Sufficient Cartilage for Most Talar Articular Defects Can Be Harvested From the Non–Loadbearing Talus: A Cadaveric Analysis



Michael C. O'Brien, B.S., M.A., Wojciech K. Dzieza, B.S., Michelle L. Bruner, M.S., and Kevin W. Farmer, M.D.

Purpose: To assess the quantity of morselized cartilage that can be harvested from the non-load-bearing portion of the talus for immediate reimplantation. **Methods:** Non-load-bearing talar cartilage was harvested from 5 cadaveric specimens using a standard arthroscopic approach. Cartilage was separated from the talus in maximum dorsiflexion at the junction of the talar head and neck, grasped, and morselized into a graft using a cartilage particulator. The volume of reclaimed cartilage was measured, and the extrapolated area of coverage was compared to average osteochondral lesions of the talus previously reported. **Results:** The total yield of cartilage graft following processing that was obtained from 5 ankle joints ranged from 0.3 mL to 2.1 mL with a mean volume of 1.3 ± 0.7 mL, yielding a theoretical 13.2 ± 7.1 cm² coverage with a 1-mm monolayer. While the average size of osteochondral lesions of the talus is difficult to estimate, they may range from 0.5 cm² to 3.7 cm² according to the literature. **Conclusions:** This study validated that it is possible to harvest sufficient amount of cartilage for an autologous morselized cartilage graft via a single-stage, single-site surgical and processing technique to address most talar articular cartilage defects. **Clinical Relevance:** Particulated cartilage autografts have shown promise in surgical management of cartilage defects. A single-site, single-staged procedure that uses a patient's autologous talar cartilage from the same joint has the potential to reduce morbidity associated with multiple surgical sites, multistaged procedure, or nonautologous tissue in ankle surgery.

Osteochondral lesions of the talus (OLTs) are defined as defects in the cartilage overlying the articular surface as well as subchondral bone of the talus. They most commonly occur following ankle trauma, leading to greater prevalence among athletes, active-duty service members, and active populations.^{1,2} Less frequently, lesions result secondary to chronic conditions, such as degenerative joint disease, joint malalignment, avascular necrosis, peripheral vascular

https://doi.org/10.1016/j.asmr.2021.05.012

disease, and endocrine or metabolic abnormalities, such as hypothyroidism or calcium metabolism abnormalities.^{1,3} Poor blood supply to the talus as well as weak regenerative capacity of the articular cartilage make these lesions challenging to treat.^{1,3} Nonoperative versus operative treatment of OLTs varies based on symptoms, which can range from pain, swelling, stiffness, locking or catching, as well as age.^{1,4} In adults, procedural treatment is often considered to prevent osteoarthritis, as successful outcomes with nonoperative treatment are present in less than one-half of patients.³

Several options for management of OLTs have emerged over the years. These include arthroscopic debridement, microfracture, osteochondral autograft transplantation (OAT) or osteochondral allograft transplantation (OCA), autologous chondrocyte implantation, matrix-associated chondrocyte implantation, and juvenile chondrocyte implantation.^{1,3,5-7} Adjuvant therapy with biological agents such as bone marrow aspirate concentrate, hyaluronic acid, and platelet-rich plasma have been used to stimulate regeneration in conjunction with OAT and microfracture.^{1,3,7} While microfracture has become the

From the University of Florida College of Medicine (M.C.O., W.K.D.); and Department of Orthopaedics and Rehabilitation, University of Florida (M.L.B., K.W.F.), Gainesville, Florida, U.S.A.

The authors report the following potential conflicts of interest or sources of funding: M.C.O., W.K.D., M.L.B., and K.W.F. report nonfinancial support from Exactech, during the course of the study. Full ICMJE author disclosure forms are available for this article online, as supplementary material.

Received November 1, 2020; accepted May 25, 2021.

Address correspondence to Kevin W. Farmer, M.D., P.O. Box 112727. Gainesville, FL 32611-2727. E-mail: farmekw@ortho.ufl.edu

^{© 2021} THE AUTHORS. Published by Elsevier Inc. on behalf of the Arthroscopy Association of North America. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). 2666-061X/201759



Fig 1. Reveille CP System. Cartilage particulator system used in the study. Each component labeled as follows: cartilage particulator (A), tissue holder (B), collection tube (C), tissue collection cup (D), and filtration tube (E).

surgical approach of choice for small talar lesions measuring less than 1.50 cm² (150 mm²) in area and less than 7 mm in depth,^{7,8} a gold standard for medium-to-large talar lesions has not been established. In addition, other systematic reviews have not demonstrated any technique to be superior to the others, even in small lesions.⁵ Finally, it is known that each of these techniques has individual drawbacks, such as multiple surgical sites, multistaged procedures, high cost, and use of nonautologous tissue.

