Title: Increase stiffness of Rotator cuff tendons in frozen shoulder on shear wave elastography

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Running title: Evaluating frozen shoulder on SWE

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ABSTRACT

Objectives: To evaluate the stiffness and morphology of the capsule, rotator cuff tendons and muscles, coracohumeral ligament (CHL), and long head of the biceps (LHB) in patients with frozen shoulder using shear wave elastography (SWE) with B-mode ultrasound.

Methods: Thirty-two patients with frozen shoulder were divided into the freezing and frozen phases. All patients had limitation of range of motion without rotator cuff tear. Stiffness was measured using SWE in the supraspinatus tendon, infraspinatus tendon, supraspinatus muscle, infraspinatus muscle, teres minor muscle, upper and lower trapezius muscles, posterior capsule, CHL, and LHB. The posterior capsule and CHL thicknesses were also investigated using B-mode ultrasound. All values were compared in the affected and unaffected shoulder in each phase.

Results: The SWE value of the supraspinatus and infraspinatus tendons in the freezing phase and of the CHL in the frozen phase were significantly greater on the affected than unaffected side ($P < 0.05$). The posterior capsule in both the freezing and frozen phases and the CHL in the frozen phase were significantly thicker on the affected than unaffected side ($P < 0.01$).

Conclusion: The SWE value of the both supraspinatus and infraspinatus tendons increased in the freezing phase, and that of the CHL also increased in the frozen phase. Not only the change in thickness of the capsule but also the change in stiffness of the rotator cuff may

correlate with frozen shoulder.

Keywords: frozen shoulder; shear wave elastography; rotator cuff; muscle; capsule; ultrasound; stiffness

INTRODUCTION

Frozen shoulder is usually described as a stiff shoulder of unknown cause [1]. The age of affected patients commonly ranges from 40 to 60 years, and patients develop pain and stiffness of their shoulders [2]. Frozen shoulder has been divided into three phases [1]. In the freezing phase, which is the first of the three phases, patients experience severe pain and gradually increasing stiffness. The pain becomes less severe and the stiffness is substantial in the frozen phase. Finally, function is gradually recovered in the thawing phase [2, 3]. In previous studies, some authors reported changes of soft tissues in patients with frozen shoulder, for example the rotator cuff tendons, the long head of the biceps (LHB) [4], the trapezius muscle [5], the capsule [6], the coracohumeral ligament (CHL) [7] and so on. However, how these tissues become stiff in each phase of frozen shoulder remains unclear, and no method to evaluate the changes in stiffness has been established.

Shear wave elastography (SWE) is an ultrasound technique that provides a quantitative measurement of stiffness by evaluating the shear wave propagation speed, which is related to the mechanical properties of soft tissue [8]. SWE is currently used to assess stiffness of skeletal muscles in association with muscular conditions or pathologies in the shoulder joint area, such as the rotator cuff muscle and the shoulder joint capsule [9-12]. Previous studies evaluating shoulder stiffness by elastography were shown in table 1. Studies focused on stiffness of shoulder muscles and tendons had been reported from 2015 and investigated relationship between stiffness and some pathologies. However, few studies have evaluated the mechanical stiffness of the soft tissues in patients with frozen shoulder.

Our hypothesis was that the soft tissues in patients with frozen shoulder are stiff on SWE and that the SWE value of the tissues changes depending on the phase. The purpose of this study was to evaluate the stiffness and morphology of the capsule, rotator cuff tendons and muscles, CHL, and LHB in patients with frozen shoulder using SWE with B-mode ultrasound.

