



## Techniques

## Osteo-core plasty: minimally invasive approach for subchondral pathologies



Katarzyna Herman<sup>a,b,c,\*</sup>, Graeme P. Whyte<sup>d,e,f,g,h</sup>, Anna Montagna<sup>a</sup>,  
Leandra Bizzoco<sup>a</sup>, Nogah Shabshin<sup>i</sup>, Dawid Szwedowski<sup>a</sup>, and Alberto Gobbi<sup>a</sup>

<sup>a</sup> O.A.S.I. Bioresearch Foundation NPO, Milan, Italy

<sup>b</sup> Department of Orthopedics and Traumatology, Brothers Hospitallers Hospital, Katowice, Poland

<sup>c</sup> Department of Medical Rehabilitation, Medical University of Silesia, Katowice, Poland

<sup>d</sup> New York University School of Medicine, New York, NY, USA

<sup>e</sup> NYU Langone Orthopedic Hospital, New York, NY, USA

<sup>f</sup> Cornell University, New York, NY, USA

<sup>g</sup> Weill Medical College, New York, NY, USA

<sup>h</sup> New York Presbyterian Hospital/Queens, New York, NY, USA

<sup>i</sup> Division of Musculoskeletal Imaging, Department of Radiology, Penn Musculoskeletal Center, Philadelphia, PA, USA

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## ABSTRACT

The subchondral bone is a critical part of the osteochondral unit, providing nutrients to the overlying articular cartilage, thereby maintaining viability of the chondral tissue. The subchondral bone also provides firm mechanical support to assist with stability of the articular cartilage and distribution of stress. Subchondral bone pathology, diagnosed as a bone marrow lesion (BML) on magnetic resonance imaging, may be seen in a variety of pathologic conditions, including knee osteoarthritis (OA). Bone marrow lesions accelerate degenerative changes in the knee joint, and treatment of these lesions may prolong joint longevity. Presently, treatment options for subchondral bone lesions are limited. Osteo-core plasty is a minimally invasive treatment for subchondral bone pathology that consists of two parts: (1) decompression of bone marrow and the administration of bone marrow aspirate concentrate (BMAC) to promote tissue healing, and (2) implantation of bone autograft to provide mechanical support. In an observational study 24 patients with bone marrow lesions have been treated with Osteo-core plasty due to symptomatic bone marrow lesions. At 2 year follow-up they showed a significant improvement in patient-reported scores compared to the preoperative assessment. Based on early clinical data Osteo-core plasty has demonstrated clinical efficacy in treatment of symptomatic bone marrow lesions associated with knee osteoarthritis.

## Introduction

Subchondral bone is a metabolically active tissue and is responsible for providing nutrition to articular cartilage, playing a crucial role in the healing of cartilage lesions. Subchondral bone is composed of two major constituents: the bone plate and the spongiosa. Pathology involving the subchondral bone compromises function of the osteochondral unit and can lead to deterioration of overlying articular cartilage. In cases of knee osteoarthritis (OA), subchondral bone marrow edema (BME) is associated with more rapid joint

\* Katarzyna Herman, Department of Orthopedics and Traumatology, O.A.S.I. Bioresearch Foundation NPO, Katowice, Poland.  
Email address: [khermanmd@gmail.com](mailto:khermanmd@gmail.com) (K. Herman).

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degeneration, and greater patient-reported pain. Numerous studies have been conducted to examine the use of biologic therapy in maintaining and improving cartilage health.<sup>1-4</sup> Importantly, however, options for the treatment of subchondral bone pathology are limited. Osteo-core plasty (OCP) is a novel, minimally invasive treatment for subchondral bone pathology, developed to limit the progression of OA and to increase joint longevity.

### *Bone marrow lesions*

There are numerous pathologies that may be described as Bone marrow lesions (BMLs). Although these lesions may have a similar appearance on magnetic resonance imaging (MRI), there is variability in the pathologic processes. BMLs may be classified according to etiology: mechanical, ischemic, or reactive, traumatic, and nontraumatic. Importantly, it must be considered whether the subchondral bone lesion is treatable and the changes to the osteochondral unit reversible.<sup>5</sup>

