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Original Research

Cell-free biomimetic scaffold for chondral and osteochondral lesions: surgical technique for custom and standardized implantation

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ABSTRACT

Introduction: Cell-free chondral and osteochondral scaffolds have been introduced to address lesions of the articular surface. A proper implantation technique is key to favor scaffold integration, regenerative processes, and positive clinical outcomes.
Objectives: The purpose of this article is to describe indications and surgical steps for both the custom traditional free-hand implantation approach and an innovative minimally invasive technique for the standardized implantation of this biomimetic cell-free scaffold (MaioRegen; Fin-Ceramica Faenza Spa).
Methods: Indications and contraindications for this scaffold implantation have been provided. The required steps for surgical preparation, implantation technique, and postoperative management have been described as well to address articular surface lesions of the knee.
Results: A dedicated instrumentation for circular implants of different sizes has been developed to allow more precise preparation of the depth and width of the defect, reducing the invasiveness and increasing implant stability. The custom free-hand technique with chisels and osteotomes remains useful when the lesion does not allow the use of the standardized instrumented technique. In case further stability of the implant is needed, fibrin glue addition should be considered.
Conclusions: By guiding the readers with the key perioperative and intraoperative steps, chondral and osteochondral defects can be addressed with the use of a cell-free scaffold, maximizing implant stability.

Introduction

Cartilage lesions of the knee are a frequent condition that affects all ages.[1–3] Along with cartilage, the subchondral bone is frequently involved in the pathological process, either primarily, as in osteochondritis dissecans, osteonecrosis, and trauma, or secondarily, the altered articular surface may progress toward early osteoarthritis (OA).[4–6] If not appropriately treated, an altered

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articular surface may increase the risk of early OA, and the involvement of the subchondral bone further increases the challenge of addressing these lesions.[7] Thus, several strategies have been developed to manage these defects, with disadvantages that include donor-site morbidity, limited availability, 2-step procedures, or significant costs coupled with unsatisfactory clinical outcomes.[8–10]

Cell-free chondral and osteochondral scaffolds have been introduced to overcome these limitations, aiming to restore the articular surface through a single surgical procedure. The function of scaffolds extends beyond simply serving as carriers for cell delivery, but they also present an ability to promote chondral or osteochondral regeneration by exploiting the self-regenerative potential of the body.[11,12] The appropriateness of these scaffolds also gained consensus among experts, as promoted by a recent International Cartilage Regeneration and Joint Preservation Society (ICRS) Consensus detailing the appropriateness for specific scenarios.[13] Different devices have been developed and applied in the clinical setting, with overall promising results.[14–16] Among these, a type I equine collagen and hydroxyapatite (HA) osteochondral scaffold have been used clinically and extensively investigated with positive long-term results.[17] To further improve the advantages of this 1-step cell-free approach, a new dedicated instrumentation with preshaped cylindrical scaffolds has been developed aiming at reducing the invasiveness of the surgical technique, increasing the reproducibility and improving the integration, regeneration, and potentially clinical outcomes.[18,19]

The purpose of this article is to describe indications and surgical techniques for both the custom traditional free-hand implantation approach and an innovative minimally invasive technique for the standardized implantation of this biomimetic cell-free scaffold.

Indications and contraindications

Currently, the indications for this scaffold are patients who have symptomatic full-thickness chondral and osteochondral defects (ICRS grades III and IV) of the knee joint; traumatic lesions, degenerative lesions, and osteochondritis dissecans; patients aged between 15 and 60 years old (although there is no precise age cut-off and the joint status prevails in the surgical indication[20]) and preferably nonobese defined as body mass index < 30 kg/m^2. Regarding defect size, the traditional custom free-hand technique is indicated for defects ranging from 2.0 cm^2 to 10 cm^2,[21] while the new instrumentation allows targeting lesions ranging from 1.2 to 2.5 cm^2 for a single defect, increasing up to 10 cm^2 for multiple defects.

Absolute contraindications to scaffold implantation are active or recent infection; rheumatic and autoimmune diseases; diffuse and severe OA; and obesity. Axial malalignment and ligament instability, if left untreated, are risk factors for failure following isolated chondral and osteochondral repair, and therefore, they are contraindications to scaffold implantation unless they are addressed before or at the time of the articular surface treatment.