METHODS

This study was designed as prospective cross-sectional study. Forty consecutive patients were recruited from September 2016 to November 2017. All patients had shoulder pain and limitation of passive/active range of motion without abnormal change in X-ray. According to previous studies, limitation of range of motion was defined as <100º in forward flexion, <10º in external rotation, and lower than the L5 level in internal rotation [1]. We defined the freezing phase as contracture with severe pain, and the frozen phase as contracture with moderate pain in this study. Therefore, the patients were divided into two phases, the freezing phase and the frozen phase, based on the Visual Analog Scale (VAS) score. VAS score was consisted of 0 to 10, and 0 was no pain and 10 was the maximum pain. Patients who had severe pain with a score of 6 to 10 points on VAS score were assigned to the freezing phase, and those who had moderate pain with 0 to 5 points were assigned to the frozen phase. The exclusion criteria for this study were a history of a rotator cuff tear, calcific tendinitis, a surgical operation around the shoulder, proximal humeral fracture, neurologic disorder, myopathy, or shoulder pain in either the affected or unaffected shoulder. Eight patients were excluded; four had a partial rotator cuff tear on ultrasound examination, three had a history of shoulder pain in the affected or un affected shoulder, and the other had a history of clavicle surgery on the affected side. Finally, 32 patients with frozen shoulder were enrolled. The mean age of the patients was 59.4 years (range, 44–80 years), and the study population comprised 13 men and 19 women. All patients underwent measurement of stiffness of the soft tissue of the affected and unaffected shoulder, and unaffected side was defined as the control in this study, using SWE. This study was approved by our institutional review board, and written informed consent was obtained from each patient.

Material property by SWE

An ultrasound system (Aixplorer; SuperSonic Imagine, Aix-en-Provence, Cedex, France) and an SL10-2 linear array transducer were used to perform the ultrasound examinations by one shoulder surgeon with 10 years of experience (TW). Patients were seated on the chair with their arms in a relaxed position at 0º of abduction and neutral rotation. Firstly, tissue fibers were detected in the supraspinatus tendon, infraspinatus tendon [13], CHL [14], LHB [15], posterior capsule [12], anterior and posterior deep regions of the supraspinatus muscle [10], infraspinatus muscle, teres minor muscle [15, 16], upper and lower trapezius muscles [5], and posterior, middle, and anterior deltoid muscles [11] using B-mode ultrasound imaging according to previous studies. SWE were showed high reliability of repeatability when the transducer was parallel to the fibers in previous study [9], therefore alignment of the ultrasound probe with the fiber orientation was achieved for all tissues. All muscles were measured at almost middle of the muscles. Finally, stiffness was measured using SWE. Although we attempted to measure the stiffness of the inferior capsule, the patients could not abduct their arms because of pain and contracture of the shoulders in our preliminary experiment. Therefore, we did not include the stiffness of the inferior capsule. The patients internally rotated their arms 30º for measurement of the posterior capsule. The transducer detected the propagation of shear waves, and the ultrasound system determined the shear wave speed in each pixel of the selected tissue. The SWE system in this study was 2D-SWE which could measure the tissue stiffness using conventional ultrasound transducer. The SWE value was calculated in a region of interest (ROI) based on a previously described method [8]. The ROI could be set up with freehand. The ROI in the supraspinatus tendon and the infraspinatus tendon were taken on superior side of the tendons to distinguish only tendons from capsule. The range for SWE value was

0 to 800 KPa. Each SWE value was measured three times, and the mean value was recorded. We tested 10 healthy shoulders (mean age: 31.0 years) and measured inter-observer reliability by two examiners.

B-mode ultrasound

The thickness of the posterior capsule and CHL were also measured using B-mode ultrasound imaging according to previous studies [12, 14]. The patients positioned their arms as for the SWE measurement. The thickness of the posterior capsule was measured 5 mm lateral to the edge of the labrum [12]. The thickness of the CHL was measured 2 mm from the coracoid process [14]. The measurement values were obtained using the software ImageJ (National Institutes of Health, Bethesda, MD, USA).

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 6.0 (GraphPad Software, San Diego, CA, USA). Mann-Whitney tests were used to compare patient age, range of motion and VAS score, and Wilcoxon signed rank tests were used to compare each value between the affected side and unaffected side. Differences were considered statistically significant at $P < 0.05$.

RESULTS

Fifteen patients were in the freezing phase and 17 were in the frozen phase. Five of 15 patients in freezing phase were men and 9 were women. Eight of 17 in frozen phase were men and 9 were women. The mean age of patients was 54.9 years in freezing phase, and 63.4 years in frozen phase. The age in frozen phase was significantly older than freezing phase. The mean Range of motion in forward flexion, external rotation, internal rotation and VAS score are indicated in Table 2 and the mean SWE values in each phase are shown in Table 3. The intra-examiner reliability of SWE by two examiners was satisfactory (ICC (2,1) of 0.992).

