Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology 14 (2018) 17–21

Contents lists available at ScienceDirect

Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology

journal homepage: www.ap-smart.com

Original Article

Mechanoreceptor profile of the lateral collateral ligament complex in the human elbow

Erica Kholinne [a, e], Hyun-Joo Lee [b], Yu-Mi Lee [c], Suk-Joong Lee [d], Maria F. Deslivia [a], Ga-Yeong Kim [e], SungJoon Lim [e], In-Ho Jeon [e, *]

[a] Department of Orthopedic Surgery, St. Carolus Hospital, Jakarta, Indonesia
[b] Department of Orthopaedic Surgery, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, Republic of Korea
[c] Department of Preventive Medicine, School of Medicine, Kyungpook National University, Republic of Korea
[d] Department of Orthopedic Surgery, Keimyung University, Dongsan Medical Center, Daegu, Republic of Korea
[e] Department of Orthopedic Surgery, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea

ARTICLE INFO

Article history:
Received 25 December 2017
Received in revised form
9 March 2018
Accepted 9 April 2018
Available online 18 May 2018

Keywords:
Mechanoreceptor
Lateral collateral ligament complex
Elbow
Human

ABSTRACT

Background: Active restraint for the elbow joint is provided by the soft tissue component, which consists of a musculoligamentous complex. A lesion of the lateral collateral ligament complex (LCLC) is thought to be the primary cause of posterolateral rotatory instability in the elbow. Its role as a protective reflexogenic structure is supported by the existence of ultrastructural mechanoreceptors. The aim of this study was to describe the existence and distribution of LCLC mechanoreceptors in the human elbow joint and to determine their role in providing joint stability.
Methods: Eight LCLCs were harvested from fresh frozen cadaver elbows. Specimens were carefully separated from the lateral epicondyle and ulna. The ligament complex was divided into 7 regions of interest and stained with modified gold chloride. Microscopic evaluation was performed for Golgi, Ruffini, and Pacinian corpuscles. The number, distribution, and density of each structure were recorded.
Results: Golgi, Ruffini, and Pacinian corpuscles were observed in LCLCs, with variable distribution in each region of interest. Ruffini corpuscles showed the highest total mechanoreceptor density. Mechanoreceptor density was higher at bony attachment sites.
Conclusion: The existence and role of each mechanoreceptor defined the purpose of each region of interest. Mechanoreceptors are beneficial for its proprioceptive feature towards a successful elbow ligament reconstruction.

Introduction

A lesion of the lateral collateral ligament complex (LCLC) is thought to be the primary cause of posterolateral rotatory instability of the elbow.[1] The functional properties of such protective mechanisms are supported by the existence of mechanoreceptors embedded in their structure.[2–5] Active restraint for the elbow joint is provided by the soft tissue component, which consists of the musculoligamentous complex.[1] Many authors[6–10] have provided information on the mechanoreceptors of the shoulder, knee, and ankle, which are less stable and thus protected by many ligaments and a thick capsule. However, the role of the ligament-muscular protective reflex of the elbow has not recently been considered due to its stable bony structure. Studies have been performed on mechanoreceptors in the elbow ligaments in felines and humans.[11,12] One study that evaluated the mechanoreceptors in the human elbow joint[11] failed to describe their spatial arrangement.

The purpose of this study was to determine the distribution of mechanoreceptors in the human elbow LCLC, i.e., the location of each mechanoreceptor and morphological evidence for LCLC reconstruction. Our hypotheses were as follow: 1) Bony attachment sites have higher mechanoreceptor density, and 2) the mechanoreceptor density at bony attachment sites is higher at the ulna compared to the radius.

---

* Corresponding author. Department of Orthopaedic Surgery, University of Ulsan, Asan Medical Center, 86 Asanbyeongwon-gil, Songpa-gu, Seoul, 138-736, Republic of Korea.

E-mail address: jeonchoi@gmail.com (I.-H. Jeon).

https://doi.org/10.1016/j.asmart.2018.04.001

Materials and methods

Cadaver dissection and specimen preparation

Institutional Board Review exemption were obtained for this study. Eight elbow joints from four fresh frozen cadavers were included in this study. Two were male with a mean age of 69 years (range, 56–79). LCLCs were harvested within 12 h after cadavers were thawed at room temperature. The ligament complex were carefully isolated from the surrounding muscle and capsule attachment. The dissection was carefully performed taking care not to damage the ligaments and preserving all portions. The attachment to the bone was peeled off. After dissection, the specimens were immersed in neutral pH, 4% paraformaldehyde solution. After at least 24 h of fixation, LCLCs were divided into 7 regions of interest with similar areas in each region (Fig. 1).