Surgical technique

The original osteochondral biomimetic scaffold (MaioRegen; Fin-Ceramica Faenza Spa) is a 3-dimensional 3-layer porous composite structure, which mimics the osteochondral anatomy. The cartilaginous layer, made up of equine type I collagen, has a smooth surface to promote articular surface gliding. The middle layer is similar to the cartilage tide mark, and it is made of a combination of type I collagen (60%) and HA (40%), while the bottom layer is made of a mineralized mixture of type I collagen (30%) and HA (70%), reproducing the subchondral bone layer.

After the original 3-layer scaffold, now called “Prime” for a depth of 6 mm, 2 new formulations have been introduced: the “Slim,” a bilayer 4 mm deep scaffold for chondral and osteochondral lesions, and the “Chondro+,” a monolayer 2 mm deep scaffold for chondral lesions with slight or no involvement of the subchondral bone. Moreover, along with the customizable squared-shaped scaffold to be shaped free-hand, these formulations are available also in 3 preshaped cylindrical sizes (1.2 cm, 1.5 cm, and 1.8 cm of diameter), which can be implanted with the new dedicated instrumentation.

Custom free-hand technique

The original surgical custom free-hand technique[21] involves the use of chisels and osteotomes for lesion preparation and removal of subchondral sclerotic bone, and the hand cutting of the scaffold in accordance with the size and shape of the lesion. This approach remains useful when the lesion does not allow the use of the standardized instrumented technique, because of its size or its shape, or if dedicated instrumentation is not available. After applying a tourniquet to the proximal part of the thigh, the incision of the skin, subcutaneous layers, and capsule can be made medially or laterally to the patella, depending on the location of the lesion. Once the chondral or osteochondral lesion is identified, the lesion is prepared by removing the injured cartilage and sclerotic subchondral bone with a scalpel and osteotome without using high-speed burs, to create an area of the specific depth to accommodate the scaffold of the desired size. The bottom of the prepared bed should be flat, and the sides of the defect should be stable and perpendicular. According to the accurate measure of the prepared bed, the smooth cartilaginous layer of the scaffold is cut with a scalpel and the subchondral bone layer with surgical scissors. The bottom layer of the scaffold is identified by its rough surface for proper orientation, and then the scaffold can be inserted with a gentle press-fit technique, making sure that the bottom layer is in contact with the bone floor. Fibrin glue on the perimeter interface between the scaffold and the host bone and on the surface layer can be applied to achieve greater stability, if needed. Finally, before and after removal of the tourniquet, knee flexion and extension cycles are performed to assess implant stability.

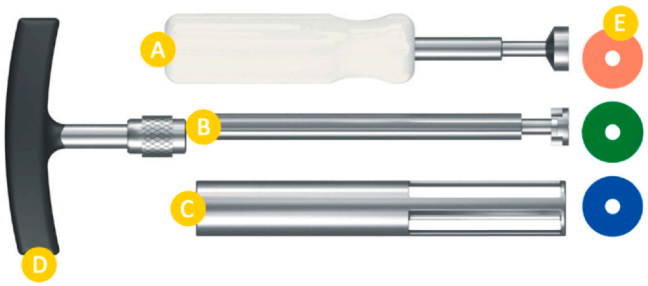

Fig. 1. Instrumentation of the standardized implantation technique. In detail: **A**, circular scalpel; **B**, Sizer; **C**, guide tube; **D**, handle; and **E**, spacers. Blue (Chondro+), Green (Slim), Orange (Prime). Images courtesy of Fin-ceramica Faenza Spa, Faenza, Italy.

Standardized implantation technique

The new dedicated instrumentation (Fig. 1) has been introduced to allow more precise preparation of the depth and width of the defect, reducing the invasiveness and increasing the implant stability. The detailed surgical procedure is described by steps in the following paragraphs.

1. Surgical preparation and access:

- Apply a tourniquet to the proximal region of the patient's thigh and prepare the surgical field. Expose the lesion area through an arthrotomy or mini-arthrotomy incision depending on the lesion site (Fig. 2).
- The minimally invasive approach through a mini-arthrotomy incision (minimum 4.5 cm) is possible for chondral or osteochondral lesions located in the condyles or trochlea.