Traumatic BMLs may result from direct (eg, ligament tear) or indirect (eg, overload) injury. Pivot shift osteochondral injury associated with traumatic anterior cruciate ligament (ACL) tears, lateral patellar dislocations and valgus injuries are a common cause of knee BMLs.<sup>6-8</sup> MRI distribution of BMLs and associated soft-tissue lesions typically reveal the mechanism of injury. In an ACL-injured knee, edema-like signals on MRI with an uninjured cortical bone layer tend to resolve spontaneously<sup>9</sup> but can last more than a year. Studies have demonstrated that BML location may influence regeneration potential. In cases of an ACL-injured knee, those lesions located on the femoral condyle tend to resolve more rapidly than those located in lateral tibia.<sup>10</sup>

Spontaneous insufficiency fractures of the knee (SIFK) are a part of the spectrum of BME syndromes in which the etiology remains unclear.<sup>11</sup> On MRI they demonstrate extensive remarkable BME-like signal that involve the articular surface. A fracture line parallel to the articular surface is commonly seen. Occasionally and even frequently, SIFK is complicated with osteonecrosis (ON). Current clinical data also demonstrate that SIFK progression to osteochondral collapse is what was earlier recognized as spontaneous ON of the knee.<sup>12,13</sup> The course of the disease is unpredictable, with spontaneous resolution in some cases, and osteochondral collapse and progression to OA in others.<sup>10</sup> SIFK typically affects males and females in the 5th to 6th decade of life.<sup>11</sup> Symptoms comprise of new onset of severe pain, rest and night pain, and loss of function. It has been shown that SIFK is commonly associated with posterior root tear of the medial meniscus and medial meniscus extrusion, supporting the role of mechanical stress in evolution of these lesions.<sup>11,14</sup> SIFK has been classified to be reversible or irreversible based on the presence of a subchondral band and its size. A subchondral band of low signal greater than 4 mm thick indicates irreversibility.<sup>15</sup> Recently, Sayyid et al<sup>16</sup> suggested a new classification of SIFK to low and high grade: if there is just BME with or without a subchondral fracture, this is considered as low grade. If there is also ON with and without cystic changes around the bone defect the lesion is considered high grade. More than 50% of the low-grade lesions improve within 1 year.<sup>16</sup>

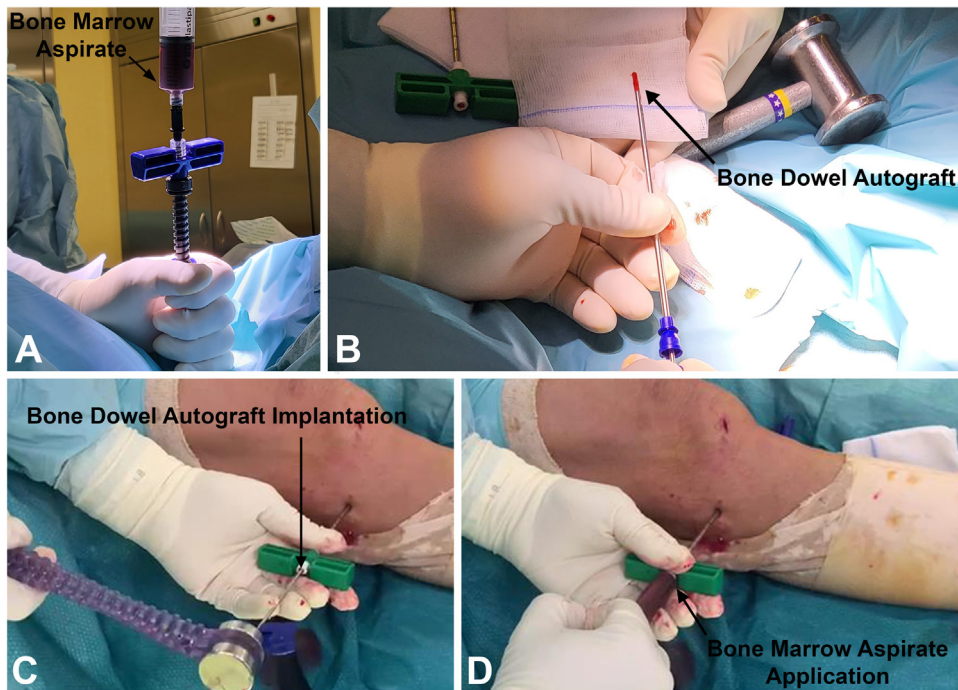
Osteonecrosis, also known as avascular necrosis is a distinct condition to SIFK. ON is an irreversible condition that causes progressive bone damage characterized by cell death subsequent to an incident of bone ischemia. It is directly caused by impaired local blood distribution in atraumatic cases and the physiology of the blood distribution is significantly altered. It is almost always a complication of underlying conditions or treatments, the most common of which being steroid use.<sup>17-19</sup> Other causes of ON include systemic diseases (ie, systemic lupus erythematosus, coagulopathies), radiation, chemotherapy, alcohol consumption, tobacco use,<sup>18</sup> subcapital fractures of the femur, and Caisson's disease. The natural course of ON frequently leads to collapse and deformation of the affected joint surface, regularly leading to joint destruction and secondary arthritis. The subchondral area of bone is principally affected, progressing to irreversible joint cartilage and subchondral bone damage. Outcomes are generally better in children than in adults due to their capacity for bone growth and remodeling.<sup>17</sup>

