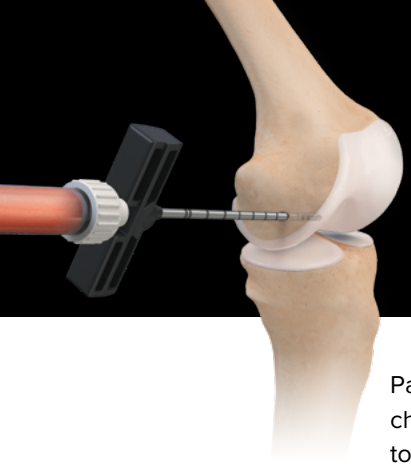

IntraOsseous BioPlasty® (IOBP®) Technique Scientific Update

A review of design rationale, techniques, and outcomes

Patients suffering from osteoarthritis (OA) commonly present with subchondral bone changes, leading researchers to suggest a defect of the subchondral bone may progress to disruption of the overlying articular cartilage, resulting in OA.[1] Scientific literature has documented the IOBP procedure's potential for treating OA, including improvement in quality of life,[2] reduction in percentage of total knee replacements, and definite advantages over calcium phosphate injections.[3] Evidence suggests the IOBP procedure can be used as a minimally invasive treatment to help heal the subchondral bone impacting OA.

Scope of the Problem

Manara M, Varenna M

A clinical overview of bone marrow edema. *Reumatismo.* 2014;66(2):184-196. doi:10.4081/reumatismo.2014.790

- Review of bone marrow lesions (BMLs), including observation via MRI, causes, and their usual self-limiting recovery without sequelae
- BML is predictive for joint replacement
  - 109 subjects w/ OA; risk of knee prosthesis over 4 years significantly increased with increase in BML scores
- OA is more likely to be found in knee compartments with higher load, such as the medial vs the lateral compartment

Takeaway

BMLs are a key indicator for identifying possible joint replacement.

Davies-Tuck ML, Wluka AE, Forbes A, Wang Y, English DR, Giles GG, O'Sullivan R, Cicuttini FM

Development of bone marrow lesions is associated with adverse effects on knee cartilage while resolution is associated with improvement—a potential target for prevention of knee osteoarthritis: a longitudinal study. *Arthritis Res Ther.* 2010;12(1):R10. doi:10.1186/ar2911

- Observed the life cycle of knee BMLs
- 271 adults had MRI of dominant knee at baseline and again 2 years later
  - 14% initially had BMLs
  - 14% developed BMLs
  - 54% with BMLs at baseline persisted
- Developing an incident BML increases odds of defects in cartilage; this occurs more with lateral BMLs than medial BMLs
- Resolution of medial BMLs was associated with reduced loss in medial tibial cartilage volume and reduced progression over time

Takeaway

BMLs do not easily resolve naturally and are found to contribute to the acceleration of harmful knee pathology.

Arthrex®

Felson DT, Niu J, Guermazi A, Roemer F, Aliabadi P, Clancy M, Torner J, Lewis CE, Nevitt MC

Correlation of the development of knee pain with enlarging bone marrow lesions on magnetic resonance imaging. *Arthritis Rheum.* 2007;56(9):2986-2992. doi:10.1002/art.22851

- Patients 50-79 years of age with OA or high risk of OA had baseline query of knee pain, then follow-up 15 months later
  - Experimental group: no pain at baseline, pain at follow-up
- 49.1% of case knees showed increase in BML score
- 32.4% of experimental knees with no BMLs initially saw new BMLs form

Takeaway

Knee pain is associated with an increase in BMLs found within compartments of the knee.

Scher C, Craig J, Nelson F

Bone marrow edema in the knee in osteoarthrosis and association with total knee arthroplasty within a three-year follow-up. *Skeletal Radiol.* 2008;37(7):609-617. doi:10.1007/s00256-008-0504-x

- Knee MRI studies over 3-year period of 25 patients in OA group and 48 patients in OA/BML group; used 4 distinguishable bone marrow edema categories:
  - None
  - Focal
  - Global
  - Cystic
- BMLs of all 4 patterns led to an 8.95 times greater likelihood of total knee arthroplasty (TKA)
  - Global pattern BMLs were 5.45 times more likely to progress to TKA than BMLs with other patterns
  - Global pattern BMLs were 13.04 times more likely to progress to TKA than patients with no BMLs
- TKA patients were 12.6 years older than those without
- Results remained significant after accounting for age difference

Takeaway

Patients with any size BML are approximately 9 times more likely to progress rapidly towards TKA than patients with no BML.