A surgical technique that applies cartilage regeneration using autologous cartilage particles has been attempted when treating cartilage defects in the knee.^{9,10} In this surgical approach, cartilage is harvested from the non-load-bearing portion of the affected joint and used to create a particulated cartilage graft ready for immediate reimplantation. Reveille Cartilage Particulator (CP) (Exactech Inc., Gainesville, FL) (Fig 1) is a device that enables preparation of cartilage particles, increasing the surface area, for immediate reimplantation. While application of this single-site, single-stage technique has shown promising results in the knee,⁹ it has not been attempted in treatment of OLTs. The purpose of this study was to assess the quantity of morselized cartilage that can be harvested from the non-load-bearing portion of the talus for immediate reimplantation. We hypothesized that this amount would be adequate for coverage of average sized OLTs.

Methods

This study was approved by the University of Florida Institutional Review Board (IRB #: 201800819). Five previously healthy cadaveric ankle specimens were obtained from MedCure (Portland, OR), stored in a -25.5° C freezer for an average of 7 days, and thawed in a 4°C fridge over the course of 2 days immediately before cartilage harvest. All 5 specimens were operated on by a single, board-certified, sports medicine fellowship—trained orthopaedic surgeon according to the procedures outlined to follow. Only specimens without significant arthritis were included in the study. Patient demographic data were unavailable.

Technique

A standard diagnostic arthroscopy was performed on each cadaveric specimen to assess the health of the ankle joint. A 2-portal arthroscopic approach was used during the harvesting technique. The ankle was engaged in maximum dorsiflexion to directly visualize the non-load-bearing cartilage on the anterior surface of the talus at the junction of talar head and neck (Fig 2). This area was chosen as it is commonly debrided during anterior impingement decompression.^{11,12} Minimal debridement of synovium was used to ensure adequate visibility. Using a curette, a small amount of cartilage was elevated from the previously identified non-load-bearing aspect of the talus. Cartilage was then separated from the anterior talar head, at the junction with the talar neck. Graspers were used to reclaim the cartilage flap that was created and remove it from the portal. The retrieved cartilage was then carefully added to the Reveille cartilage particulator to diminish fragment loss from the transfer. These steps were repeated until all visible non-load-bearing cartilage had been reclaimed. Extreme care was taken to leave the remaining cartilage in the joint intact.

The particulator was added to a saline-filled collection tube to aid in filtration and morselization. Together, they were threaded onto a drill and tissue was morselized for at least 2 minutes at 1500 rpm. Excess saline was decanted using a plunging process. The total volume of processed cartilage reclaimed was measured using a syringe demarcated in 0.1-mL increments (Fig 3).



Fig 2. Cross-section of the ankle joint. Lateral view of a cross-section of the ankle demonstrating the distal tibia (1), body of talus (2), and the non—load-bearing cartilage (3) at the junction of the head (4) and neck of talus.

Outcomes of Interest

The primary outcome of interest in this study was the volume of morselized cartilage that could be reclaimed from the non—load-bearing aspect of the anterior talus. The defect coverage size was extrapolated from the volume of morselized cartilage using a theoretical formula (Fig 4) and compared to the size of average OLTs reported in the literature.

Results

The total volume of particulated cartilage graft following processing among the 5 specimens ranged from 0.3 mL to 2.1 mL with a mean volume of 1.3 ± 0.7 mL (Table 1).

Discussion

This cadaveric study demonstrates that an adequate amount of cartilage can be harvested from the non-load-bearing area of the talus to create a morselized cartilage graft sufficient for coverage of average talar defects.

The size, thickness, and location of OLTs may vary among patients and depend on radiographic versus arthroscopic assessment. Direct visualization with arthroscopy remains the gold standard of estimating the lesion size and choosing appropriate treatment.¹³ Small talar defects have been repeatedly defined as less than 1.5 cm². Nevertheless, according to the studies done on various surgical approaches to treatment, the mean talar defect size may range from 0.5 cm² to 3.7 cm², with thickness of the subchondral involvement ranging from 0.5 cm to 2 cm (Table 2).¹⁴⁻²² In addition to the size and thickness, OLTs can be distinguished by location on the talus using a 9-grid model, with most lesions occurring in the centromedial and centrolateral zones.²³ Finally, the defects may be graded differently using a 4-stage classification created by Berndt and Harty that uses involvement of subchondral bone, detachment of cartilage, and displacement.