Modified gold chloride staining

A modified gold chloride staining method was applied to the specimens.[13] Vials consisting of fresh lemon juice and 98% formic acid solution in a 3:1 ratio were prepared. The vials were transferred and shaken (Penetron Swirling Shaker Model Mark IV, SPI Supplies, Sunkay Laboratories, Tokyo, Japan) inside a fume hood (A-MB-1200TYPE; DH science, Daejeon, Korea) for 30 min. Gold chloride solution (gold chloride solution 200 mg/dL in deionized water, HT1004; Sigma-Aldrich, MO, USA) was poured into the solution vials and then processed with a shaker for 90 min. This process was repeated for subsequent batches with recycled gold chloride solution from previous batches by using a filtering process. The gold chloride solution was subsequently discarded and specimens were soaked in 2.5% formic acid solution and processed with a shaker for at least another 12 h. Specimens were repeatedly washed clean of gold chloride solution 3 times with running distilled water for 5 min. Each specimen was then transported to a conical tube prefilled with 30% sucrose solution and stored at 4 °C for 1–2 days. After a specimen sank to the conical tube bottom, it was then transferred to a new vial containing 30% sucrose and optimum cutting temperature compound (OCT). These vials were then processed with a shaker for 2 h. Once this process finished, the stained specimens were embedded in 30% sucrose and OCT compound in a 3:2 ratio and frozen according to a previous technique.[14] Frozen specimens were sectioned parallel to their longitudinal (horizontal) axis and perpendicular to their vertical axis with a cryosectioning machine (Leica CM3050-S Research Cryostat; Leica Biosystems, Nussloch, Germany) at 30-μm thickness and attached to a microscope glass slide.

Microscopic examination

Inverted light microscopy was used for mechanoreceptor observation. The Freeman and Wyke classification and Hagert et al. modification were used to evaluate types and numbers of Golgi, Ruffini, and Pacinian corpuscles.[15,16]

The slides were first examined under low-power magnification (100×) and subsequently at higher magnification (200×) in order to identify each receptor. Mechanoreceptor structure was evaluated on previous slides and lateral serial slides to determine whether the structures were consistently present. A confirmed structure was counted as one unit. Discontinuous objects with uncertain or doubtful morphology were not counted. We reconfirmed each structure using 400 × magnification in order to minimize any misreading or potential bias that might alter quantification. Mechanoreceptors were evaluated and recorded according to their bony attachment at the humeral, ulnar, or radial site, and at the ligament mid-substance.

Density calculation

To measure ligament volume, we customized software that automatically measured the dimension of each ligament fragment. The volume on one slide was multiplied by 30 μm to determine the total dimension. The volume of each compartment was calculated. The density was defined as the number of mechanoreceptors