2. Lesion identification:

- Once the chondral or osteochondral lesion to be treated has been identified (Fig. 3), use Sizers of different diameters to select the correct diameter of the bed to be prepared (Fig. 4). The diameter must be large enough to include the entire chondral or osteochondral lesion. If Hoffa's tissue is hypertrophic at the defect level, it is preferable to remove it to avoid the formation of adherence.
- Place the Sizer centered on the lesion, insert the guide wire through its distal hole, and hammer the guide wire to its final position. Remove the Sizer leaving the guide wire in place.
- Insert the circular scalpel of the same diameter as the Sizer previously used, through the guide wire (Fig. 5). Cut the cartilage by rotating the circular scalpel. Then remove the circular scalpel, leaving the guide wire in place.
- Check that the cartilage incision includes the entire chondral layer of the lesion.

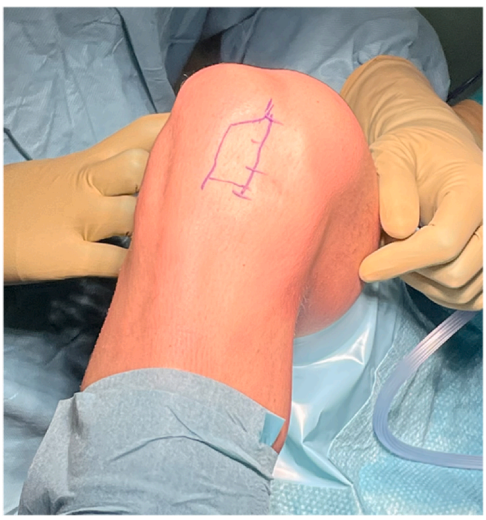

Fig. 2. Surgical position and access.

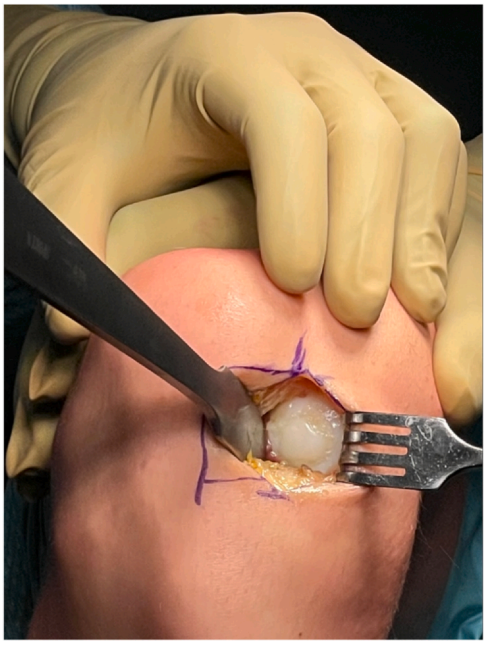

Fig. 3. Identification of the lesion.

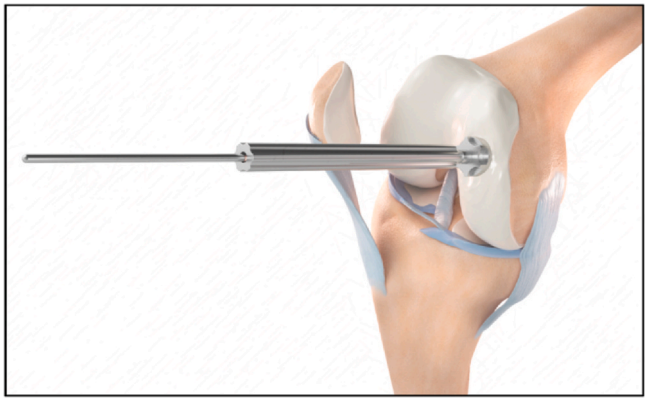

Fig. 4. Sizer positioning. Image courtesy of Fin-ceramica Faenza Spa, Faenza, Italy.

3. Reamer assembly:

- Assemble the reamer (of the same diameter as the Sizer and circular scalpel previously used) with the appropriate handle, guide tube, and spacer. Insert the reamer into the guide tube. Apply the selected spacer and secure the handle through the lock/unlock mechanism, ensuring that the handle is well-connected and stable.
- The spacer must be selected according to the depth of the lodge to prepare (2.5 mm, 4.5 mm, or 7 mm, respectively for the scaffold versions Chondro+, Slim, or Prime).

