

Subchondral Injections of Biologics for advanced DDD and Endplates

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Disclosure



- Founding Governor, World Institute of Regenerative Medicine (WIRM)
- Founder and Co-Chairman, Latin American Pain Society (LAPS)
- Founder and Chairman, NY/NJ Annual Pain Medicine Congress since Nov 2011
- Co-founder and President, Advanced Spine on Park Avenue, New York
- Chair of sections, World Institute of Pain (WIP)
- Past President (2018-2019) and Director Emeritus, ASIPP (2019-Current)
- Executive Director, NYSIPP
- Former Director, Weill Cornell Pain Medicine Fellowship program and Pain Division
- Section Editor, Regenerative Medicine, Pain Physician, official journal of ASIPP
- Associate editor – Pain Practice, Official journal of WIP
- Section Editor, Regenerative Medicine, Journal of Pain and Neuroscience – Official journal of ASPN

SAVE THE DATE!

NOVEMBER 5-8, 2026



15th Annual New York & New Jersey Pain Medicine Congress

Evolving Advanced Pain Therapies

How do Biologics work: Sooner the better

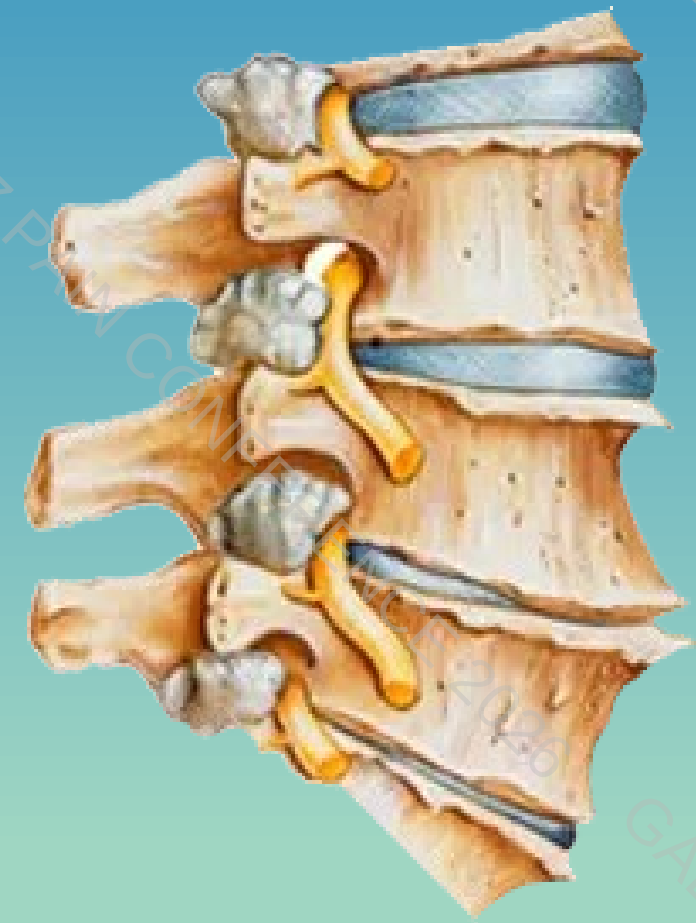
Goal: Create ideal Tissue Homeostasis

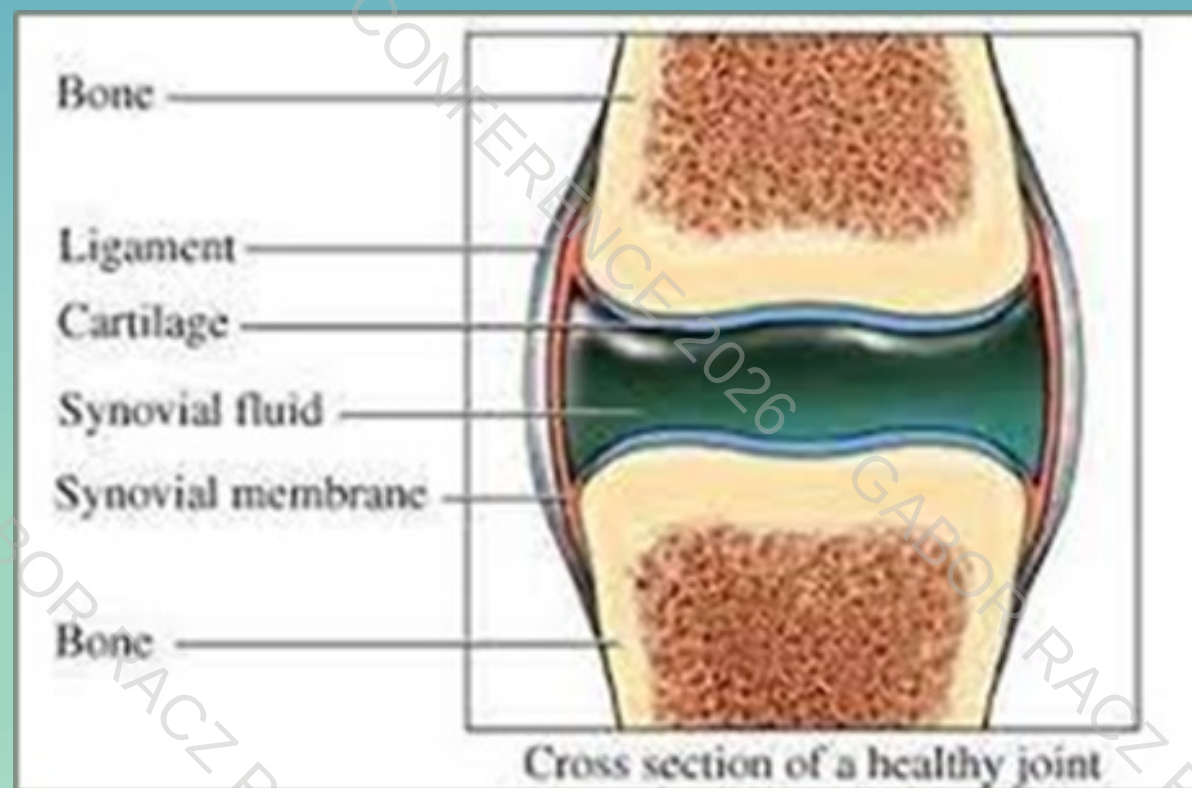
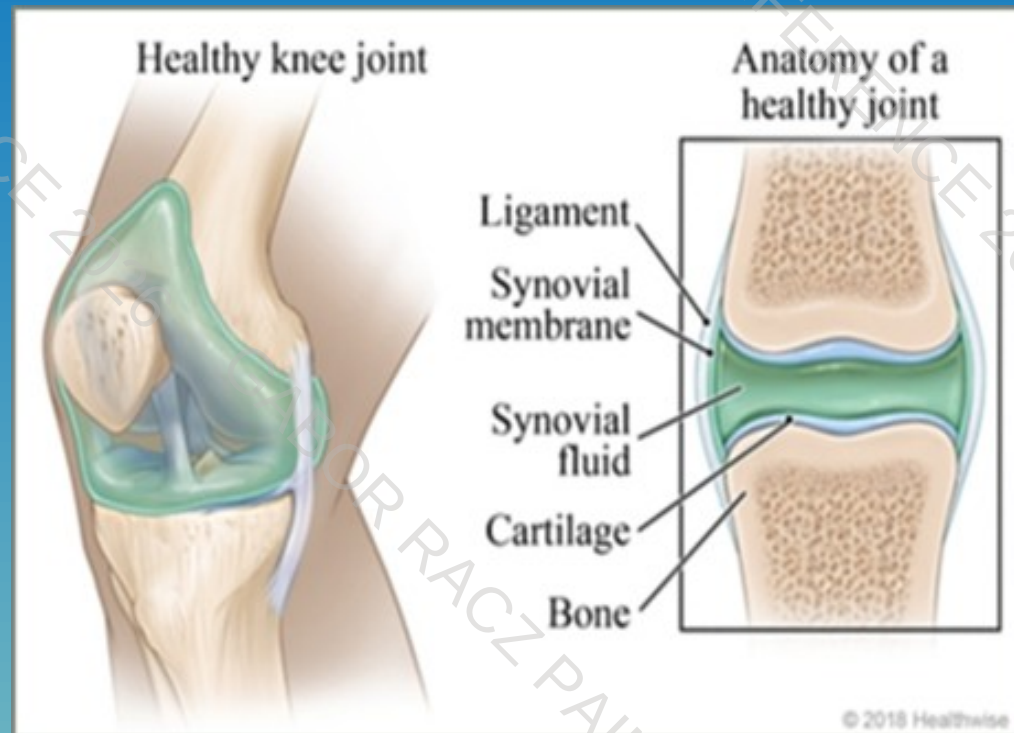
Mild to moderate degeneration:

- Usually PRP /growth factors work by **proliferating and multiplying** the existing cellular mass

For severe degeneration:

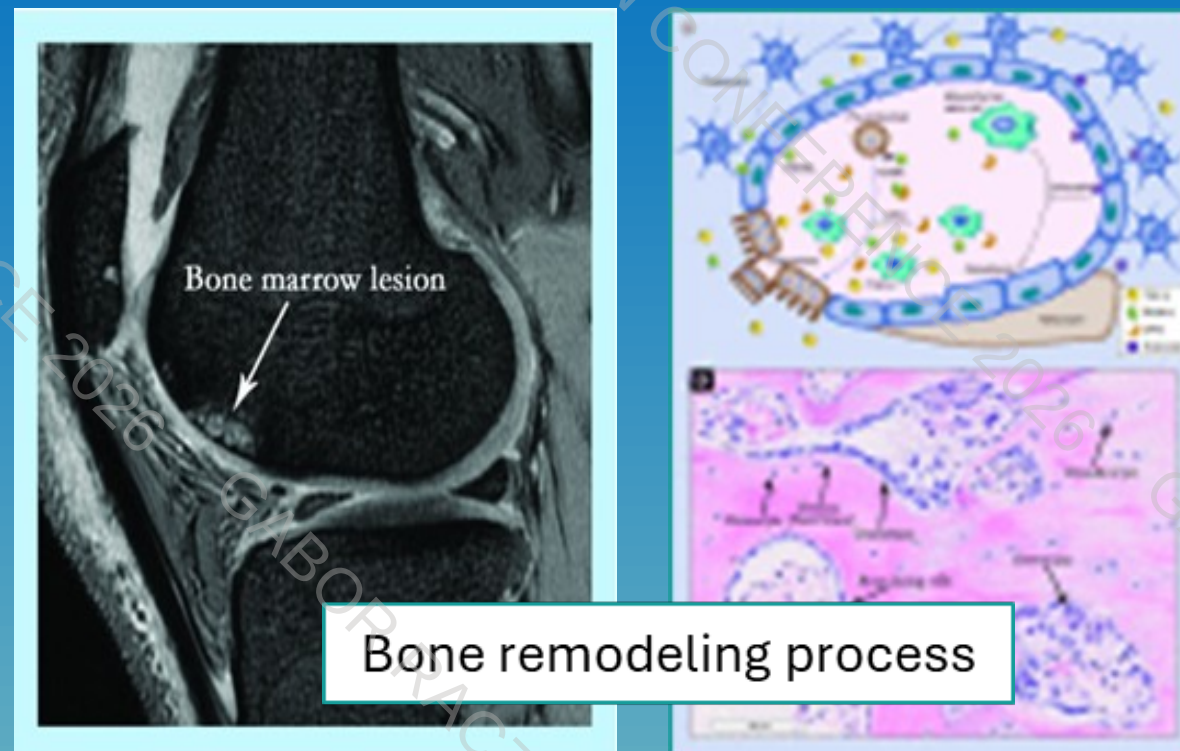
- Regenerative process involves cellular **differentiation** and providing the progenitor cells
- Maximize the cell delivery to the **multiple effective sites** to expedite the regenerative process