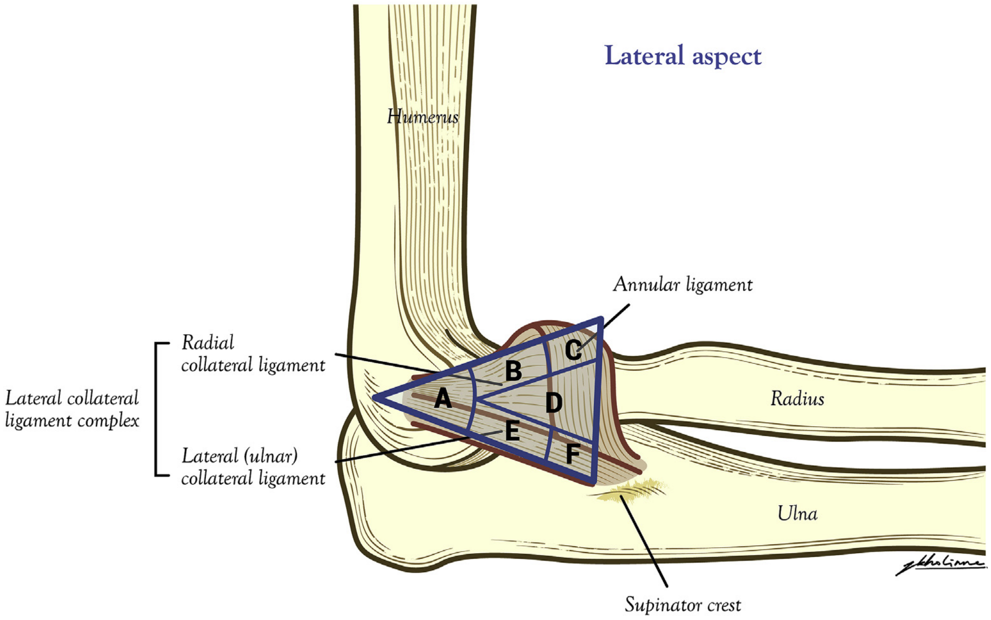

Fig. 1. Topographic diagram showing 7 regions of interest in the LCLC.
A: Humeral bony attachment; B: Radial collateral ligament mid-substance; C: Radial bony attachment and annular ligament; D: Inter-ligament mid-substance; E: Lateral ulnar collateral ligament mid-substance; F: Ulnar bony attachment.

divided by the unit volume (unit/cm^3). Density was compared between bony attachment and mid-substance, annular ligament and mid-substance, and between individual bony attachment sites (humeral, radial and ulnar site). The bony attachment of the radial collateral ligament (RCL) was represented by the annular ligament.

Statistical analysis

The Kruskal-Wallis test was used to evaluate the dominant receptor in the LCLC. Posttest analysis was performed using Dunn's test. Density evaluation comparing bony attachment sites and mid-substance, and annular ligament and mid-substance, was performed using the Wilcoxon signed-rank test. Posttest study for each bony attachment site was performed using the Friedman test.

Result

We observed Ruffini, Pacinian, and Golgi corpuscles in the LCLC (Figs. 2–4).

All mechanoreceptors were embedded in the ligament substance. Most were surrounded by loose connective synovial tissue and medium-to-large vessels. Free nerve endings were observed closely for ultrastructure.

Density of mechanoreceptors

1. Median total corpuscle density was higher at bony attachment sites than at mid-substance sites; however, the difference was not statistically significant (p value > 0.05). In addition, Golgi corpuscles at mid-substance sites showed higher density than at bony attachment sites (Table 1).
2. Median total corpuscle density was higher at the annular ligament compared to mid-substance, with no statistically significant difference ($p > 0.05$). For each corpuscle, the results are shown in Table 2.
3. Posttest results revealed no significant difference between each bony attachment site (humeral, radial, and ulnar site), as shown in Table 3.

Discussion

Stability of the elbow joint depends on both osteoligamentous and muscular structures. The elbow is a trochleogingylomoid -hinged joint, with naturally stable morphology. Both lateral and medial ligamentous complexes add some stability to the elbow joint against varus and valgus forces.[17] Ultrastructural components such as mechanoreceptors provide reflexogenic protection for the elbow joint. Mechanoreceptors are transducers of unit-converting stimuli (nerve signal) from one system to another. This stimulus is not solely single but rather a repetitive wave pattern discharge when the mechanoreceptor is stimulated. The process of transmission of a mechanical stimulus to an electrical response is important for kinesthesis and joint proprioception.[9,18] The role of mechanoreceptors has been extensively studied in the knee because it is the most mobile joint.

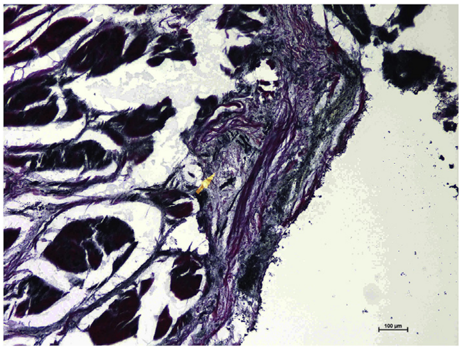

Fig. 2. The Ruffini corpuscle is coil-shaped with partial encapsulation. It has arborizing nerve branches with bulbous terminals. It is a low threshold and slow-adapting mechanoreceptor (magnification 200×).