4. Reaming procedure:

- Insert the reamer, assembled as described above, through the wire guide. Prepare the bed of the lesion paying particular attention to the depth, referring to the laser markings on the reamer blades. Proceed with reaming by visually checking the depth until the desired level.
- Hold the reamer perpendicular to the housing surface, taking care not to bend or tilt the wire guide. Hold the guide tube firmly and rotate the reamer to erode the tissue. Proceed to the final stop (Fig. 6). Reaming slowly and taking care of axiality with the guide wire during this step is important in order to avoid oval holes or not perpendicular walls of the prepared bed.

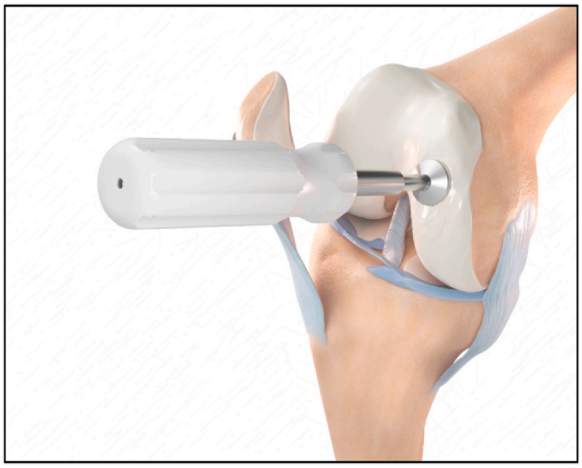

Fig. 5. Circular scalpel positioning. Image courtesy of Fin-ceramica Faenza Spa, Faenza, Italy.

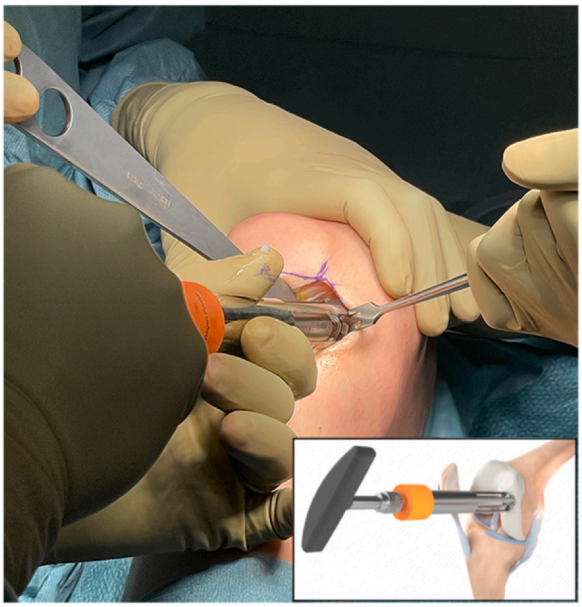

Fig. 6. Reaming procedures. Image courtesy of Fin-ceramica Faenza Spa, Faenza, Italy.

- If there is insufficient surgical space to securely and stably insert the reamer assembled with the guide tube, assemble the reamer with the handle alone. Prepare the bed of the lesion paying particular attention to the milling depth, referring to the laser markings on the reamer blades. Take care to keep the reamer perpendicular to the housing surface. The laser markings indicate the 3 possible depths for the scaffold versions.

5. Lesion prepared bed check and scaffold implantation

- Check the depth of the prepared bed (Fig. 7) created using the Sizer and referring to the notches and laser markings indicating the depth measurement. If the depth is not as expected and is not compatible with the device to be implanted, repeat the previous step until the correct depth is reached. The instrumentation is designed to place the scaffold at the level of the surrounding cartilage. In case the implanted scaffold is more prominent, it is preferable to go deeper with the preparation of the lesion, as a protruding scaffold could compromise the stability of the implant. Finally, remove all instruments, including the wire guide.

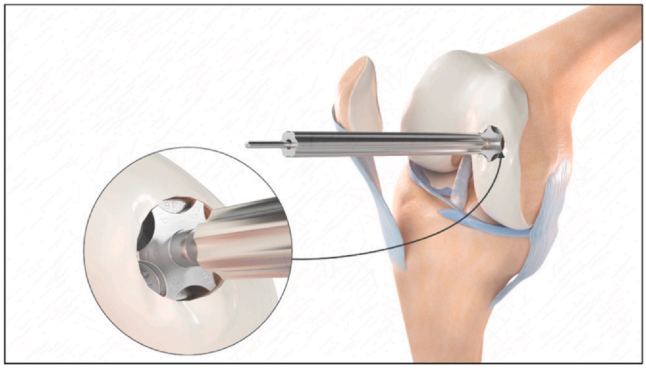

Fig. 7. Check the lesion depth with the Sizer. Illustration courtesy of Fin-ceramica Faenza Spa, Faenza, Italy.