Measurement on SWE

The SWE value of the supraspinatus and infraspinatus tendons in the freezing phase were significantly greater on the affected than unaffected side ($P < 0.05$), although there was no significant difference in the frozen phase (Fig. 1). The B-mode and SWE images in the supraspinatus tendon in the freezing phase and the CHL in the frozen phase are shown in Figure 2. The color showed the relative stiffness of the tissues in the SWE images. As stiffness of the tissue increased with SWE value increased, the color changed from blue to greenish-yellow, yellow and red by gradation. On the affected side, the supraspinatus tendon was colored mostly yellow (medium hard) and the CHL was colored yellow and red (hard) on SWE, although those on the unaffected side were blue and greenish yellow (soft). This indicated that the supraspinatus tendon in the freezing phase (yellow) was stiffer than on the unaffected side (blue and greenish-yellow). The CHL in the frozen phase (yellow and red) was also stiffer than those on the unaffected side (blue and greenish-yellow). The SWE value of the CHL in the frozen phase was significantly greater on the affected than unaffected side ($P < 0.05$), although there was no significant difference in the freezing phase (Fig. 1). In contrast, the SWE values of the muscles in the shoulder, LHB, and posterior capsule were not significantly different between the two sides (Fig. 3).

Measurement on B-mode ultrasound

The mean thickness of the posterior capsule in the freezing phase was 1.3 ± 0.2 mm on the affected side and 0.9 ± 0.3 mm on the unaffected side, and that in the frozen phase was 1.2 ± 0.4 mm on the affected side and 0.9 ± 0.3 mm on the unaffected side (Fig. 4). The mean thickness of the CHL in the freezing phase was 3.7 ± 1.0 mm on the affected side and 3.4 ± 0.7 mm on the unaffected side, and that in the frozen phase was 4.4 ± 1.4 mm on the affected side and 3.3 ± 1.1 mm on the unaffected side (Fig. 4). The posterior capsule in both phases and the CHL in the frozen phase was significantly thicker on the affected than unaffected side ($P < 0.01$) (Figs. 4, 5).

DISCUSSION

In the present study, the SWE value of the supraspinatus and infraspinatus tendons increased in the freezing phase and decreased in the next phase. It might show that there was reversible stiffness change in rotator cuff tendons in frozen shoulder. Morikawa et al. suggested that degeneration of the rotator cuff enthesis contributed to increased stiffness in an animal model [17]. Krepkin et al. demonstrated that the SWE value was increased in the degenerated supraspinatus tendon [13]. Ichinose et al. reported that the risk of tendon rupture was increased in rotator cuff tendons with a greater elastic modulus [18]. These studies showed that increased stiffness in the rotator cuff is associated with degeneration. Thus, our results might suggest that SWE detects reversible stiffness change of the rotator cuff that may correlate with frozen shoulder.

However, the SWE value of the CHL on the affected side increased in the frozen phase, and the CHL in the frozen phase was thicker on the affected than unaffected side on B-mode ultrasound imaging. Mengiardi et al. indicated that the CHL became thicker in patients with frozen shoulder using magnetic resonance arthrography, and Homsi et al. showed similar results with using B-mode ultrasound [7, 19]. Moreover, Wu et al. reported that the CHL elastic modulus was larger on the affected than unaffected side of frozen shoulders using SWE [14]. These results are consistent with our findings. However, the previous studies did not show in which phase the CHL was stiffer. Our study may be the first to demonstrate the changes in stiffness in each phase and the change in the CHL stiffness in the frozen phase.

The CHL anatomically extends from coracoid process to the supraspinatus, infraspinatus and subscapularis and spreads beneath the floor of the subacromial bursa and superior side of the capsule [20]. In our study, SWE value of the rotator cuff tendon increased in the freezing phase, and SWE value of the CHL increased and the CHL was thickened in the frozen phase. These data might suggest that stiffness change of the rotator cuff may involve in stiffness and thickness change of the CHL in the patients with frozen shoulder.