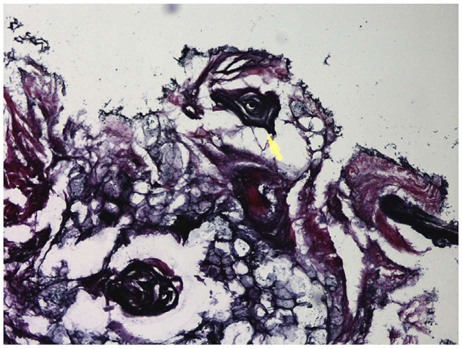

Fig. 3. The Pacinian corpuscle was observed as a rounded, ovoid corpuscle with a thick lamellar capsule. It has low threshold and rapidly adapting mechanoreceptor characteristics, and was embedded in ligament fibers (magnification 200×).

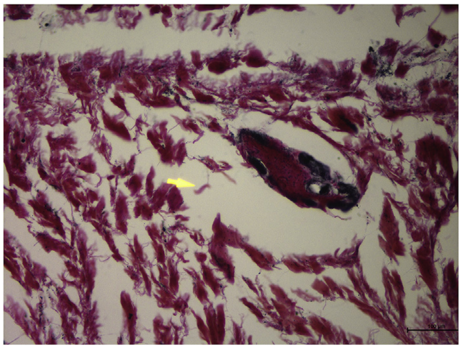

Fig. 4. The Golgi corpuscle is large and spherical with partial encapsulation. It comprises a group of arborizing dendritic receptors, and is a high-threshold, rapidly-adapting mechanoreceptor (magnification 200×).

The existence of mechanoreceptors has been reported in the elbow joint but the distribution and spatial arrangement have not been adequately described.[11,12] Our study described both distribution and density based on region of interests for each type of mechanoreceptors. Density is important because it represents a functional map, rather than simple anatomy.

We found that Ruffini corpuscles showed the highest density all LCLCs. Ruffini corpuscles are always active, even when the joint is static. This slow-adapting corpuscle will signal static joint position, changes in intra-articular pressure, and the direction, amplitude, and velocity of joint movements. This corpuscle also regulates reflex changes over muscle tone in a continuous or tonic flow. Any extreme torque within the joint caused by extension, flexion, and rotation will signal Ruffini corpuscles.[9] All of these features are important for joint positioning and protection. Ruffini corpuscles are found to function in combination with Pacinian corpuscles. Pacinian corpuscles will signal mechanical stimuli at the onset or cessation of a movement.[19] Unlike Ruffini corpuscles, Pacinian corpuscles are rapid-adapting. They respond to acceleration, quick joint movement, and vibration. The end result is a brief reflex change over muscle tone acting around the joint, analogous to an

Table 1
Density of mechanoreceptors at bony attachment sites compared to mid-substance sites.

Location	Mechanoreceptors			
	Golgi corpuscle	Ruffini corpuscle	Pacinian corpuscle	Total
Bony attachment (Range)	3.9 (1.8–7.3)	9.8 (9.4–10.0)	3.2 (0–4.2)	16.0 (13.0–20.8)
Mid-substance (Range)	6.8 (3.7–8.6)	4.0 (2.8–11.0)	0 (0–3.7)	11.4 (10.2–18.4)
p-value	0.375	0.250	0.500	0.125

Table 2
Density of mechanoreceptors at mid-substance sites compared to the annular ligament.

Location	Mechanoreceptors			
	Golgi corpuscle	Ruffini corpuscle	Pacinian corpuscle	Total
Mid-substance (Range)	6.8 (3.7–8.6)	4.0 (2.8–11.0)	0 (0–3.7)	13.2
Annular ligament (Range)	0 (0.0–0.0)	11.5 (8.0–12.8)	0 (0.0–0.0)	17.3
p-value	0.063	0.625	–	0.250

Table 3
Comparison between mechanoreceptors at each bony attachment site.

Location	Mechanoreceptors			
	Golgi corpuscle	Ruffini corpuscle	Pacinian corpuscle	Total
Humerus	4.3	14.2	2.9	21.1
(Range)	(1.5–9.1)	(12.2–16.2)	(0–4.6)	(15.3–27.4)
Ulna	8.4	8.2	9.6	19.9
(Range)	(6.2–13.6)	(0–13.6)	(0–13.6)	(18.5–40.7)
Radius	0	14.1	0	14.17
(Range)	(0.0–0.0)	(8.2–19.1)	(0.0–0.0)	(8.2–19.1)
p-value	0.039	0.472	0.050	0.174