In advanced stages of OA, subchondral BMLs may be encountered, particularly if there is high-grade chondral injury present, or if there are cystic changes.<sup>20</sup> Patients who suffer from knee OA that is associated with BMLs tend to report greater pain intensity compared to those cases of OA not associated with BMLs.<sup>21</sup> Histologic analysis has demonstrated that BMLs in cases of OA represent hemorrhage, bone necrosis, fibrosis, and trabecular abnormalities, as opposed to actual bone edema.<sup>22-24</sup> Additionally, the presence of subchondral bone cysts in cases of BMLs are associated with a greater incidence of total knee arthroplasty treatment compared to cases of BMLs without associated subchondral cysts.<sup>25,26</sup> Importantly, however, bone cysts are not specific to OA and may be presented in other conditions such as rheumatoid arthritis, ON, or SIFK.<sup>27</sup>

### *Diagnostic imaging of bone marrow lesions*

The diagnosis of BMLs is based on MRI. These lesions usually appear as hyperintense areas within the trabecular subchondral bone at the site of increased mechanical stress on fat-saturated T2-weighted and short tau inversion recovery sequences. These signal changes intensify after intravenous administration of contrast agents. Although crucial for early diagnosis of conditions associated with BMLs, the prognostic value of MRI remains controversial with regard to the ability to predict development of OA. Differential diagnosis of BMLs identified on MRI includes stress fractures, Sudeck's syndrome, primary bone tumors or metastases, ON, infection, rheumatoid arthritis, and transient osteoporosis.

The etiology of BMLs may only be identified after more aggressive and irreversible conditions when similar clinical presentations have been excluded. Differentiation between bone bruises and transient osteoporosis poses a great diagnostic challenge. The absence of additional focal lesions in the subchondral bone is a very sensitive and specific sign of transient osteoporosis that differentiates it from chronic conditions. In cases involving complex regional pain syndrome, there should be focus on associated clinical findings



**Figure.** A, Bone marrow aspirate extracted from iliac crest. B, Autologous bone dowel after extraction from iliac crest. C, Implantation of bone dowel autograft into subchondral bone lesion of lateral femoral condyle. D, Application of bone marrow aspirate into site of subchondral bone lesion of lateral femoral condyle.

such as skin atrophy, sensorimotor impairment, and contractures. Intravenous contrast is used to improve the diagnostic value of MRI in neoplastic conditions.

If subchondral fracture is suspected, computed tomography should be performed. Studies have attempted to use genetic and biochemical markers from serum or joint tissue for early diagnosis. However, these methods are in the early stages of development and their role is presently unclear. Although plain radiographs are not the gold standard for the diagnosis of BMLs, they are especially useful to identify OA. Subchondral bone sclerosis is typically seen on plain radiographic imaging of OA, which results from new bone deposition on preexisting trabeculae and trabecular compression, leading to microfractures and callus formation.<sup>28</sup> On MRI, bone sclerosis may resemble the subchondral low-signal-intensity areas seen in SIFK. However, in cases of knee OA, the MRI signal changes are localized and there is associated loss of overlying articular cartilage. SIFK presents on MRI a more extensive subchondral signal change in association with preserved articular cartilage, although there may be progression to osteochondral collapse and eventual degenerative joint failure.<sup>11</sup>