Fig 3. Cartilage paste postprocessing. Cartilage grafts after harvest and processing with the cartilage particulator.

$$defect \ size \ (cm^2) = \frac{cartilage \ paste \ (cm^3)}{layer \ thickness \ (0.1 \ cm)}$$

Fig 4. Theoretical cartilage defect coverage formula. The formula developed to estimate the theoretical defect size coverage that could be covered with a 1-mm layer of morselized cartilage graft.

Surgical treatments of cartilage defects of the talus vary greatly. Thus, outcomes are equally variable and depend on several factors, including the size or depth of the lesion, previous history of trauma to the ankle joint, and type of intervention. These techniques also target healing differently, including cartilage repair, cartilage regeneration, and cartilage replacement. Studies have shown that microfracture works well for smaller lesions,^{8,19,24} has a low complication rate, minimal post-operative pain, and is less technically demanding for the surgeon.^{25,26} Despite its benefits, there has been disagreement regarding the longevity of efficacy.^{26,27}

For larger lesions, OAT and OCA have shown promising results. In OAT and OCA, a graft from the ipsilateral knee (autograft) or off-the-shelf allograft, respectively, are used to mimic native hyaline cartilage in the ankle joint. Autografts have shown to be effective,²⁸ even in long-term studies with second-look arthroscopy.^{22,29} Still, they are associated with donor-site morbidity.³⁰⁻³² While allografts can help restore joint function and reduce pain,^{4,16,33} they do not completely halt the development of degenerative arthritic changes and are, therefore, not the best long-term treatment.^{3,18,34}

Autologous chondrocyte implantation has shown promising outcomes when attempting to mimic hyaline cartilage in the ankle joint^{20,25}; however, it has been shown that the cell-grown grafts do not always fully incorporate themselves into the cartilage defect or turn into hyaline cartilage.³ Matrix-associated chondrocyte implantation has provided the benefit of more even distribution of the chondrocytes at the implantation site and avoidance of de-differentiation of chondrocytes without the need for a covering layer.¹⁵ These 2 options are high in cost and require staged surgeries. Finally, another technique that applies minced or particulated articular cartilage obtained from juvenile allograft donors has been recently presented, however, it has not been studied in depth.^{14,35,36}

While microfracture has become the surgical approach of choice for small talar lesions measuring less than 1.5 cm², no single surgical technique seems to be superior.⁵ To date, the only option for a single-site, single-stage procedure applied to osteochondral defects in the ankle joint has been done with the use of particulated allograft cartilage implantation.^{14,35,36} A single-site, single-staged procedure with autologous cartilage graft application has only been applied in the knee. Massen et al.⁹ followed a cohort that underwent autologous minced cartilage transfer in osteochondral lesions of the knee. Despite the

small size of the cohort, the authors reported satisfactory outcomes at 2-year follow-up and demonstrated the safety and cost-effectiveness of this approach in comparison with other techniques available for treatment of osteochondral defects in the knee. Although this technique has not been done for OLTs, it would be reasonable to assume similar conclusions when treating the ankle joint.

The avascular nature of cartilage tissue in the joint limits the absorption of anabolic factors. Particulated cartilage allows for increased surface area, which has shown improved absorption of these anabolic factors into the extracellular matrix of cartilaginous tissue, better interaction with marrow elements, and heightened potential for chondrocyte growth.³⁷⁻⁴⁰ Tissue grafts prepared with Reveille CP (Exactech Inc.) are composed primarily of tissue small particles between 0.3 mm and 1.0 mm in diameter. This 10-fold increase in the surface area allows for high cellular viability and interaction, which has been previously demonstrated with fluorescent microscopy. A theoretical 1-mm layer of cartilage paste can be applied to the defect, which allows for appropriate replacement of overlying cartilage and helps avoid cartilage hypertrophy (Exactech Internal Study; Data on File at Exactech). Using this principle, the area of coverage could be calculated using a theoretical formula (Fig 4). Therefore, the amount of processed cartilage reclaimed in this study could over up to 13.2 cm^2 , which should be of sufficient quantity to cover average talar defects reported in the literature. It would be reasonable then to consider intraoperative cartilage reclamation with subsequent grafting using this system as a surgical option for typical talar defects. Providing the benefit of a single-stage and single-site procedure, this technique demonstrates promise as another surgical approach to repair osteochondral defects of the talus.