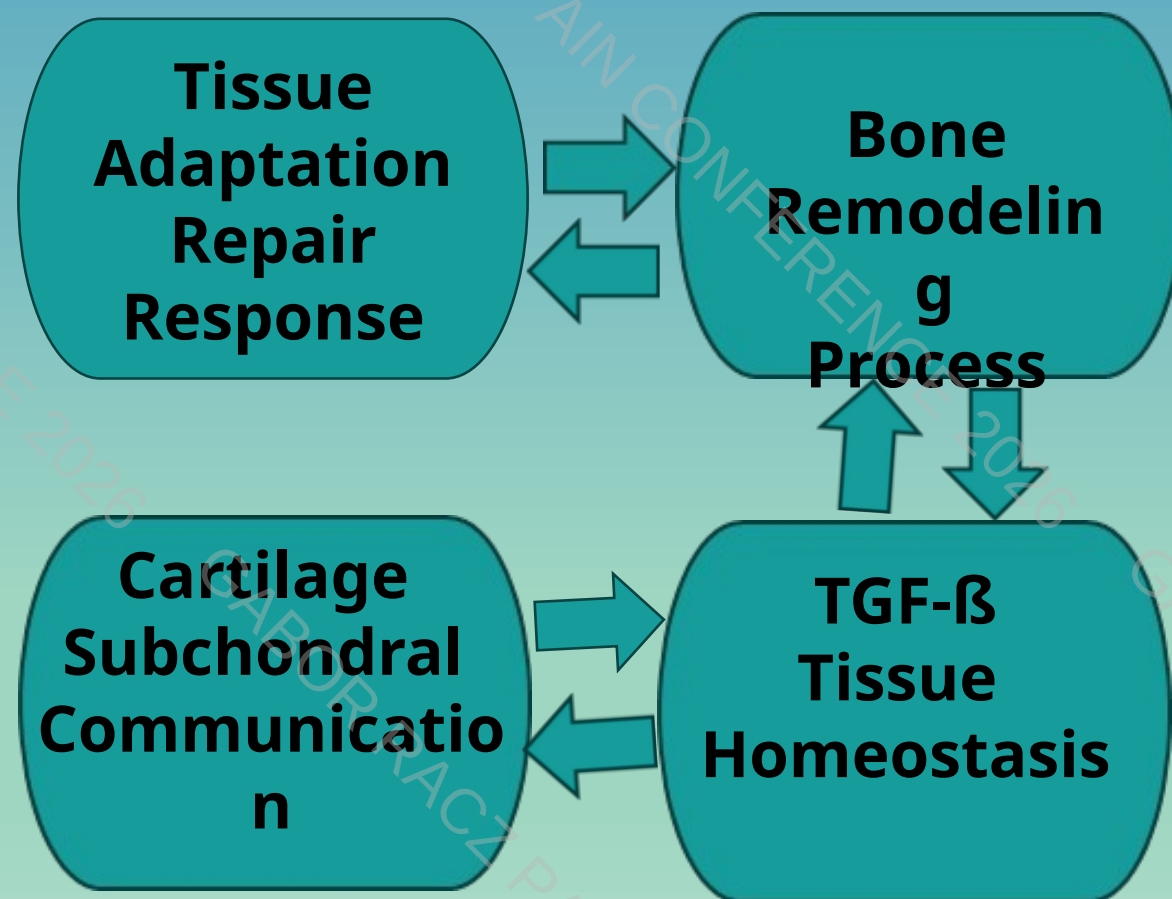
Joint: A complex biological system

- **Cartilage homeostasis:** Dynamic balance between cartilage synthesis and degradation
- **Cross-communication Between:**
 1. Articular cartilage
 2. Synovial membrane
 3. Synovial fluid
 4. Subchondral bone
- In OA, homeostasis depends on **cross-communication** bet' subchondral bone and cartilage



Subchondral bone for joint repair in OA

- **Tissue adaptation and repair responses** are evident in subchondral tissues
- **Bone remodeling process (Bone Homeostasis)** is balance between **Osteoblast** (MSCs) and **Osteoclasts** (Monocytes + Macrophages) activities
- In OA, osteoclasts release **TGF- β** , which **modulates MSC activity** for bone remodeling activity in subchondral bone
- **MSCs in subchondral bone** a novel approach for **cartilage regeneration**