BME is always present in cases of ON; however, this is not a specific finding and there are numerous conditions that must be considered as the inciting factor. In ON of the knee, a “double-line sign” is typically seen on T2-weighted scans. This consists of an inner high-signal-intensity band, representing vascularized granulation tissue, and an outer low-signal-intensity band, representing the new sclerotic bone.<sup>11</sup> The most concerning complication of ON is subchondral collapse, which occurs more frequently in the setting of larger BMLs, particularly if a lesion is greater than one-third of the condyle on mid-coronal magnetic resonance scans, or the middle and posterior one-third of the condyle on mid-sagittal magnetic resonance scans.<sup>29</sup>

### Surgical technique

The surgical technique was developed by the senior author (A.G.), and initial clinical data have demonstrated good clinical outcomes.<sup>30-32</sup> Firstly, bone marrow (BM) is aspirated from the ipsilateral iliac crest using a sharp trocar with a hollow aspiration sleeve (Figure). The trocar should be introduced between the cortices into cancellous bone. Proper positioning of the trocar is confirmed by aspiration of 1 ml of bone marrow. The sharp needle stylet is then replaced by a blunt trocar. A Marrow Cellution system (Marrow Cellution, Aspire Medical Innovation, Germany) is used to collect 10 mL of bone marrow aspirate (BMA). The closed tip canula reduces aspiration of the peripheral blood. Additionally a multilevel aspiration allows the surgeon to reach a large area inside the marrow space resulting in higher concentration of nucleated cells. This system has been shown to acquire BMA that is similar in composition to the BMA obtained by other commercially available systems, without the need for additional manipulation such as centrifugation or chemical separation. BMA with the aforementioned system has been shown to collect BM that contains high concentrations of CFU-fs/mL and CD34+/mL. Furthermore, the level of CFU-fs/mL has been shown to be significantly higher when compared to cen-

trifuged BMA in side-by-side comparison, using samples obtained from the contralateral iliac crests of test subjects.<sup>33</sup> In OCP, there is no requirement for centrifugation of the BMA, thereby enabling the surgeon to precisely apply the aspirate to the target necrotic zone without risk of contamination. Once BMA has been extracted, a sharp trocar is used to harvest bone dowels from the site of bone marrow aspiration (Figure).

The patient is positioned in standard supine fashion for knee arthroscopy and is anaesthetized. Concomitant treatment of associated pathology such as chondral injury, meniscal tear, and ligament injury is performed prior OCP. Additionally, osteotomy to normalize bony alignment about the knee is performed concurrently if indicated. Anteroposterior and lateral fluoroscopic images are taken at the time of the procedure. These images are examined alongside the preoperative MRI study, allowing for precise placement of the guide pin at the location of BME. A cannula is inserted over the guide pin, and the guide pin is then removed. The autologous bone dowels are inserted through the cannula using a blunt trocar and positioned within the BML (Figure). BMA is then injected into the BML through the cannula (Figure). The trocar is reinserted and left in place for 5 to 7 minutes to allow the BMA to clot. Final arthroscopic examination is performed to confirm extra-articular placement of the OCP.

### Postoperative protocol

Rehabilitation to address concomitant procedures is incorporated into the postoperative protocol and is patient specific. Early postoperative rehabilitation is focused on pain control, preserving range of motion, and limiting muscular atrophy. Immediately after the procedure, passive motion is initiated, and cryotherapy is applied to minimize pain and swelling. Isometric and isotonic exercises are introduced on the first postoperative day. Touchdown weight bearing begins 3 to 4 weeks postoperatively and full weight bearing is allowed 6 weeks postoperatively. Pool therapy is used to help regain a normal gait pattern and is initiated after the surgical wounds are healed. Postoperative MRI may be performed after 3 and 6 months to monitor the effects of treatment. A decrease in hyper-intense signal in T2-weighted images is expected to be seen at 3 months postoperatively, with full resolution of the bone marrow lesion after 6 months.

### Results

We recently conducted an observational study of 24 patients (mean age  $53 \pm 17$  years) with symptomatic BMLs of the knee who were treated with the OCP and then followed prospectively. Each patient was evaluated before surgery and 2 years postoperatively using the Knee Injury and Osteoarthritis Outcome Score (KOOS) subsets of symptoms, pain, activity of daily living (ADL), sport, and quality of life. At 2-year follow-up, all patients showed a significant improvement in patient-reported scores compared to the preoperative assessment, with KOOS scores all significantly improved: symptoms ( $p = .0005$ ), pain ( $p = .0003$ ), ADL ( $p = .0053$ ), sport ( $p = .0014$ ), and quality of life ( $p < .0001$ ). Median range KOOS symptoms improved from 48.00 [36.25-68.00] to 85.50 [61.75-100.0], KOOS pain from 51.50 [39.25-67.75] to 90.50 [69.25-100.0], KOOS ADL from 51.50 [40.00-79.50] to 90.00 [62.00-100.0], KOOS sport from 27.50 [15.00-48.75] to 75.00 [26.25-100.0], KOOS quality of life from 30.00 [25.00-43.00] to 72.00 [44.00-100.0]. No serious adverse events were observed during the study.