accelerator and brake pedal. Once the joint moves, an action potential will cease until it reaches a plateau or rests.[20] The concurrent equilibrium action between the two receptors is important for joint stabilization. In our study, the two corpuscles showed the highest density at bony attachments, especially at the humeral site. This is explained by its function as a conjoint bony attachment for merged RCL and lateral ulnar collateral ligament (LUCL) structures. These will transmit signals from their bony attachment sites to execute an efferent signal for the joint to move or halt. Hence, anatomic and careful bony site attachment preservation in LCLC reconstruction should never be underestimated for this reason. Among all bony site attachments, mechanoreceptors are the lowest in density at the radial site. This indicates that humero-ulnar soft tissue plays a greater role as a stabilizer compared with the radial site. The broad LUCL footprint at the supinator crest compared to that of the RCL have may value for this reason. However, prevention of posterolateral rotatory instability inevitably involves both the LUCL and RCL.[1,17] The other possible reason is that the radial bony attachment site is a merger between the RCL and annular ligament. This is still not solely a bony attachment but rather a transition from one ligament to another.

Golgi corpuscles were mostly found in the mid-substance. When present solely in the joint ligaments, these high-threshold receptors are responsible for tension, joint position, and movement direction. They are not stimulated unless extreme degrees of joint displacement occur. Golgi corpuscles act as reflex inhibitors to motor unit activity over the joint.[19]

The annular ligament is a broad extension of the RCL, encircling the radial head and docked to the sigmoid notch. It acts in unison with the proximal radio-ulnar joint in stabilizing the radial head.[16,21] Ruffini corpuscles were shown to be present in this structure at higher density than at the mid-substance site. This supported the role of the annular ligament as a radial head stabilizer.

In an anterior cruciate ligament (ACL) study, Pacinian and Golgi corpuscles were found to be more numerous than Ruffini corpuscles. Being a very mobile and non-hinged joint, the knee is more prone to extreme position changes, fast acceleration, and deceleration compared to the hinged trochleogingylomoid elbow joint. It is understandable why Pacinian corpuscles, which function in quick response and velocity control and Golgi corpuscles, which function in reflex inhibition control, are most numerous in the ACL.[19] Therefore, we postulated that the ratios between mechanoreceptors depend on the specific type of joint. However, whether these ratios are altered in certain repetitive activities, such as playing baseball, are still unclear.

Our study results should remind every surgeon to reconstruct elbow ligaments from both biomechanical and histological perspectives. Anatomic reconstruction to a bony attachment will increase the likelihood of mechanoreceptor recovery. Hence, this will result in a stable reconstructed elbow joint.

There are several limitations in our study. Our small number of cadavers from various age groups may have under-powered the study. Nevertheless, a pilot study will not require traditional power and statistical analysis.[22] The age of cadavers and time from death to fixation were also potential confounding factors. Several studies showed an age effect. A postmortem period of several hours before freezing also influences the shape and number of mechanoreceptors due to necrosis.[23] The other limitation is that we did not use control staining methods such as hematoxylin-eosin or immunereactive stains because the entire specimen was stained with gold chloride to determine the distribution of mechanoreceptors. In future studies, other staining methods should be used to compare these results. However, our study highlighted several new findings such as the study was valuable for the large volume of specimens observed and the clinical implications for LCLC reconstruction.

Conclusions

The existence and role of each mechanoreceptor defined the purpose of each region of interest. Besides its major property as proprioceptive apparatus, mechanoreceptors play a role in ligamentization for successful reconstruction, particularly at bony attachment sites.

Author contributions

EK contributed to the study concept and design, data analysis, and drafting of the manuscript. HJL, SJL, MFD, GYK, SJL contributed to the study design and drafting of the manuscript. YML contributed to statistical analysis. IHJ contributed to the study design and critical revision of the manuscript.

Conflicts of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding and support statement

We appreciate the support from the Global Frontier R&D Program on Human-centered Interaction for Coexistence and funding by the National Research Foundation of Korea via the Korean Government (MSIP) (grant no. 2017–0522).

Acknowledgments

We thank Jessica Kholinne, B.Des. (Glitch Network, Jakarta, Indonesia) for the medical illustrations.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.asmart.2018.04.001.