Dragos C. Ilas et al. Future Sci OA. **2017** Nov; 3(4): FSO228

Subchondral bone as injection target

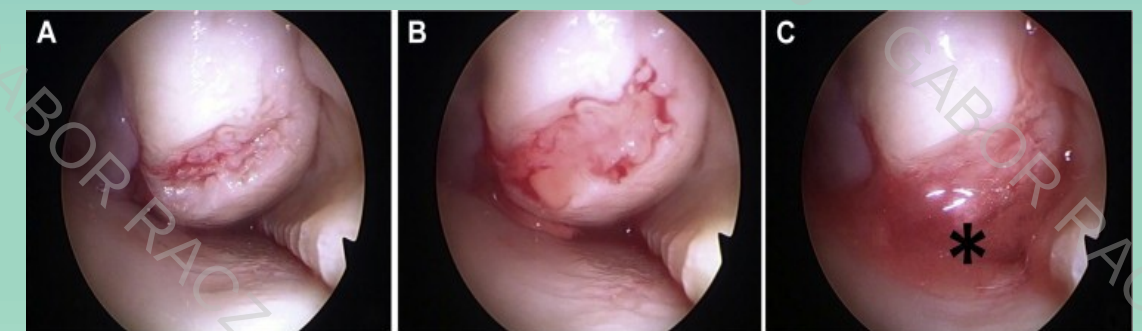
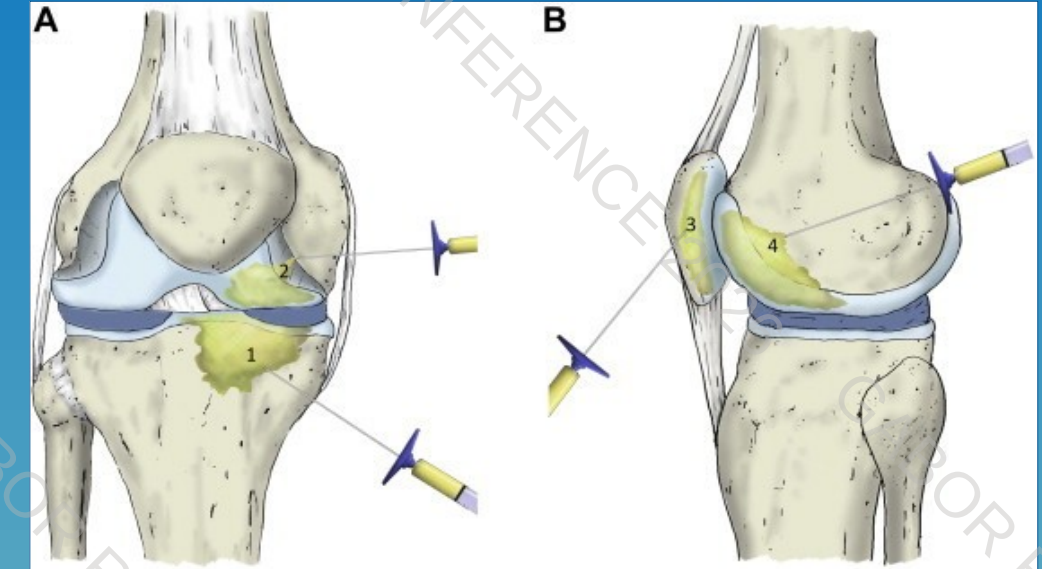
- **Cartilage homeostasis:** Cross-communication among articular cartilage + subchondral bone + synovium

- Commun
are more

“Intraosseous is inaccurate. It should be precisely called “subchondral”

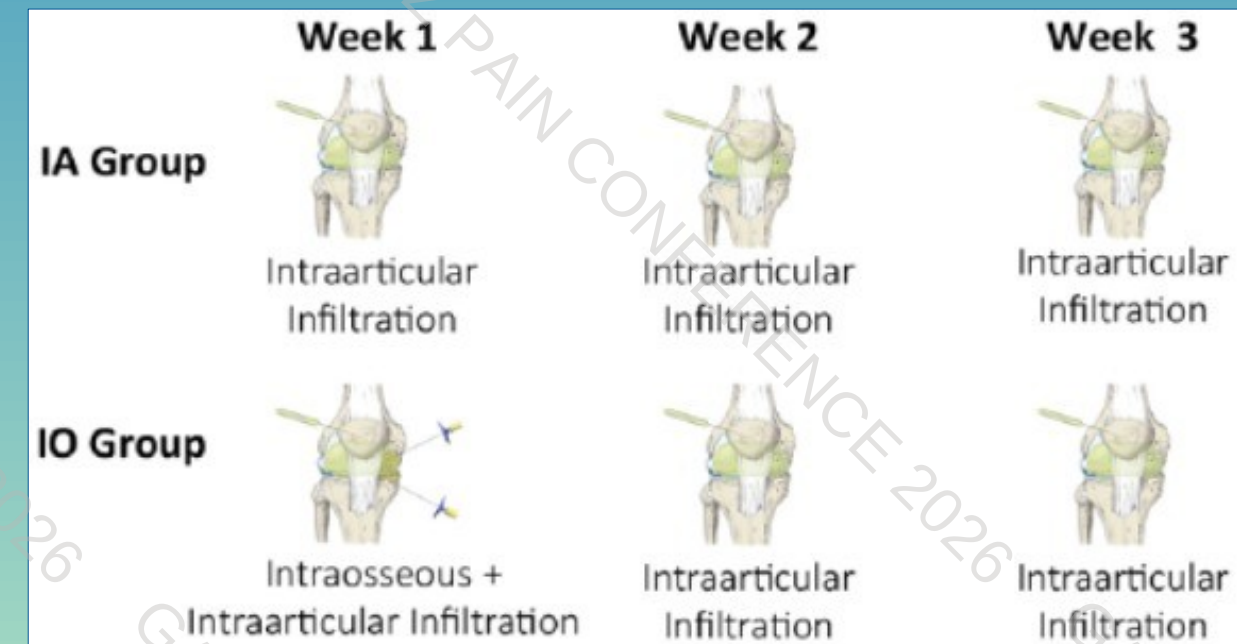
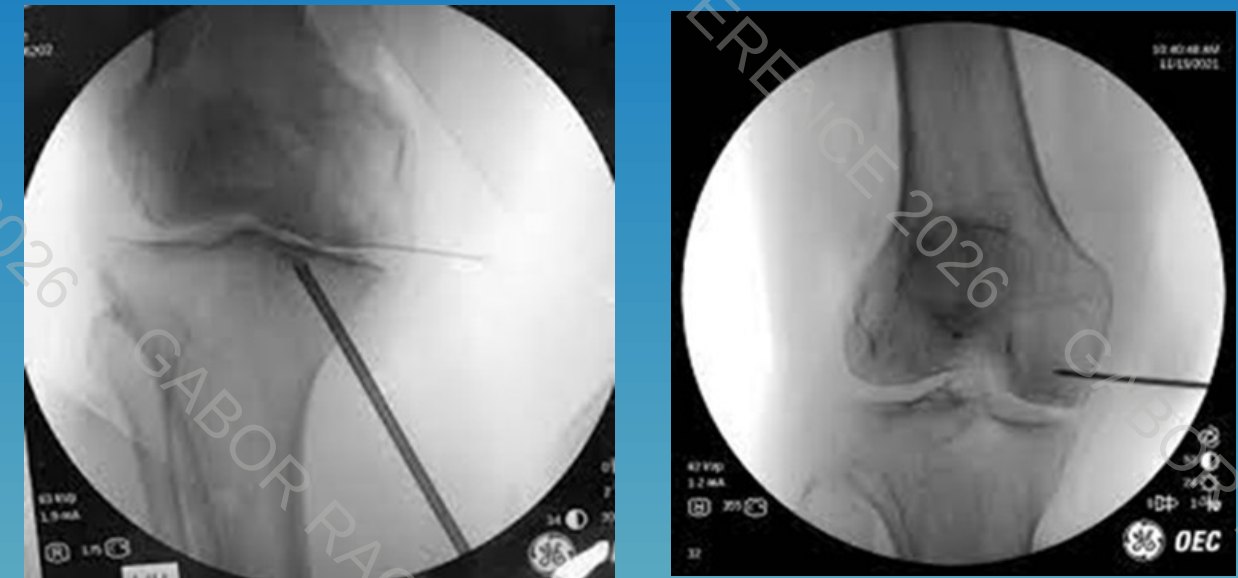
- Combination of **intra-articular** and **subchondral** biologics injections re-establishes cross communication, and can treat severe OA