### Discussion

It is important to appreciate the role of subchondral bone. BMLs involving the osteochondral unit are not necessarily pathologic processes that initially involve the articular cartilage. Arteriovenous complexes have been shown to penetrate the subchondral bone plate and reach into the calcified cartilage layer.<sup>34</sup> Additionally, Lane et al demonstrated increased vascular perforation at areas of increased stress, suggesting that the subchondral bone reacts to greater loads by enhancing blood supply.<sup>34</sup> Conversely, in cases of OA, joint overload is known to inhibit natural processes of remodeling and there is disruption of nutrient flow from the subchondral bone to the overlying articular cartilage. MacKay et al showed that subchondral bone quality is associated with radiographic knee OA progression.<sup>35</sup>

Studies have compared clinical outcomes of cartilage restoration procedures when performed in association with lesions that involved subchondral BME. Autologous chondrocyte implantation, when performed in the presence of severe subchondral bone marrow edema, is associated with poorer clinical outcomes. BME has been shown to be a reliable prognostic factor in the first year after treatment of cartilage lesions using autologous chondrocyte implantation.<sup>36</sup> Furthermore, the persistence of edema signs in the subchondral bone is a factor predicting poor clinical outcome after microfracture surgery.

Biologic adjuncts to treat cartilage injury are becoming increasingly researched and are likely to prove beneficial in preserving joint health. BMA is a readily available source of mesenchymal stromal cells and growth factors, including platelet-derived growth factor, transforming growth factor-beta, and bone morphogenetic proteins (BMP-2, BMP-7), which have anabolic and anti-inflammatory effects. While BMAC is an attractive source of mesenchymal stromal cells for clinical use, there is clear benefit to the use of BM isolates that do not require separate processing, such as centrifugation.

OCP is a novel, minimally invasive procedure that has demonstrated clinical efficacy, based on early clinical data, in the treatment of symptomatic BME associated with knee OA and other conditions. This treatment may be particularly beneficial for younger, active patients who wish to better manage pain and avoid or delay the need for more invasive procedures such as total knee arthroplasty.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