Changes in the shoulder joint capsule reportedly contribute to frozen shoulder [6, 19, 21-25]. Global capsular inflammation and synovitis are involved in capsular fibrosis in patients with adhesive capsulitis [6, 21]. A previous ultrasound study showed that the inferior capsule was thicker in the affected than unaffected shoulder [22], and some studies using magnetic resonance imaging and magnetic resonance arthrography also showed thickening of the rotator cuff interval and axillary pouch [19, 23-25]. In the present study, the posterior capsule was significantly thicker on the affected than unaffected side in the freezing and frozen phases. These results are similar to previous studies. Conversely, Takenaga et al. investigated the stiffness of the posterior and posteroinferior capsules in throwing shoulders of healthy college baseball players using SWE and reported that each capsule on the throwing side became stiffer than that on the non-throwing side [12]. In the present study, we performed measurements using their methods. However, the SWE value of the posterior capsule was not significantly different between the affected and unaffected sides. One reason for this might be that it is difficult to accurately measure the stiffness of the posterior capsule using SWE because of the limitation of the SWE machine. Mo et al. indicated that the stiffness could not be measured accurately in thin layers because the shear wave speed measured by SWE decreased when ROI thickness decreased [26]. Moreover, according to the protocol of the SWE machine that we used, the limit of spatial resolution (mean of axial and lateral measures) in this machine was >2 mm. In this study, the mean thickness of the posterior capsule was 1.23 mm; therefore, the stiffness of the posterior capsule could not be measured. In a previous study, the inferior capsule was thicker than about 4 mm in patients with adhesive capsulitis using B-mode ultrasound [22]. It might be possible to measure the SWE value of the inferior capsule with these authors' methods, but further study is needed.

This study has several limitations. First, although the SWE values on the affected side were compared with those on the unaffected side, whether the unaffected side was a truly healthy shoulder remains unclear. It has been reported that 14% of patients with frozen shoulders [27], therefore control in our study had potential becoming frozen shoulder. However, we excluded patients with a history of shoulder pain and who showed rotator cuff injury on ultrasound imaging in the unaffected side. Second, degenerative change should not be an exclusion criteria, since it may be common in middle-aged population. However, this study was investigated the frozen shoulder without abnormal change on the image (like a rotator cuff tear, osteoarthritis, and so on), and clarified an unknown pathological condition of the frozen shoulder. In the future, study included the patients with abnormal change on the image should be also needed. Third, because this study was preliminary, the sample size was small. Fourth, the patients were divided into the freezing and frozen phase according to only VAS score in this study, because there was no clear classification divided into two phases in frozen shoulder. Finally, this was a cross-sectional study, and the changes in stiffness with time were unclear. We plan to verify the changes in stiffness in a future longitudinal study.

CONCLUSION

The SWE value of the both supraspinatus and infraspinatus tendon increased in the freezing phase, and that of the CHL also increased in the frozen phase. The posterior capsule was thicker on the affected side on B-mode ultrasound imaging in both phases. Because the rotator cuff tendon became stiffer in the early phase, not only the change in thickness of the capsule but also the change in stiffness of the rotator cuff may correlate with frozen shoulder.