Mikel Sanchez et al. Arthrosc Tech. 2014 Dec; 3(6): e713–e717

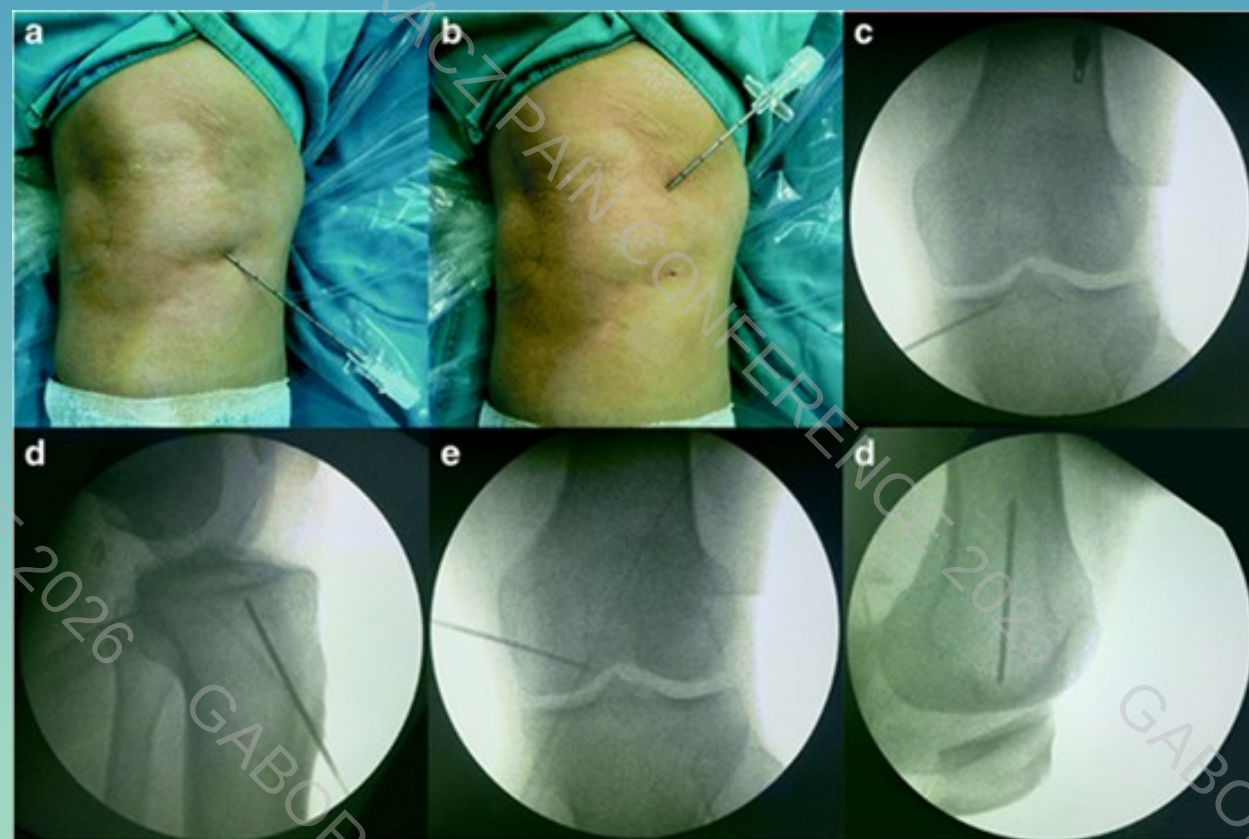
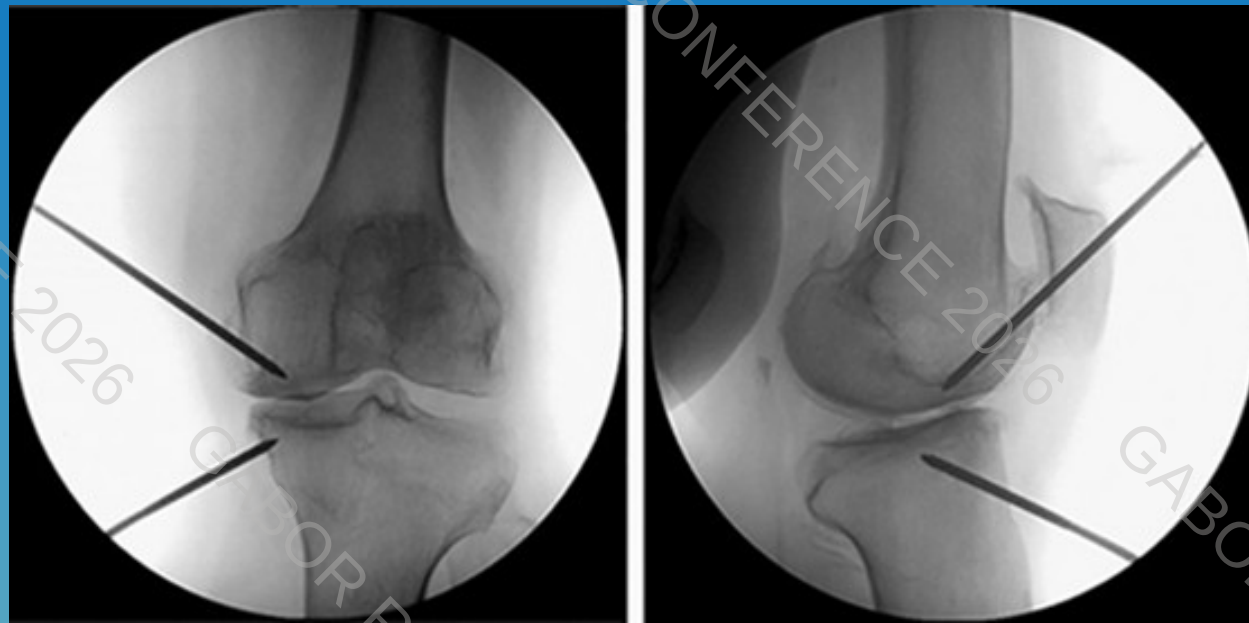