## Ethics approval

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

## References

- Gobbi A, Lad D, Karnatzikos G. The effects of repeated intra-articular PRP injections on clinical outcomes of early osteoarthritis of the knee. *Knee Surg Sports Traumatol Arthrosc.* 2015;23(8):2170–2177. doi:10.1007/S00167-014-2987-4.
- Imhof H, Breitenseher M, Kainberger F, Rand T, Trattnig S. Importance of subchondral bone to articular cartilage in health and disease. *Top Magn Reson Imaging.* 1999;10(3):180–192. doi:10.1097/00002142-199906000-00002.
- Herman K, Gobbi A. Evidence-based approach to orthobiologics for osteoarthritis and other joint disorders. *Phys Med Rehabil Clin N Am.* 2023;34(1):71–81. doi:10.1016/j.pmr.2022.08.019.
- Kuebler D, Schnee A, Moore L, et al. Short-term efficacy of using a novel low-volume bone marrow aspiration technique to treat knee osteoarthritis: a retrospective cohort study. *Stem Cells Int.* 2022;2022:1–7. doi:10.1155/2022/5394441.
- Roemer FW, Frobell R, Hunter DJ, et al. MRI-detected subchondral bone marrow signal alterations of the knee joint: terminology, imaging appearance, relevance and radiological differential diagnosis. *Osteoarthritis Cartilage.* 2009;17(9):1115–1131. doi:10.1016/j.joca.2009.03.012.
- Bretlau T, Tuxøe J, Larsen L, Jørgensen U, Thomsen HS, Lausten G. Bone bruise in the acutely injured knee. *Knee Surg, Sports Traumatol, Arthroscopy.* 2002;10(2):96–101. doi:10.1007/s00167-001-0272-9.
- Koga H, Nakamae A, Shima Y, et al. Mechanisms for noncontact anterior cruciate ligament injuries. *Am J Sports Med.* 2010;38(11):2218–2225. doi:10.1177/0363546510373570.
- Viskontas DG, Giuffre BM, Duggal N, Graham D, Parker D, Coolican M. Bone bruises associated with ACL rupture. *Am J Sports Med.* 2008;36(5):927–933. doi:10.1177/0363546508314791.
- Costa-Paz M, Muscolo DL, Ayerza M, Makino A, Aponte-Tinco L. Magnetic resonance imaging follow-up study of bone bruises associated with anterior cruciate ligament ruptures. *Arthroscopy: The J Arthroscopic & Related Surg.* 2001;17(5):445–449. doi:10.1053/jars.2001.23581.
- Marcacci M, Andriolo L, Kon E, Shabshin N, Filardo G. Aetiology and pathogenesis of bone marrow lesions and osteonecrosis of the knee. *EFORT Open Rev.* 2016;1(5):219–224. doi:10.1302/2058-5241.1.000044.
- Gorbachova T, Melenevsky Y, Cohen M, Cerniglia BW. Osteochondral lesions of the knee: differentiating the most common entities at MRI. *RadioGraphics.* 2018;38(5):1478–1495. doi:10.1148/rg.2018180044.
- Fujita S, Arai Y, Honjo K, Nakagawa S, Kubo T. A case of spontaneous osteonecrosis of the knee with early and simultaneous involvement of the medial femoral condyle and medial tibial plateau. *Case Rep Orthop.* 2016;2016:1–7. doi:10.1155/2016/2574975.
- Hussain ZB, Chahla J, Mandelbaum BR, Gomoll AH, LaPrade RF. The role of meniscal tears in spontaneous osteonecrosis of the knee: a systematic review of suspected etiology and a call to revisit nomenclature. *Am J Sports Med.* 2019;47(2):501–507. doi:10.1177/0363546517743734.
- Yao L, Stanczak J, Boutin RD. Presumptive subarticular stress reactions of the knee: MRI detection and association with meniscal tear patterns. *Skeletal Radiol.* 2004;33(5):260–264. doi:10.1007/s00256-004-0751-4.
- Lecouvet FE, van de Berg BC, Maldague BE, et al. Early irreversible osteonecrosis versus transient lesions of the femoral condyles: prognostic value of subchondral bone and marrow changes on MR imaging. *AJR Am J Roentgenol.* 1998;170(1):71–77. doi:10.2214/ajr.170.1.9423603.
- Sayyid S, Younan Y, Sharma G, et al. Subchondral insufficiency fracture of the knee: grading, risk factors, and outcome. *Skeletal Radiol.* 2019;48(12):1961–1974. doi:10.1007/s00256-019-03245-6.
- Herman K, Pękala P, Szwedowski D, Grabowski R, Cholewiński J. Avascular Necrosis. In: Gobbi A, Lane JG, Longo UG, Dallo I, eds. *Joint Function Preservation.* Cham: Springer; 2022:161–171. doi: 10.1007/978-3-030-82958-2\_14.
- Karim AR, Cherian JJ, Jauregui JJ, Pierce T, Mont MA. Osteonecrosis of the knee: review. *Ann Transl Med.* 2015;3(1). doi:10.3978/J.ISSN.2305-5839.2014.11.13.
- Gobbi A, Alvarez R, Irlandini E, Dallo I. Current Concepts in Subchondral Bone Pathology. In: Gobbi A, Lane JG, Longo UG, Dallo I, eds. *Joint Function Preservation.* Cham: Springer; 2022:161–171. doi: 10.1007/978-3-030-82958-2\_15.
- Dallo I, Gobbi A. Knee osteochondral lesions treatments. *Joint Function and Preservation.* 2022:337–344. doi:10.1007/978-3-030-82958-2\_21.
- Yusuf E, Kortekaas MC, Watt I, Huizinga TWJ, Kloppenburg M. Do knee abnormalities visualised on MRI explain knee pain in knee osteoarthritis? A systematic review. *Ann Rheum Dis.* 2011;70(1):60–67. doi:10.1136/ard.2010.131904.
- Zanetti M, Bruder E, Romero J, Hodler J. Bone marrow edema pattern in osteoarthritic knees: correlation between MR imaging and histologic findings. *Radiology.* 2000;215(3):835–840. doi:10.1148/RADIOLOGY.215.3.R00JN05835.
- Taljanovic MS, Graham AR, Benjamin JB, et al. Bone marrow edema pattern in advanced hip osteoarthritis: quantitative assessment with magnetic resonance imaging and correlation with clinical examination, radiographic findings, and histopathology. *Skeletal Radiol.* 2008;37(5):423–431. doi:10.1007/S00256-008-0446-3.
- Xu L, Hayashi D, Roemer FW, Felson DT, Guermazi A. Magnetic resonance imaging of subchondral bone marrow lesions in association with osteoarthritis. *Semin Arthritis Rheum.* 2012;42(2):105–118. doi:10.1016/J.SEMARTHRT.2012.03.009.
- Tanamas SK, Wluka AE, Pelletier JP, et al. The association between subchondral bone cysts and tibial cartilage volume and risk of joint replacement in people with knee osteoarthritis: a longitudinal study. *Arthritis Res Ther.* 2010;12(2):R58. doi:10.1186/AR2971.
- Gobbi A, Dallo I. Case report: Osteo-Core-Plasty technique for the treatment of a proximal tibial subchondral cystic lesion. *Aspire Med Innovation.* 2021.
- Lecouvet FE, Malghem J, Maldague BE, van de Berg BC. MR imaging of epiphyseal lesions of the knee: current concepts, challenges, and controversies. *Radiol Clin North Am.* 2005;43(4):655–672. doi:10.1016/J.RCL.2005.02.002.
- Gupta KB, Duryea J, Weissman BN. Radiographic evaluation of osteoarthritis. *Radiol Clin North Am.* 2004;42(1):11–41. doi:10.1016/S0033-8389(03)00169-6.
- Sakai T, Sugano N, Nishii T, Haraguchi K, Yoshikawa H, Ohzono K. Osteonecrosis of the patella in patients with nontraumatic osteonecrosis of the femoral head: MRI findings in 60 patients. *Acta Orthop Scand.* 2000;71(5):447–451. doi:10.1080/000164700317381108.
- Dallo I, D'Ambrosi R, Szwedowski D, Mobasheri A, Gobbi A. Minimally invasive cell-based therapy for symptomatic bone marrow lesions of the knee: a prospective clinical study at 1 year. *Stem Cells Dev.* 2022;31(15-16):488–497. doi:10.1089/scd.2021.0283.
- Szwedowski D, Dallo I, Gobbi A. Osteo-core plasty: a minimally invasive approach for subchondral bone marrow lesions of the knee. *Arthrosc Tech.* 2020;9(11):e1773–e1777. doi:10.1016/j.eats.2020.07.023.
- Gobbi A, Arbas AJ, Dallo I. Proximal Tibial Subchondral Cystic Lesion Treatment with Osteo-Core-Plasty. In: Gobbi A, Lane JG, Longo UG, Dallo I, eds. *Joint Function Preservation.* Cham: Springer; 2022:237–246. doi: 10.1007/978-3-030-82958-2\_21.