Basic Science Studies

Madry H, van Dijk CN, Mueller-Gerbl M

The basic science of the subchondral bone. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(4):419-433. doi:10.1007/s00167-010-1054-z

- The subchondral plate's purpose is to absorb most of the mechanical force in diarthrodial joints
- The tight connection of articular cartilage and subchondral bone via the calcified zone from the subchondral plate causes this surface to be remodeled in early OA (specifically, regions of articular cartilage damages)
- Subchondral anatomy and structure vary from joint to joint and do not provide a universal standard for subchondral characteristics

Takeaway

By taking most of the force in joint movement, subchondral bone causes remodeling of the articular cartilage impacting the progression of OA.

Brem MH, Schlechtweg PM, Bhagwat J, Genovese M, Dillingham MF, Yoshioka H, Lang P

Longitudinal evaluation of the occurrence of MRI-detectable bone marrow edema in osteoarthritis of the knee. *Acta Radiol.* 2008;49(9):1031-1037. doi:10.1080/02841850802339413

- 23 patients with degenerative articular cartilage lesions of grade 3 or lower had baseline MRI and 3-month follow-up MRI; 12 of 23 had 6-month MRI follow-up as well
- 71.4% of detected subchondral BMLs had overlaying cartilage defect present
- BMLs were nonstatic during the recordings as there was no statistical difference of BMLs score

Takeaway

BMLs follow no set pattern of growth and occur at random.

Clinical Studies

Di Matteo B, Polignano A, Onorato F, La Porta A, Iacono F, Bonanzinga T, Raspugli G, Marcacci M, Kon E

Knee intraosseous injections: a systematic review of clinical evidence of different treatment alternatives. *Cartilage*. 2021;13(1_suppl):1165S-1177S. doi:10.1177/1947603520959403

- Summary of 12 studies examining intraosseous injections of platelet-rich plasma (PRP) or mesenchymal cell products into the knee for patients with knee OA, all with a minimum of 5 patients and 6-month follow-up
- Conversion rates to TKA:
  - Calcium phosphate (CaP): 26.68%
  - PRP: 15.45%
  - Bone marrow concentrate (BMC): 10%

Takeaway

Intraosseous injections lower the conversion rate to TKA, with BMC leading to the lowest conversion rate and CaP injections to the highest.

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Sánchez M, Delgado D, Sánchez P, Muiños-López E, Paiva B, Granero-Moltó F, Prósper F, Pompei O, Pérez JC, Azofra J, Padilla S, Fiz N

Combination of intra-articular and intraosseous injections of platelet-rich plasma for severe knee osteoarthritis: a pilot study. *Biomed Res Int*. 2016;2016:4868613. doi:10.1155/2016/4868613

- 14 patients with severe OA with severity degrees of 3 or 4 on the Ahlbäck scale
- Each patient received 1 intra-articular PRP treatment and 2 intraosseous PRP injections
- Statistically significant improvement was reported in symptoms, pain, activities of daily living, sports/recreation, and QOL scores at 8 and 24 weeks
  - 84.2% improvement in symptoms, activities of daily living, quality of life, and pain
  - 76.92% improvement for sports/recreation

Takeaway

Intraosseous PRP injections can improve quality of life for patients by 85% and improve sport/recreation function by 75%.

Ivković A, Glavčić M, Vuletić F, Janković S

Core decompression combined with intraosseous autologous conditioned plasma injections decreases pain and improves function in patients with symptomatic knee bone marrow lesions. *Biomedicines*. 2023;11(7):1799. doi:10.3390/biomedicines11071799

- Prospective case series following 20 patients receiving IO injection of PRP to treat symptomatic bone marrow lesions in the knee.
- Significant improvements in both pain (NPRS) and function (KOOS) were found at all timepoints.
  - At 1-week follow-up, NPRS improved from 8.3 ± 0.8 to 1.5 ± 1.0 ($P \leq .001$) and KOOS improved from 33.4 ± 10.6 to 53.9 ± 13.6 ($P \leq .001$)
  - This trend continued across study duration, with a mean NPRS score of 1.4 at 12-month follow-up and a total KOOS increase of 44.6 points from the baseline (average 78 at 12-month follow-up)
- Whole-Organ Magnetic Resonance Imaging Score improved from 66.1 ± 19.4 prior to surgery to 58.0 ± 15.9 ($P < .001$) after 3 months.