IO + IA PRP for Severe Knee OA

- 60 pts, F/U 2, 6 and 12 months
- Two groups: PRP -IA group, PRP IO + IA
- IA + IO PRP showed superior outcomes at 6 and 12 mos. compared with IA PRP



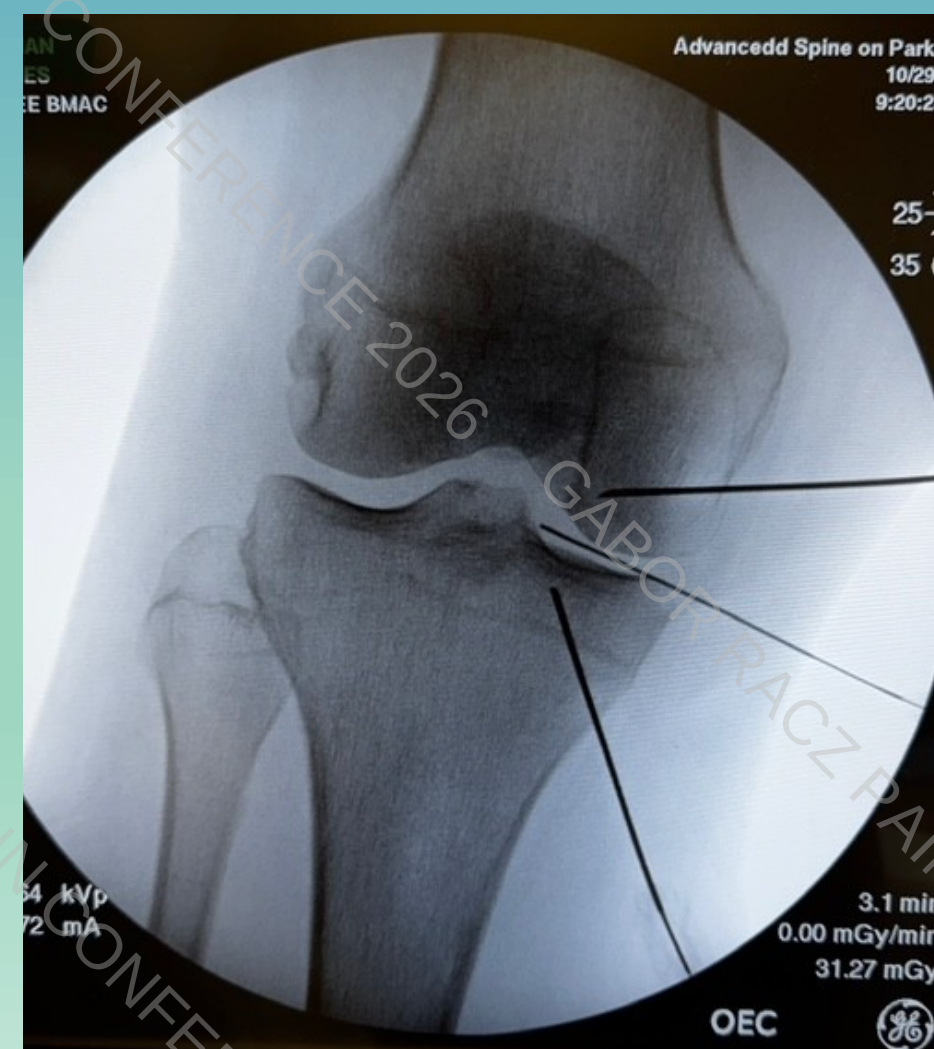
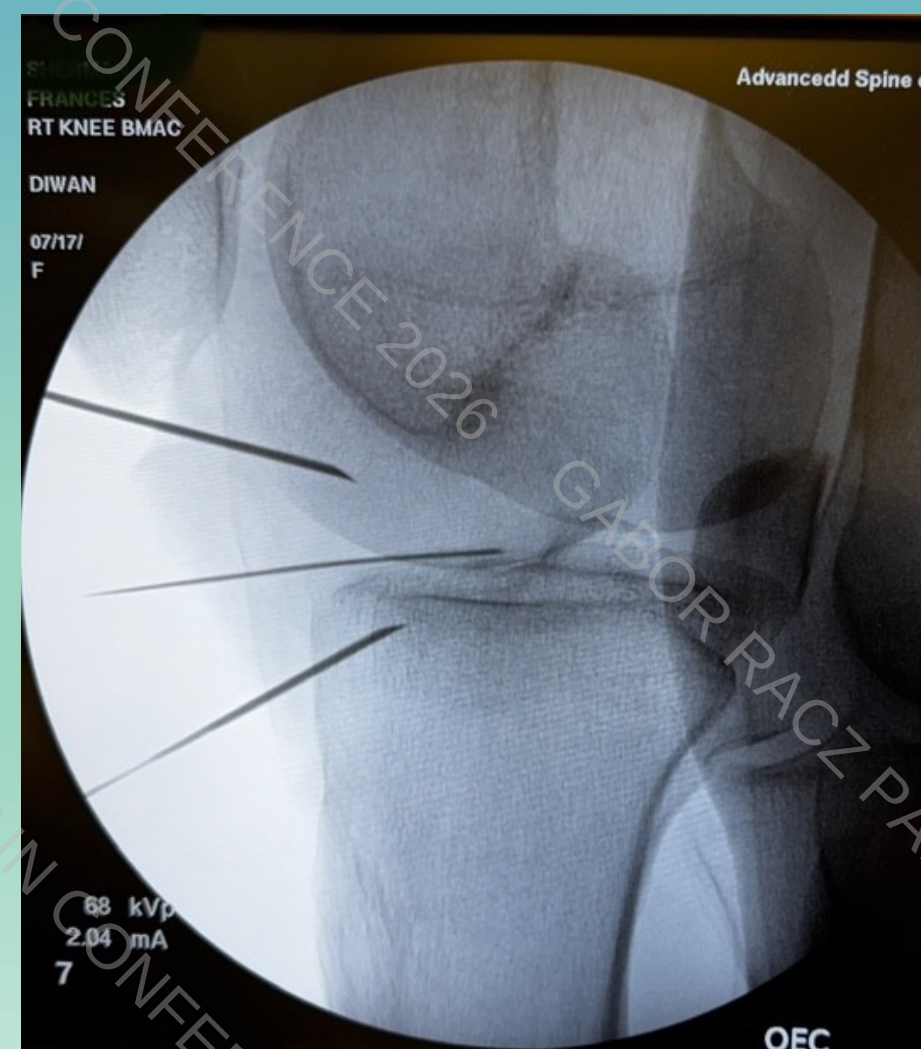
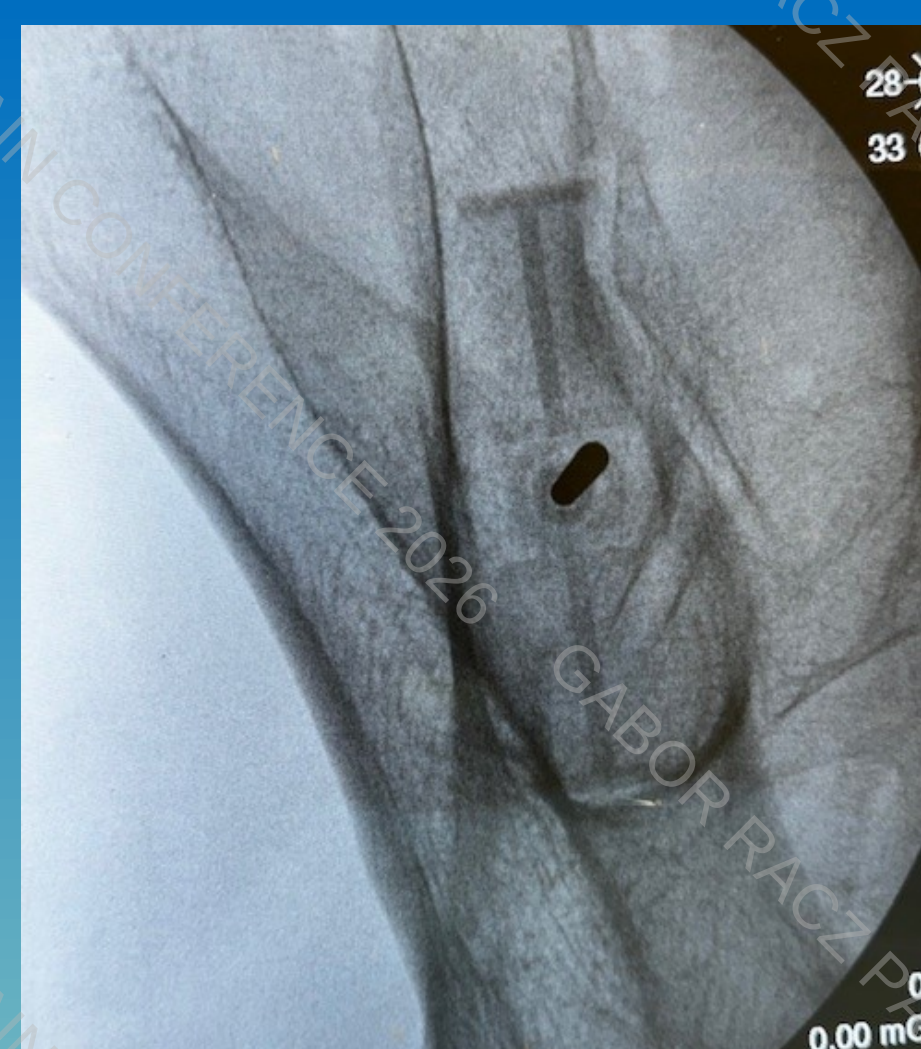
Mikel Sánchez, Diego Delgado, Orlando Pompei. Cartilage. 2019 Apr;10(2):245-253