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Tables

Author	Year	Machine	Technique	Inference of study
Itoigawa et al.	2015	SuperSonic	SWE	Elasiticity of the supraspinatus muscle.
Hatta et al.	2015	SuperSonic	SWE	Reliability of the supraspinatus muscle.
Wu et al.	2015	SuperSonic	SWE	Elasiticy of the CHL in adhesive capsulitis.
Takenaga et al.	2015	SuperSonic	SWE	Stiffness of the posterior and posteroinferior capsule in baseball player.
Muraki et al.	2015	Hitachi-Aloka	strain	Elasiticity of the supraspinatus muscle and tendon.
Ishikawa et al.	2015	Hitachi-Aloka	strain	Association between the activity and elasticity of muscles around shoulder.
Hatta et al.	2016	SuperSonic	SWE	Elasiticity of the supraspinatus muscle after rotator cuff repair.
Hatta et al.	2016	SuperSonic	SWE	Reliabolity of the deltoid muscle.
Leong et al.	2016	Supersonic	SWE	Stiffness of upper trapezius in athletes with rotator cuff tendinopathy.
Hatta et al.	2016	SuperSonic	SWE	Elasiticity of the supraspinatus muscle after the margin convergence technique.
Yamauchi et al.	2016	SuperSonic	SWE	Effect of stretching to measure elasiticy of muscles around shoulder.
Rosskopf et al.	2016	Siemens	SWE	Reliability of the supraspinatus muscle.
Lee et al.	2016	Toshiba	strain	Association between MRI tendinosis grade and stiffness in supraspinatus tendon.
Kusano et al.	2017	SuperSonic	SWE	Effect of stretching to measure elasiticy of infraspinatus muscle.
Hatta et al.	2017	SuperSonic	SWE	Correlation between extensibility and elasiticity of the supraspinatus muscle.
Fukuyoshi et al.	2017	SuperSonic	SWE	Elasiticity of the anteroinferior labrum after arthroscopic Bankert repair.
Umehara et al.	2017	SuperSonic	SWE	Effect of stretching to measure elasiticy of muscles around shoulder.
Hou et al.	2017	Siemens	SWE	The Rotator cuff tendon softning in rotator cuff desease.
Krepkin et al.	2017	Siemens	SWE	Association between MRI T2/T2* mapping and elasiticity in the supraspinatus tendon.
Baumer et al.	2017	Siemens	SWE	Reliability of the supraspinatus muscle and tendon.
Dischler et al.	2017	Siemens	SWE	The supraspinatus mussle elasticity in competitive swimers.
Gilbert et al.	2017	Siemens	SWE	Correlation with fatty degenaration using MRI in the supraspinatus muscle.
Itoigawa et al.	2018	SuperSonic	SWE	Correlation between extensibility and elasiticity of the supraspinatus muscle.
Gimbini et al.	2018	SuperSonic	SWE	Correlation between extensibility and elasiticity of the supraspinatus muscle.
Nishishita et al.	2018	SuperSonic	SWE	Effect of stretching to measure elasiticy of the supraspinatus muscle.
Baumer et al.	2018	Siemens	SWE	Association between age and elasticity of the rotator cuff.
Kim et al.	2018	Toshiba	strain	Correlation with muscle activity around shoulder.
Demirel et al.	2018	Toshiba	strain	Elasiticity of the supraspinatus muscle in impingement syndrome.
Yuri et al.	2018	Hitachi-Aloka	strain	Elasiticity of the supraspinatus muscle.
Yuri et al.	2018	Hitachi-Aloka	strain	Correlation with fatty degenaration using MRI in the supraspinatus muscle.

Table 1: Previous studies about evaluating shoulder stiffness using elastography.

SWE: shear wave elastography

	Freezing phase	Frozen phase	P value
Age (y)	54.9 ± 9.8	63.4 ± 8.1	< 0.05
Forward flexion (°)	90.3 ± 9.2	91.2 ± 7.6	0.91
External rotation (°)	4.0 ± 6.6	2.6 ± 5.6	0.45
Internal rotation	Buttock level	Buttock level	0.38
Visual Analog Scale	7.5 ± 0.8	2.9 ± 1.7	< 0.01

Table 2: The mean of age, range of motion and Visual Analog Scale in the frozen and freezing phases.

		Freezing phase			Frozen phase		
		unaffected side (Kpa)	affected side (KPa)	* (P < 0.05)	unaffected side (KPa)	affected side (Kpa)	
SSp tendon		178.1 ± 73.3	280.4 ± 125.3	*	244.3 ± 100.9	245.0 ± 76.0	
ISp tendon		240.8 ± 91.5	318.4 ± 110.7	*	285.7 ± 88.5	268.8 ± 116.6	
posterior capsule		82.4 ± 73.9	123.8 ± 99.7		96.0 ± 119.2	96.9 ± 99.3	
CHL		239.9 ± 113.8	270.3 ± 142.5		214.1 ± 91.1	287.2 ± 135.3	*
LHB		194.3 ± 98.8	210.3 ± 103.2		233.3 ± 119.4	241.2 ± 113.6	
SSp muscle	AD	25.4 ± 7.6	27.9 ± 9.0		22.5 ± 8.2	21.8 ± 6.5	
	PD	25.6 ± 9.1	24.7 ± 10.7		22.4 ± 10.1	18.9 ± 4.9	
Trapezius	Upper	65.2 ± 22.6	58.1 ± 23.3		55.7 ± 22.8	63.5 ± 19.7	
	Lower	20.6 ± 13.6	26.2 ± 17.5		24.2 ± 12.8	21.7 ± 17.1	
ISp muscle		19.8 ± 4.8	20.5 ± 9.7		21.5 ± 9.1	18.5 ± 4.9	
Teres minor		37.8 ± 23.8	37.7 ± 25.9		28.0 ± 13.9	24.6 ± 6.7	
Deltoid	Posterior	24.5 ± 10.6	26.7 ± 13.1		28.5 ± 15.3	28.9 ± 21.8	
	Middle	26.5 ± 8.5	31.4 ± 10.2		37.8 ± 23.6	24.5 ± 4.9	
	Anterior	25.6 ± 8.0	26.4 ± 12.3		31.7 ± 13.1	27.2 ± 11.3	

Table 3: Shear wave elastography values in the freezing and frozen phases.