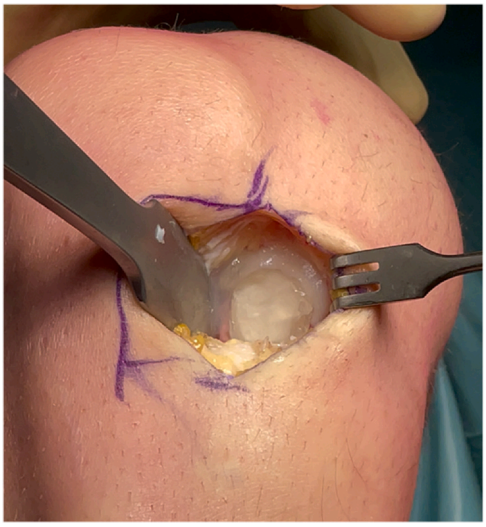

Fig. 8. Scaffold implantation.

6. Scaffold implantation

- Once the bed of the lesion is prepared, apply the appropriate device according to the lesion depth (Fig. 8). If the prepared bed depth is greater than expected, implant the Slim device in place of Chondro+, implant the Prime device in place of Slim or retrieve the bone debris and compact it to the bottom of the housing with the Sizer if the Prime version was implanted. The implant can be positioned press-fit. If additional stability is needed, it can be sealed with fibrin glue.

7. Stability check and tourniquet release

- Release the tourniquet. Stabilization of the device is facilitated by subchondral bone bleeding and subsequent coagulation. Wait approximately 2 minutes for the device to be filled with subchondral blood. Check the mechanical stability of the device with a few flexion-extension cycles of the joint. If the scaffold is mobilized or delaminated check both the size and depth of the prepared lesion bed and implant a new scaffold accordingly. Close the surgical site according to standard procedures.

Postoperative care

The postoperative care depends on the location of the treated lesion. In general, the rehabilitation includes active and passive flexion-extension and isometric and isotonic muscle-strengthening exercises. For condylar lesions, flexion-extension and muscle-strengthening exercises are permitted from the first postoperative days, while loading is not permitted for the first 3 to 4 weeks. In the following weeks, the patient can progressively load until reaching full weight bearing between 6 and 8 postoperative weeks. For patellofemoral lesions, active and passive flexion-extension exercises are allowed after a week, while isometric and isotonic muscle-

strengthening exercises, as well as loading, are allowed partially for the first 2 weeks. In the following weeks, patients can progressively load until reaching full weight bearing between 4 and 5 postoperative weeks.

Discussion

This study described the surgical technique for the application of a cell-free biomimetic scaffold for the treatment of chondral and osteochondral lesions.

Cartilage lesions require precise surgical procedures to ensure consistent results in different clinical scenarios. To this aim, the dedicated instrumentation allows to deliver a preformed scaffold that can offer significant advantages compared to the previous free-hand technique. This can increase the standardization of the surgical procedure, reducing the variability associated with the surgeon's manual skills. The reproducibility of cartilage reconstruction procedures in orthopedics is of considerable importance to increase the treatment success, given the unique challenges and limited self-healing capabilities of cartilage tissue.[22,23] In addition, the increased precision of the dedicated instruments and the standardized circular shape of the scaffold can facilitate contact with surrounding structures, promoting a tighter adhesion and a better migration of cartilage cells at the scaffold level, resulting in greater integration with the host tissue. This can positively influence implant stability and tissue regeneration, providing a more favorable environment for the regenerative processes to occur.

