*, gastrocnemius medialis; *GL*, gastrocnemius lateralis; *Gr*, gracilis; *ISP*, infraspinatus; *LvS*, levator scapulae; *PL*, peroneus longus; *Q*, quadriceps; *RF*, rectus femori; *Sar*, sartorius; *Sol*, Soleus; *SoP*, soft palate; *SpC*, Splenius capitis; *SSp*, supraspinatus; *T*, trapezius; *TA*, tibialis anterior; *TB*, triceps brachii; *TM*, teres minor; *Tg*, tongue; *VI*, vastus intermedius; *VL*, vastus lateralis; *VM*, vastus medialis

failed to be a significant quantitative marker of histologic changes due to aging, gender or physical activity [122, 123]. Fiber-type composition and muscle performance are known to be different between men and women [124]. Decreases of the

number and the size of the fibers, fat degeneration and corrupted connective tissue occur with aging. In response to changes in neuromuscular activity or mechanical loading, muscle has great adaptive potential called muscle plasticity.

Thus, considering physical activity leading to angiogenesis and muscular fiber changes, and inactivity leading to sarcopenia and fat infiltration, we could expect that muscle plasticity would induce stiffness changes. However, SWE did not reveal the quantitative stiffness changes expected in relation to the specific muscle histology of samples extracted from females or males, athletes, juniors or seniors [30, 125].

Lastly, skeletal muscle significantly participates in multiple bodily functions and the general metabolism. To date, the biomechanical behaviors of skeletal muscle in response to general metabolism stimuli, such as corticosteroids, and hormonal levels have not been studied. Such plasticity related to various metabolic and mechanical demands might partly explain the large inter- and intra-individual variability. Individual factors that influence stiffness have not been identified yet.

Feasibility in clinical routine

Actually, SWE of skeletal muscle remains in the field of research, and no guideline on the use of SWE in medical practice exists yet. Moreover, most of US scanners are not equipped with systems that allow realizing SWE. Given the influence of the many technical factors on stiffness measurements cited above, knowledge of the anatomy of the studied muscle, the basic muscular biomechanical concepts and the limits of the SWE method (in particular the role of anisotropy) is needed before using SWE on skeletal muscle.

SWE has potential in both research and clinical settings. In the field of biomechanics, SWE of muscle can be used to estimate muscle force during contraction, stretching and torque [18]. In sports, muscle elasticity is a critical determinant of muscle performance. Stiffness analysis of muscle could prevent injury and improve training and muscle performance. Increased muscle stiffness limits joint range of motion, whereas decreased muscle stiffness is known to predispose to joint partial dislocation [126]. In the field of physical therapy and haptics, SWE may have a promising future in the detection and evaluation of muscular regions that are tender and abnormal to palpation. Even if the majority of palpatory tests demonstrate poor or fair reliability, muscle stiffness changes measured by manual palpation are claimed to be important clinical features of the diagnostics of joint dysfunction. In medical practice, ultrasonography of muscle is mainly used in muscle-tendon pain syndrome and trauma as well as in the first examination of soft tissue masses. Real-time SWE could be easily implemented at the end of ultrasonic examination. SWE could be helpful in diagnosing muscle injuries and compartment syndrome, evaluating muscle-tendon pain syndrome, evaluating a patient for surgery and judging the effectiveness of rehabilitation. SWE has the potential to increase the understanding of several muscular pain syndromes classified as “idiopathic” when other imaging results are normal.

How should we analyze SWE in practice and research? First, the value of muscle stiffness could be a diagnostic and prognostic tool since significant quantitative changes have been observed in muscle diseases and with muscle solicitation as contraction and stretching. In addition to quantitative data, qualitative analyses of stiffness, i.e., the regional distribution of stiffness within the elastogram, could be an interesting feature to characterize biomechanical changes of muscle, especially in extreme age or during muscle load while the elastogram shows a heterogeneous stiffness pattern.

Limitations and future perspectives

Although SWE has potential in both research and clinical settings, several challenges need to be faced. First, the technical challenges need to be understood. More effective algorithms should be developed to identify the anisotropic properties of muscles. For each technique, the “gold standard conditions” (muscle and joint positioning, material setup, acoustic wave frequency, rheologic fit) need to be clarified to harmonize measurements. The probe should be aligned along the direction of muscle fibers as confirmed in B-mode [21, 22]. Better temporal and spatial resolutions of the shear wave should be improved to allow a tri-dimensional and dynamic analysis of stiffness. For complex and large muscles, the stiffness should be measured in the direction of muscle shortening. Second, larger cohorts are needed to properly determine the accuracy of SWE for the characterization of muscular diseases. Third, the relationships among muscle histology, plasticity and stiffness need to be explored. Investigations of the relationship between muscle structure and stiffness as well the relationship between muscle function and stiffness are challenging and require a multidisciplinary approach including biology, biomechanics, biophysics and clinical experience. Finally, the role of the tissular environment (subcutaneous, bone, fascia) on muscle stiffness needs to be clarified. The tissular environment around the muscle seems to influence stiffness in two ways: (1) by creating artifacts or attenuation effects that corrupt stiffness measurements or (2) by increasing tension and pressure in the muscular compartment to ensure sufficient muscular force [26, 91, 97]. In the first instance, artifact and attenuation effects are limitations of the SWE method, and it appears necessary to define the conditions in which such effects occur to avoid over- or underestimated stiffness values. In the second instance, SWE could allow understanding the mechanics of fascia in vivo and their role in force generation.

Conclusion

Shear wave imaging is a promising non-invasive tool for analyzing the biomechanical properties of muscles in healthy and pathologic conditions, and its scope should be broadened in the near future.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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