Future Directions

The results of this study call for further assessment of clinical application and outcomes for routine use of this surgical approach. Since it is up to the experience and

Table 1. Amount of Cartilage Paste Available for Transfer

Sample No.	Volume of Cartilage after Processing, mL	Theoretical Defect Size Coverage, cm ²
1	0.3	3
2	1.0	10
3	1.8	18
4	2.1	21
5	1.4	14
Mean \pm SD	1.3 ± 0.7	13.2 ± 7.1

NOTE. The volume of cartilage paste following processing is reported for each specimen. Corresponding theoretical defect size coverage using the formula from Figure 4 is reported for each specimen.

SD, standard deviation.

Table 2. Summary of Average Talar Defect Sizes in the Published Literature

Study	Talar Defect Area, cm ²	Talar Defect Depth, cm	Sample Size
Coetzee et al., 2013 ¹⁴	Mean, 1.25 cm^2 (range, 0.5-3.0 cm^2)	Mean, 0.7 cm (range, 0.3-2 cm)	n = 24
Magnan et al., 2012 ¹⁵	Mean, $2.36 \pm 0.49 \text{cm}^2$		n = 30
El-Rashidy et al., 2011 ¹⁶	Mean, 1.5 cm^2 (range, 0.8- 2.16 cm ²)		n = 42
Becher et al., 2010 ¹⁷	Range, 0.5-2.0 cm ²		n = 45
Hahn et al., 2010 ¹⁸	Mean, 2.67 cm^2		n = 13
Choi et al., 2009 ¹⁹	Mean, $1.17 \pm 0.55 \text{ cm}^2$	Mean, 0.577 ± 0.245 cm	n = 120
Giannini et al., 2008 ²⁰	Mean, 1.6 cm^2		n = 46
Nam et al., 2009 ²¹	Mean, 2.73 cm^2 (range, 0.8-1.00 cm^2)		n = 11
Baltzer and Arnold, 2005 ²²	Mean, 1.7 cm^2 (maximum, 3.7 cm^2)		n = 41

judgment of the surgeon to make an arthroscopic assessment of non—load-bearing cartilage, development of a device or software that helps outline the non—loadbearing zone of articular cartilage on the talus would make this procedure more standardized and replicable. In addition, development of a definitive treatment protocol and surgical instrumentation for cartilage reclamation and reimplantation could add to the time and cost-effectiveness of this procedure. The potential to reduce morbidity associated with multiple surgical sites, multi-staged procedure, or nonautologous tissue in ankle surgery calls for further investigation of this technique for application in the future.

Limitations

This study has several limitations. First, the demographics of the cadavers used in cartilage reclamation were not available; therefore, the variability in death, duration of storage, cartilage degeneration since time of death, mechanisms of death, and functional status of the ankle joint before death could not be determined. All specimens, however, were noted to have minimal osteoarthritis and deemed appropriate for cartilage harvest. Second, the small sample of this cadaveric study poses a challenge to its applicability and does not eliminate room for variability in the amount of cartilage that could be harvested from the non-load-bearing areas of the talus in a diverse population of living patients. Third, it cannot be determined how well the cartilage graft would incorporate into a defect with significant subchondral bone involvement, making its potential use limited to shallow defects. Finally, while this study adds evidence to the theoretical quantity of cartilage that can be reclaimed and turned into a morselized cartilage graft in cadavers, the long-term secondary clinical effects of this harvest on the ankle joint are not yet known.

Conclusions

This study validated that it is possible to harvest sufficient amount of cartilage for an autologous morselized cartilage graft via a single-stage, single-site surgical and processing technique to address most talar articular cartilage defects.

Acknowledgments

We thank Chris Koenig for coordinating cadaver procurement, Thien Doan for Exactech support and consultation, and Thiago Love-Leonor for Exactech device and surgical tech support during the trial.