Besides the new instrumentation, the change from a square or rectangular shape of the implanted scaffold to a round shape presents the benefits itself. The choice of a round scaffold introduces the advantage of a better adaption to curved joint surfaces. The importance of scaffold shape was demonstrated by a study by Drobnic et al comparing the same scaffold implanted in the same model either as a circular or rectangular implant. The results showed how the corners of a scaffold constitute weak points of the implant.[24] The presence of localized stresses present in the rectangular shape of the implant can be more prone to deformation and dislocation of the scaffold. This could alter the surface layer of the scaffold leading to delamination, rupture of the cartilaginous surface, particle release-induced synovitis, and failure of the implant, especially if combined with aggressive rehabilitation.[25] A study by Kon et al on the early stability of implanted scaffolds evaluated through magnetic resonance imaging documented partial detachment in 13%, a complete filling in only 67%, and a complete integration of the grafted cartilage in only 53% of the implants after 6 months.[26] These problems could be related to the free-hand square or rectangular implantation technique and are overcome by the circular shape of the scaffold, which does not suffer from the corner point weakness, is more precise and can offer better stability of the scaffold thus favoring a better integration. Biomechanical studies that have evaluated the effects of graft and defect geometry have shown that the primary stability of osteochondral autografts or allografts in the initial postimplantation period is greater when the graft and defect match.[27,28] Compared to lesion preparation with osteotomes and chisels and scaffold sizing by hand, the standardized instrumentation ensures matching equal length of defects and scaffolds.

A further possibility to improve the stability of the scaffold is the use of fibrin glue. Fibrin glue is able to improve the intrinsic cohesion of the contact layers and the fixation force on the joint surface.[24,25] The use of a press-fit implant without other stabilization methods could in fact result in a lack of stability resulting in slow integration of the scaffold and adverse postoperative events,[26] especially when the free-hand technique is used. In this case, fixation with fibrin glue could allow for a safer early mobilization (thus reducing the risk of joint adhesion and arthrofibrosis) and progressive loading.[24,25] Moreover, in addition to mechanical action, fibrin glue can also play a biological role, which served as the rationale for its use in cartilage treatments for decades and recently even as a suitable scaffold for chondrocyte transplantation.[29–31] In this perspective, fibrin glue could promote implant integration not only mechanically, but also biologically, representing itself as a scaffold for host cells and promoting tissue formation at the host-scaffold interface.[25]

The depth of a scaffold is another important parameter, as it should allow to replace the damaged osteochondral structure while preserving the adjacent healthy tissue.[32] In this regard, the dedicated instrumentation allows precise preparation of the defect depth and the implantation of an appropriate scaffold, avoiding protrusion in cartilage implants which may lead to fibrillation at the graft edges and degenerative changes in the opposing articular surfaces, which would result in softening and fibrillation of the cartilage layer.[33] Studies evaluating the effects of altered joint biomechanics due to protruding osteochondral grafts indicate a clear relationship between altered contact mechanics and subsequent damage to articular cartilage surfaces.[32] The introduction of the dedicated instruments improved the surgical technique by making the scaffold implantation more precise, standardized, and reproducible, overall improving the scaffold-to-lodging ratio and consequently the stability of the construct.

Future studies are needed to evaluate whether the introduction of the new technique with dedicated instruments and circular implants of different sizes and depths will translate into better results in terms of scaffold integration and, more importantly, patient outcomes.

Ethics approval

Complete written informed consent was obtained from the patient for the publication of this study and accompanying images.

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Declaration of Competing Interest

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Authorship contributions

L.A.: methodology, writing—review and editing; L.D.M.: methodology, data curation, writing—original draft preparation; A.D.M.: methodology, writing—review and editing; A.B.: methodology, data curation, writing—original draft preparation; S.Z.: supervision; G.F.: conceptualization, writing—review and editing, supervision. All authors have read and agreed to the published version of the manuscript.