References

1. Dunning CE, Zarzour ZD, Patterson SD, Johnson JA, King GJ. Ligamentous stabilizers against posterolateral rotatory instability of the elbow. *J Bone Jt Surg Am*. 2001;83-A(12):1823–1828.
2. Ekholm J, Eklund G, Skoglund S. On the reflex effects from the knee joint of the cat. *Acta Physiol Scand*. 1960;50:167–174.
3. Kim AW, Rosen AM, Brander VA, Buchanan TS. Selective muscle activation following electrical stimulation of the collateral ligaments of the human knee joint. *Arch Phys Med Rehabil*. 1995;76(8):750–757.
4. Palmer I. Pathophysiology of the medical ligament of the knee joint. *Acta Chir Scand*. 1958;115(4):312–318.
5. Solomonow M, Baratta R, Zhou BH, et al. The synergistic action of the anterior cruciate ligament and thigh muscles in maintaining joint stability. *Am J Sports Med*. 1987;15(3):207–213.
6. Schultz RA, Miller DC, Kerr CS, Micheli L. Mechanoreceptors in human cruciate ligaments. A histological study. *J Bone Joint Surg Am*. 1984;66(7):1072–1076.
7. Skoglund S. Anatomical and physiological studies of knee joint innervation in the cat. *Acta Physiol Scand Suppl*. 1956;36(124):1–101.
8. Wu X, Song W, Zheng C, Zhou S, Bai S. Morphological study of mechanoreceptors in collateral ligaments of the ankle joint. *J Orthop Surg Res*. 2015;10:92.
9. Zimny ML, Wink CS. Neuroreceptors in the tissues of the knee joint. *J Electromyogr Kinesiol Off J Int Soc Electrophysiol Kinesiol*. 1991;1(3):148–157.
10. Witherspoon JW, Smirnova IV, McIff TE. Neuroanatomical distribution of mechanoreceptors in the human cadaveric shoulder capsule and labrum. *J Anat*. 2014;225(3):337–345.
11. Petrie S, Collins JG, Solomonow M, Wink C, Chuinard R, D'Ambrosia R. Mechanoreceptors in the human elbow ligaments. *J Hand Surg*. 1998;23(3):512–518.
12. Phillips D, Petrie S, Solomonow M, Zhou BH, Guanche C, D'Ambrosia R. Ligamentomuscular protective reflex in the elbow. *J Hand Surg*. 1997;22(3):473–478.
13. O'Connor BL, Gonzales J. Mechanoreceptors of the medial collateral ligament of the cat knee joint. *J Anat*. 1979;129(Pt 4):719–729.
14. Witherspoon JW, Smirnova IV, McIff TE. Improved gold chloride staining method for anatomical analysis of sensory nerve endings in the shoulder capsule and labrum as examples of loose and dense fibrous tissues. *Biotech Histochem Off Publ Biol Stain Commission*. 2014;89(5):355–370.
15. Freeman MA, Wyke B. The innervation of the knee joint. An anatomical and histological study in the cat. *J Anat*. 1967;101(Pt 3):505–532.
16. Hackl M, Wegmann K, Ries C, Lappen S, Scaal M, Muller LP. Annular ligament reconstruction with the superficial head of the brachialis: surgical technique and biomechanical evaluation. *Surg Radiol Anat SRA*. 2017;39(6):585–591.
17. O'Driscoll SW, Bell DF, Morrey BF. Posterolateral rotatory instability of the elbow. *J Bone Joint Surg Am*. 1991;73(3):440–446.
18. Macefield VG. Physiological characteristics of low-threshold mechanoreceptors in joints, muscle and skin in human subjects. *Clin Exp Pharmacol Physiol*. 2005;32(1-2):135–144.
19. Zimny ML. Mechanoreceptors in articular tissues. *Am J Anat*. 1988;182(1):16–32.
20. Rowe MJ, Tracey DJ, Mahns DA, Sahai V, Ivanusic JJ. Mechanosensory perception: are there contributions from bone-associated receptors? *Clin Exp Pharmacol Physiol*. 2005;32(1-2):100–108.
21. Anderson A, Werner FW, Tucci ER, Harley BJ. Role of the interosseous membrane and annular ligament in stabilizing the proximal radial head. *J Shoulder Elbow Surg*. 2015;24(12):1926–1933.
22. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. *J Psychiatr Res*. 2011;45(5):626–629.
23. Aydog ST, Korkusuz P, Doral MN, Tetik O, Demirel HA. Decrease in the numbers of mechanoreceptors in rabbit ACL: the effects of ageing. *Knee Surg Sports Traumatol Arthrosc Off J ESSKA*. 2006;14(4):325–329.