Takeaway

A combination of core decompression and intraosseous injection of PRP to treat BMLs in the knee is a safe and effective procedure that provides rapid pain relief and a significant increase in joint function up to one year postoperatively.

de Castro JC, Henares-Esguerra EL, Olivia S Tamayo-Shih MB, Wang D, Chang Chien GC

Photoactivated leucocyte-rich platelet-rich plasma treatment in reduction of bone marrow edema in hip osteoarthritis. *Regen Med*. 2022;17(8):521-531. doi:10.2217/rme-2021-0165

- Case study of a 65-year-old female patient with hip OA treated with leukocyte-rich PRP injections in affected site in the bone weekly for 4 sessions
- Harris hip score improved post treatment
  - Pretreatment: 69.43
  - 2 months post treatment: 79.65
  - 3 months post treatment: 93.65
- BML reduced progressively from initial MRI and at 1, 2, and 3 months

Takeaway

PRP injections into affected hip OA sites promote healing of BMLs and may lead to increases in Harris hip scores.

Hernigou P, Bouthors C, Bastard C, Flouzat Lachaniette CH, Rouard H, Dubory A

Subchondral bone or intra-articular injection of bone marrow concentrate mesenchymal stem cells in bilateral knee osteoarthritis: what better postpone knee arthroplasty at fifteen years? A randomized study. *Int Orthop.* 2021;45(2):391-399. doi:10.1007/s00264-020-04687-7

- 60 patients with painful bilateral knee OA of similar Kellgren-Lawrence (KL) grades treated with BMC injections
  - One side received intra-articular (IA) injection, the other subchondral (SC) injection (chosen randomly)
- Short-term KL grade progression rate was lower in SC group than IA group
  - 11 knees in IA group and 2 knees in SC group progressed to higher KL grade at 2-year time point
- Mean BML volume significantly regressed in the SC group but not the IA group ($P = .01$)
  - Preoperative mean BML volume was 2.9 cm^3 in SC group and 2.6 cm^3 in IA group
  - At 2-year follow-up SC group BML volume was reduced to 2.1 cm^3, while no change was made in IA group
- At most recent follow-up (15 years), transition to knee arthroplasty incidence was significantly lower ($P = .01$) in SC group
  - 12 of 60 knees (20%) in the SC group transitioned to arthroplasty, while 42 of 60 knees (70%) in the IA group did

Takeaway

Subchondral injection of BMC in bilateral knee OA patients significantly improved clinical outcome measures and reduced transition-to-arthroplasty rates, as compared to intra-articular BMC injections.

Kasik CS, Martinkovich S, Mosier B, Akhavan S

Short-term outcomes for the biologic treatment of bone marrow edema of the knee using bone marrow aspirate concentrate and injectable demineralized bone matrix. *Arthrosc Sports Med Rehabil*. 2019;1(1):e7-e14. doi:10.1016/j.asmr.2019.07.001

- Short-term outcomes study of 20 patients with symptomatic knee BMLs treated with the IOBP® procedure
  - Mean age 51.7 years, mean follow-up 14.5 months
- 19 of 20 patients experienced a reduction in VAS pain scores and an increase in International Knee Documentation Committee (IKDC) functional scores
  - Mean VAS pain was reduced from 7 preoperatively to 1.3 at latest follow-up
  - Mean IKDC functional score improved from 29.2 to 66.1
- Kaplan-Meier survival analysis demonstrated 1-year joint preservation survivorship of 93%, with all others transitioning to TKA
  - 75% of BMLs demonstrated complete healing on postoperative MRI

Takeaway

The IOBP procedure demonstrates excellent short-term results in functional improvement and pain reduction when treating BMLs of the knee.

References

1. Madry H, van Dijk CN, Mueller-Gerbl M. The basic science of the subchondral bone. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(4):419-433. doi:10.1007/s00167-010-1054-z
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3. Di Matteo B, Polignano A, Onorato F, et al. Knee intraosseous injections: a systematic review of clinical evidence of different treatment alternatives. *Cartilage*. 2021;13(1_suppl):1165S-1177S. doi:10.1177/1947603520959403