References

1. Widuchowski W, Widuchowski J, Trzaska T. Articular cartilage defects: study of 25,124 knee arthroscopies. *Knee.* 2007;14(3):177–182. https://doi.org/10.1016/j.knee.2007.02.001
2. Vannini F, Spalding T, Andriolo L, et al. Sport and early osteoarthritis: the role of sport in aetiology, progression and treatment of knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(6):1786–1796. https://doi.org/10.1007/s00167-016-4090-5
3. De Marziani L, Sangiorgio A, Bensa A, Boffa A, Andriolo L, Filardo G. Intra-articular injections in sport-active patients with degenerative cartilage lesions or osteoarthritis of the knee: a systematic review. *J Exp Orthop.* 2023;10(1):112. https://doi.org/10.1186/s40634-023-00674-0
4. Keeney M, Pandit A. The osteochondral junction and its repair via bi-phasic tissue engineering scaffolds. *Tissue Eng Part B Rev.* 2009;15(1):55–73. https://doi.org/10.1089/ten.teb.2008.0388
5. Pape D, Filardo G, Kon E, van Dijk CN, Madry H. Disease-specific clinical problems associated with the subchondral bone. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(4):448–462. https://doi.org/10.1007/s00167-010-1052-1
6. Madry H, Kon E, Condello V, et al. Early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(6):1753–1762. https://doi.org/10.1007/s00167-016-4068-3
7. Schinhan M, Gruber M, Vavken P, et al. Critical-size defect induces unicompartmental osteoarthritis in a stable ovine knee. *J Orthop Res.* 2012;30(2):214–220. https://doi.org/10.1002/jor.21521
8. Hangody L, Füles P. Autologous osteochondral mosaicplasty for the treatment of full-thickness defects of weight-bearing joints: ten years of experimental and clinical experience. *J Bone Jt Surg Am.* 2003;85-A(Suppl 2):25–32. https://doi.org/10.2106/00004623-200300002-00004
9. Beer AJ, Tauro TM, Redondo ML, Christian DR, Cole BJ, Frank RM. Use of allografts in orthopaedic surgery: safety, procurement, storage, and outcomes. *Orthop J Sports Med.* 2019;7(12):2325967119891435. https://doi.org/10.1177/2325967119891435
10. Ogura T, Merkely G, Bryant T, Winalski CS, Minas T. Autologous chondrocyte implantation “Segmental-Sandwich” technique for deep osteochondral defects in the knee: clinical outcomes and correlation with magnetic resonance imaging findings. *Orthop J Sports Med.* 2019;7(5):2325967119847173. https://doi.org/10.1177/2325967119847173
11. Andriolo L, Reale D, Di Martino A, Boffa A, Zaffagnini S, Filardo G. Cell-free scaffolds in cartilage knee surgery: a systematic review and meta-analysis of clinical evidence. *Cartilage.* 2021;12(3):277–292. https://doi.org/10.1177/1947603519852406
12. Boffa A, Solaro L, Poggi A, Andriolo L, Reale D, Di Martino A. Multi-layer cell-free scaffolds for osteochondral defects of the knee: a systematic review and meta-analysis of clinical evidence. *J Exp Orthop.* 2021;8(1):56. https://doi.org/10.1186/s40634-021-00377-4
13. Filardo G, Andriolo L, Angele P, et al. Scaffolds for knee chondral and osteochondral defects: indications for different clinical scenarios. A consensus statement. *Cartilage.* 2021;13(1_suppl):1036S–1046S. https://doi.org/10.1177/1947603519894729
14. Verhaegen J, Clockaerts S, Van Osch GJVM, Somville J, Verdonk P, Mertens P. TruFit plug for repair of osteochondral defects-where is the evidence? Systematic review of literature. *Cartilage.* 2015;6(1):12–19. https://doi.org/10.1177/1947603514548890
15. Boffa A, Merli G, Andriolo L, Lattermann C, Salzmann GM, Filardo G. Synovial fluid biomarkers in knee osteoarthritis: a systematic review and quantitative evaluation using BIPEDs criteria. *Cartilage.* 2021;13(1_suppl):82S–103S. https://doi.org/10.1177/1947603520942941
16. Kon E, Filardo G, Perdisa F, Venieri G, Marcacci M. Clinical results of multilayered biomaterials for osteochondral regeneration. *J Exp Orthop.* 2014;1(1):10. https://doi.org/10.1186/s40634-014-0010-0
17. Di Martino A, Perdisa F, Filardo G, et al. Cell-free biomimetic osteochondral scaffold for the treatment of knee lesions: clinical and imaging results at 10-year follow-up. *Am J Sports Med.* 2021;49(10):2645–2650. https://doi.org/10.1177/03635465211029292
18. Christensen BB, Foldager CB, Jensen J, Jensen NC, Lind M. Poor osteochondral repair by a biomimetic collagen scaffold: 1- to 3-year clinical and radiological follow-up. *Knee Surg Sports Traumatol Arthrosc.* 2016;24(7):2380–2387. https://doi.org/10.1007/s00167-015-3538-3
19. Perdisa F, Kon E, Sessa A, et al. Treatment of knee osteochondritis dissecans with a cell-free biomimetic osteochondral scaffold: clinical and imaging findings at midterm follow-up. *Am J Sports Med.* 2018;46(2):314–321. https://doi.org/10.1177/0363546517737763
20. Filardo G, Andriolo L, Sessa A, et al. Age is not a contraindication for cartilage surgery: a critical analysis of standardized outcomes at long-term follow-up. *Am J Sports Med.* 2017;45(8):1822–1828. https://doi.org/10.1177/0363546517695088
21. Sessa A, Perdisa F, Di Martino A, Zaffagnini S, Filardo G. Cell-free biomimetic osteochondral scaffold: implantation technique. *JBJS Essent Surg Tech.* 2019;9(3):e27. https://doi.org/10.2106/JBJS.ST.18.00089
22. Benthien JP, Behrens P. Reviewing subchondral cartilage surgery: considerations for standardised and outcome predictable cartilage remodelling: a technical note. *Int Orthop.* 2013;37(11):2139–2145. https://doi.org/10.1007/s00264-013-2025-z
23. Skjold-Ødegaard B, Søreide K. Standardization in surgery: friend or foe? *Br J Surg.* 2020;107(9):1094–1096. https://doi.org/10.1002/bjs.11573
24. Drobnic M, Perdisa F, Kon E, Cefalì F, Marcacci M, Filardo G. Implant strategy affects scaffold stability and integrity in cartilage treatment. *Knee Surg Sports Traumatol Arthrosc.* 2018;26(9):2774–2783. https://doi.org/10.1007/s00167-017-4737-x
25. Filardo G, Drobnic M, Perdisa F, Kon E, Hribernik M, Marcacci M. Fibrin glue improves osteochondral scaffold fixation: study on the human cadaveric knee exposed to continuous passive motion. *Osteoarthr Cartil.* 2014;22(4):557–565. https://doi.org/10.1016/j.joca.2014.01.004