References

- 1. Dekker TJ, Dekker PK, Tainter DM, Easley ME, Adams SB. Treatment of osteochondral lesions of the talus: A critical analysis review. *JBJS Rev* 2017;5:1.
- **2.** Orr JD, Dawson LK, Garcia EJ, Kirk KL. Incidence of osteochondral lesions of the talus in the United States Military. *Foot Ankle Int* 2011;32:948-954.
- **3.** Looze CA, Capo J, Ryan MK, et al. Evaluation and management of osteochondral lesions of the talus. *Cartilage* 2017;8:19-30.
- **4.** Adams SB, Viens NA, Easley ME, Stinnett SS, Nunley JA. Midterm results of osteochondral lesions of the talar shoulder treated with fresh osteochondral allograft transplantation. *J Bone Joint Surg Am* 2011;93:648-654.
- Dahmen J, Lambers KTA, Reilingh ML, van Bergen CJA, Stufkens SjoerdAS, Kerkhoffs GMMJ. No superior treatment for primary osteochondral defects of the talus. *Knee Surg Sports Traumatol Arthrosc* 2018;26:2142-2157.
- **6.** Rungprai C, Tennant JN, Gentry RD, Phisitkul P. Management of osteochondral lesions of the talar dome. *Open Orthop J* 2017;11:743-761.
- 7. Gianakos AL, Yasui Y, Hannon CP, Kennedy JG. Current management of talar osteochondral lesions. *World J Orthop* 2017;8:12.
- **8.** Chuckpaiwong B, Berkson EM, Theodore GH. Microfracture for osteochondral lesions of the ankle: outcome analysis and outcome predictors of 105 cases. *Arthroscopy* 2008;24:106-112.
- **9.** Massen FK, Inauen CR, Harder LP, Runer A, Preiss S, Salzmann GM. One-step autologous minced cartilage procedure for the treatment of knee joint chondral and osteochondral lesions: A series of 27 patients with 2-year follow-up. *Orthop J Sports Med* 2019;7:232596711985377.
- Salzmann GM, Calek A-K, Preiss S. Second-generation autologous minced cartilage repair technique. *Arthrosc Tech* 2017;6:e127-e131.
- 11. Walsh SJ, Twaddle BC, Rosenfeldt MP, Boyle MJ. Arthroscopic treatment of anterior ankle impingement: A

prospective study of 46 patients with 5-year follow-up. *Am J Sports Med* 2014;42:2722-2726.

- **12.** McCrum MDCL, Arner MDJW, Lesniak MDB, Bradley MDJP. Arthroscopic anterior ankle decompression is successful in National Football League Players. *Am J Orthop* 2018;47(1).
- 13. Takao M, Uchio Y, Naito K, Fukazawa I, Ochi M. Arthroscopic assessment for intra-articular disorders in residual ankle disability after sprain. *Am J Sports Med* 2005;33:686-692.
- 14. Coetzee JC, Giza E, Schon LC, et al. Treatment of osteochondral lesions of the talus with particulated juvenile cartilage. *Foot Ankle Int* 2013;34:1205-1211.
- **15.** Magnan B, Samaila E, Bondi M, Vecchini E, Micheloni GM, Bartolozzi P. Three-dimensional matrixinduced autologous chondrocytes implantation for osteochondral lesions of the talus: Midterm results. *Adv Orthop* 2012;2012:1-9.
- **16.** El-Rashidy H, Villacis D, Omar I, Kelikian AS. Fresh osteochondral allograft for the treatment of cartilage defects of the talus: A retrospective review. *J Bone Joint Surg Am* 2011;93:1634-1640.
- Becher C, Driessen A, Hess T, Longo UG, Maffulli N, Thermann H. Microfracture for chondral defects of the talus: Maintenance of early results at midterm followup. *Knee Surg Sports Traumatol Arthrosc* 2010;18: 656-663.
- **18.** Hahn DB, Aanstoos ME, Wilkins RM. Osteochondral lesions of the talus treated with fresh talar allografts. *Foot Ankle Int* 2010;31:277-282.
- **19.** Choi WJ, Park KK, Kim BS, Lee JW. Osteochondral lesion of the talus: Is there a critical defect size for poor outcome? *Am J Sports Med* 2009;37:1974-1980.
- **20.** Giannini S, Buda R, Vannini F, Di Caprio F, Grigolo B. Arthroscopic autologous chondrocyte implantation in osteochondral lesions of the talus: Surgical technique and results. *Am J Sports Med* 2008;36:873-880.
- **21.** Nam EK, Ferkel RD, Applegate GR. Autologous chondrocyte implantation of the ankle: A 2- to 5-year followup. *Am J Sports Med* 2009;37:274-284.
- 22. Baltzer AWA, Arnold JP. Bone-cartilage transplantation from the ipsilateral knee for chondral lesions of the talus. *Arthroscopy* 2005;21:159-166.
- **23.** Elias I, Jung JW, Raikin SM, Schweitzer MW, Carrino JA, Morrison WB. Osteochondral lesions of the talus: Change in MRI findings over time in talar lesions without operative intervention and implications for staging systems. *Foot Ankle Int* 2006;27:157-166.
- 24. Lee K-B, Bai L-B, Chung J-Y, Seon J-K. Arthroscopic microfracture for osteochondral lesions of the talus. *Knee Surg Sports Traumatol Arthrosc* 2010;18:247-253.
- 25. Murawski CD, Kennedy JG. Operative treatment of osteochondral lesions of the talus. *J Bone Joint Surg* 2013;95:1045-1054.