33. Scarpone M, Kuebler D, Chambers A, et al. Isolation of clinically relevant concentrations of bone marrow mesenchymal stem cells without centrifugation. *J Transl Med.* 2019;17(1). doi:[10.1186/S12967-018-1750-X](https://doi.org/10.1186/S12967-018-1750-X).
34. Lane LB, Villacin A, Bullough PG. The vascularity and remodelling of subchondrial bone and calcified cartilage in adult human femoral and humeral heads. An age- and stress-related phenomenon. *J Bone Joint Surg Br.* 1977;59(3):272–278. doi:[10.1302/0301-620X.59B3.893504](https://doi.org/10.1302/0301-620X.59B3.893504).
35. MacKay JW, Kapoor G, Driban JB, et al. Association of subchondral bone texture on magnetic resonance imaging with radiographic knee osteoarthritis progression: data from the Osteoarthritis Initiative Bone Ancillary Study. *Eur Radiol.* 2018;28(11):4687. doi:[10.1007/S00330-018-5444-9](https://doi.org/10.1007/S00330-018-5444-9).
36. Niemeyer P, Salzmann G, Steinwachs M, et al. Presence of subchondral bone marrow edema at the time of treatment represents a negative prognostic factor for early outcome after autologous chondrocyte implantation. *Arch Orthop Trauma Surg.* 2010;130(8):977–983. doi:[10.1007/S00402-010-1049-8](https://doi.org/10.1007/S00402-010-1049-8).