26. Kon E, Delcogliano M, Filardo G, Busacca M, Di Martino A, Marcacci M. Novel nano-composite multilayered biomaterial for osteochondral regeneration: a pilot clinical trial. *Am J Sports Med.* 2011;39(6):1180–1190. https://doi.org/10.1177/0363546510392711
27. Kock NB, Van Susante JLC, Buma P, Van Kampen A, Verdonschot N. Press-fit stability of an osteochondral autograft: Influence of different plug length and perfect depth alignment. *Acta Orthop.* 2006;77(3):422–428. https://doi.org/10.1080/17453670610046352
28. Kordás G, Szabó JS, Hangody L. Primary stability of osteochondral grafts used in mosaicplasty. *Arthroscopy.* 2006;22(4):414–421. https://doi.org/10.1016/j.arthro.2005.12.011
29. Filardo G, Kon E, Roffi A, Di Martino A, Marcacci M. Scaffold-based repair for cartilage healing: a systematic review and technical note. *Arthroscopy.* 2013;29(1):174–186. https://doi.org/10.1016/j.arthro.2012.05.891
30. Scotti C, Mangiavini L, Boschetti F, et al. Effect of in vitro culture on a chondrocyte-fibrin glue hydrogel for cartilage repair. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(10):1400–1406. https://doi.org/10.1007/s00167-009-1014-7
31. Kim MK, Choi SW, Kim SR, Oh IS, Won MH. Autologous chondrocyte implantation in the knee using fibrin. *Knee Surg Sports Traumatol Arthrosc.* 2010;18(4):528–534. https://doi.org/10.1007/s00167-009-0905-y
32. Bowland P, Ingham E, Jennings L, Fisher J. Review of the biomechanics and biotribology of osteochondral grafts used for surgical interventions in the knee. *Proc Inst Mech Eng H.* 2015;229(12):879–888. https://doi.org/10.1177/0954411915615470
33. Nakagawa Y, Suzuki T, Kuroki H, Kobayashi M, Okamoto Y, Nakamura T. The effect of surface incongruity of grafted plugs in osteochondral grafting: a report of five cases. *Knee Surg Sports Traumatol Arthrosc.* 2007;15(5):591–596. https://doi.org/10.1007/s00167-006-0253-0