SSp: supraspinatus, ISp: infraspinatus, CHL: coracohumeral ligament, LHB: long head of the biceps, AD: anterior deep region, PD: posterior deep region

Figures

Figure 1: The mean (±SD) shear wave elastography (SWE) values of the rotator cuff tendon and other surrounding tissues in the freezing and frozen phases.

The SWE value of the supraspinatus and infraspinatus tendon in the freezing phase and the CHL in the frozen phase were significantly greater on the affected (gray histogram) than unaffected side (white histogram, $*P < 0.05$).

SSp: supraspinatus, ISp: infraspinatus, CHL: coracohumeral ligament, LHB: long head of the biceps

Figure 2: B-Mode ultrasound and shear wave elastography (SWE) images of (a) the supraspinatus tendon in the freezing phase and (b) the coracohumeral ligament in the frozen phase.

On the affected side, the supraspinatus tendon was colored mostly yellow and the coracohumeral ligament (white arrow) was colored yellow and red on SWE, although those on the unaffected side were blue and greenish yellow. This indicates that the

supraspinatus tendon and coracohumeral ligament were stiff.
T: supraspinatus tendon, H: humeral head, G: greater tuberosity, C: coracohumeral ligament

Figure 3: Shear wave elastography (SWE) values of muscles and other tissues in shoulder in freezing and frozen phases.

The SWE values were not significantly different between the two phases.
SSp: supraspinatus, ISp: infraspinatus, AD: anterior deep, PD: posterior deep, P: posterior, M: middle, A: anterior

Figure 4: (a) Thickness of the posterior capsule and (b) coracohumeral ligament in the freezing and frozen phase.

The posterior capsule in both phases and the coracohumeral ligament in the frozen phase were significantly thicker on the affected than unaffected side ($P < 0.01$).

Figure 5: Thickness of the posterior capsule on the affected and unaffected side on B-mode ultrasound imaging.

The posterior capsule (between white arrows) was thicker on the affected than on the unaffected side.
G: glenoid, H: humeral head

Fig. 1

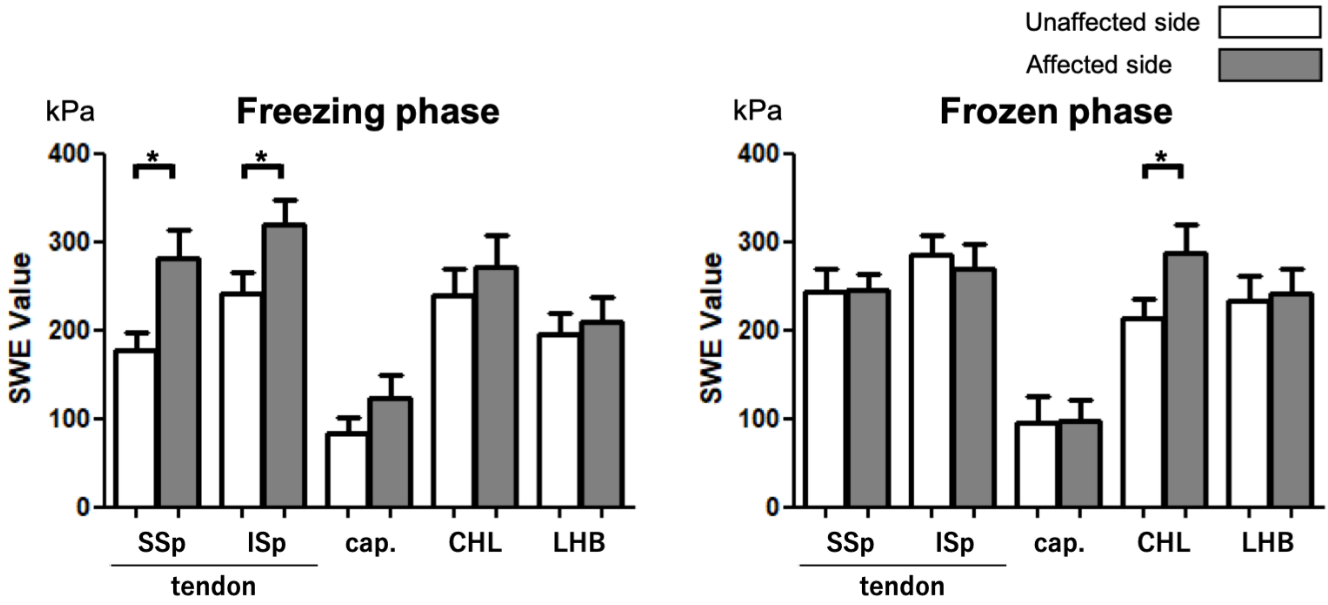
Unaffected side
Affected side
kPa
Freezing phase
400
300
200
100
0
SWE Value
*
*
SSp
ISp
cap.
CHL
LHB
tendon
kPa
Frozen phase
400
300
200
100
0
SWE Value
*
SSp
ISp
cap.
CHL
LHB
tendon