- 26. Polat G, Erşen A, Erdil ME, Kızılkurt T, Kılıçoğlu Ö, Aşık M. Long-term results of microfracture in the treatment of talus osteochondral lesions. *Knee Surg Sports Traumatol Arthrosc* 2016;24:1299-1303.
- 27. Ferkel RD, Zanotti RM, Komenda GA, et al. Arthroscopic treatment of chronic osteochondral lesions of the talus: Long-term results. *Am J Sports Med* 2008;36:1750-1762.
- 28. VanTienderen RJ, Dunn JC, Kusnezov N, Orr JD. Osteochondral allograft transfer for treatment of osteochondral lesions of the talus: A systematic review. *Arthroscopy* 2017;33:217-222.
- **29.** Lee C-H, Chao K-H, Huang G-S, Wu S-S. Osteochondral autografts for osteochondritis dissecans of the talus. *Foot Ankle Int* 2003;24:815-822.
- **30.** Hangody L, Vásárhelyi G, Hangody LR, et al. Autologous osteochondral grafting—Technique and long-term results. *Injury* 2008;39:32-39.
- **31.** Laprade R, Botker J. Donor-site morbidity after osteochondral autograft transfer procedures. *Arthroscopy* 2004;20:e69-e73.
- **32.** Reddy S, Pedowitz DI, Parekh SG, Sennett BJ, Okereke E. The morbidity associated with osteochondral harvest from asymptomatic knees for the treatment of osteochondral lesions of the talus. *Am J Sports Med* 2007;35:80-85.
- **33.** Gross AE, Agnidis Z, Hutchison CR. Osteochondral defects of the talus treated with fresh osteochondral allograft transplantation. *Foot Ankle Int* 2001;22:385-391.
- 34. Raikin SM. Fresh Osteochondral allografts for largevolume cystic osteochondral defects of the talus. *J Bone Joint Surg Am* 2009;91:2818-2826.
- **35.** Kruse DL, Ng A, Paden M, Stone PA. Arthroscopic De Novo NT® juvenile allograft cartilage implantation in the talus: A case presentation. *J Foot Ankle Surg* 2012;51:218-221.
- **36.** DeSandis BA, Haleem AM, Sofka CM, O'Malley MJ, Drakos MC. Arthroscopic treatment of osteochondral lesions of the talus using juvenile articular cartilage allograft and autologous bone marrow aspirate concentration. *J Foot Ankle Surg* 2018;57:273-280.
- **37.** Lu Y, Dhanaraj S, Wang Z, et al. Minced cartilage without cell culture serves as an effective intraoperative cell source for cartilage repair. *J Orthop Res* 2006;24:1261-1270.
- **38.** Fortier LA, Barker JU, Strauss EJ, McCarrel TM, Cole BJ. The role of growth factors in cartilage repair. *Clin Orthop Relat Res* 2011;469:2706-2715.
- **39.** Frisbie DD, Lu Y, Kawcak CE, DiCarlo EF, Binette F, McIlwraith CW. In vivo evaluation of autologous cartilage fragment-loaded scaffolds implanted into equine articular defects and compared with autologous chondrocyte implantation. *Am J Sports Med* 2009;37(1_suppl): 71-80.
- **40.** Levinson C, Cavalli E, Sindi DM, et al. Chondrocytes from device-minced articular cartilage show potent outgrowth into fibrin and collagen hydrogels. *Orthop J Sports Med* 2019;7:232596711986761.