Fig. 2

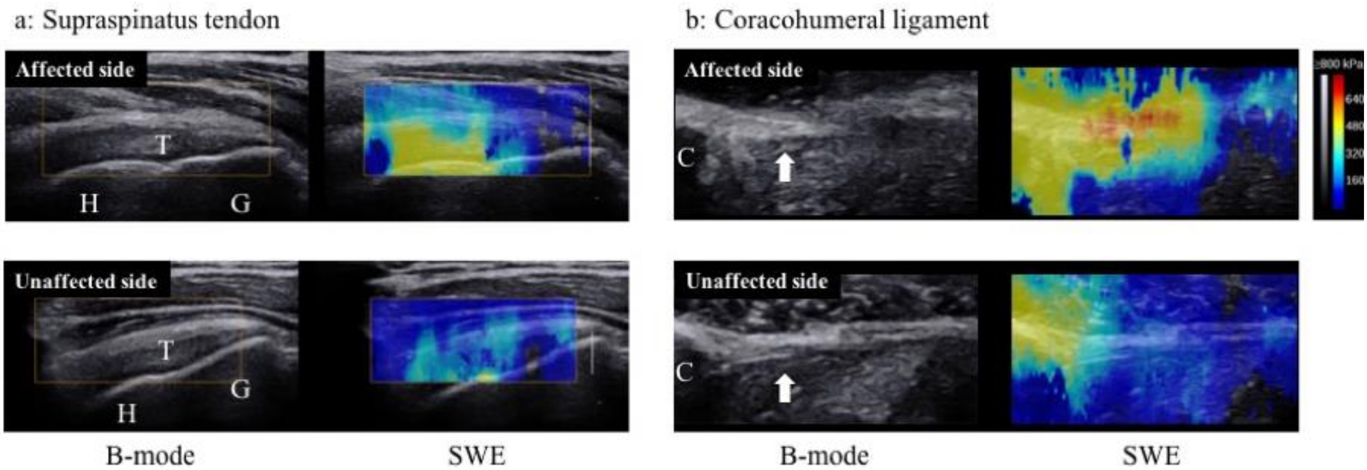
a: Supraspinatus tendon
b: Coracohumeral ligament
Affected side
T
H
G
C
Unaffected side
T
G
H
C
B-mode
SWE
B-mode
SWE

Fig. 3

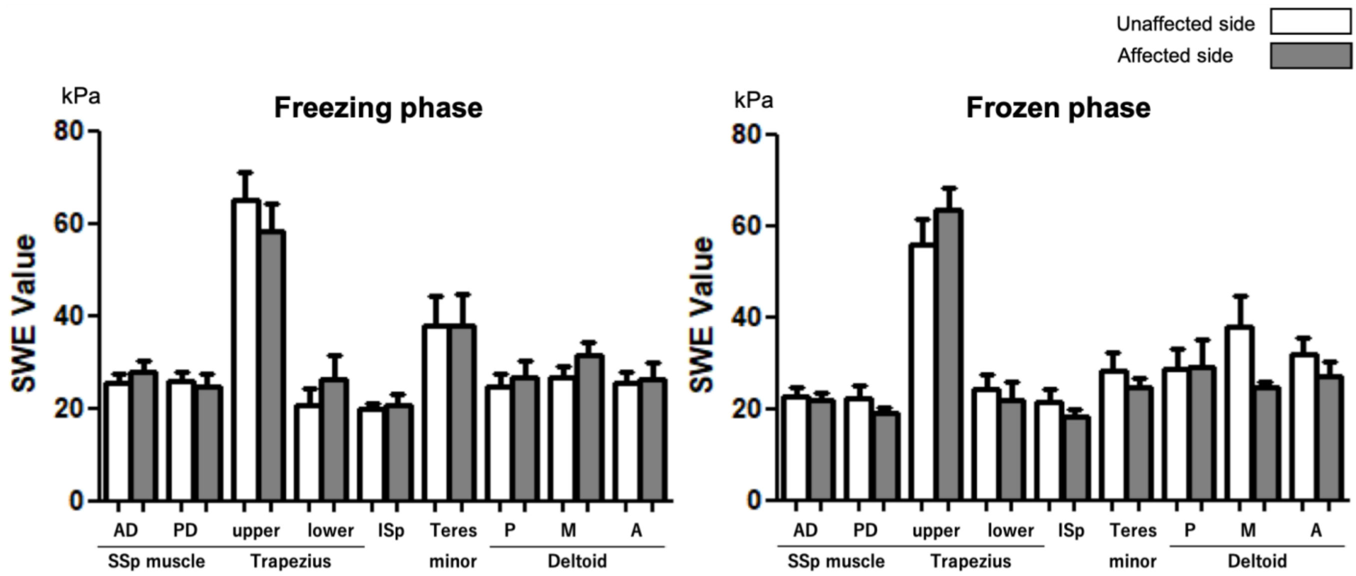

Fig. 4

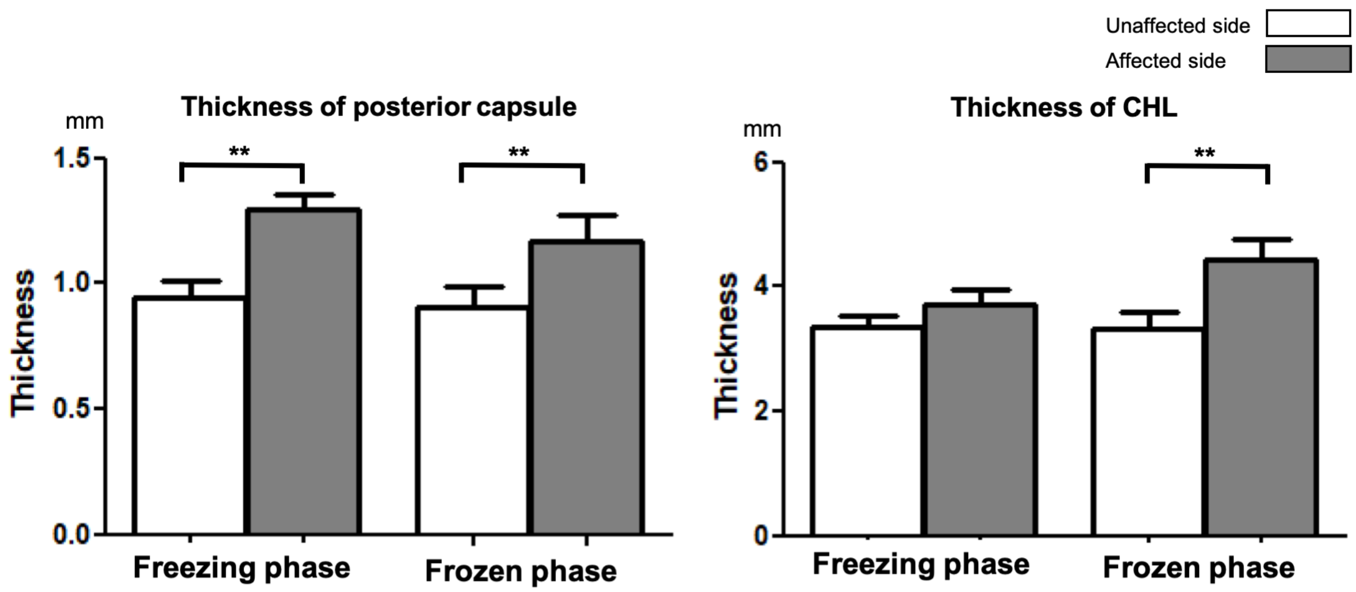

Fig. 5