IA + Dual IO Infiltrations of PRGF Rx for Knee OA

- 79 pts. with grade 3-4 KOA, F/U at 11 mos.
- retrospective review
- One-IA + two-IO (Dual) PGRF infiltrations
- 88% pts showed a significant pain reduction
- The combination of IA + IO infiltrations of PRGF is a safe and efficacious

*Antonio Ríos Luna, Homid Fahandezh-Saddi Díaz, Manuel Villanueva Martínez et al.
J Clin Med. 2023 Jul 6;12(13):4512*

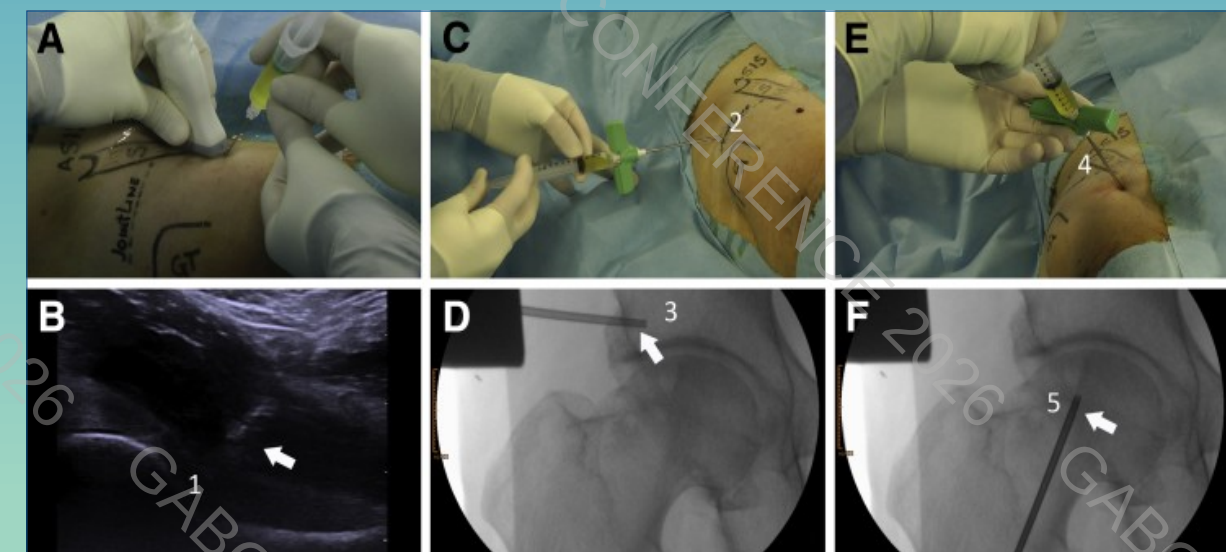
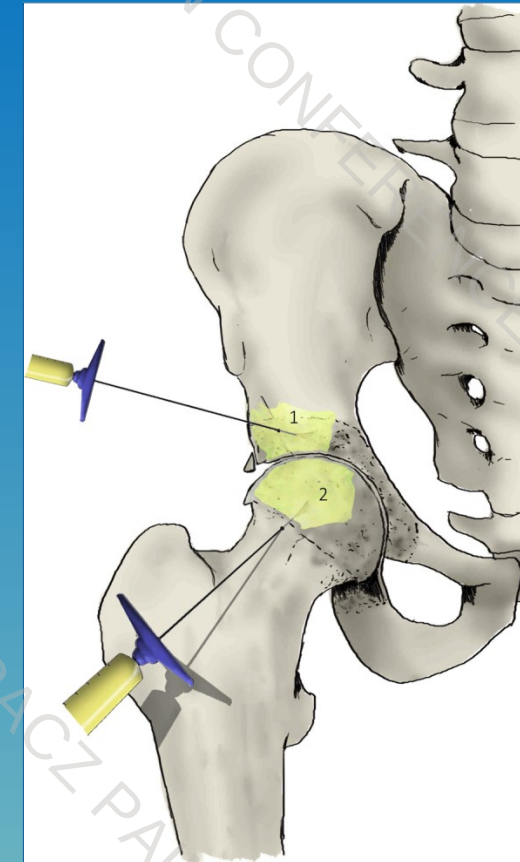


Dual SC + IA Injections of BAMC for Knee OA at ASPA

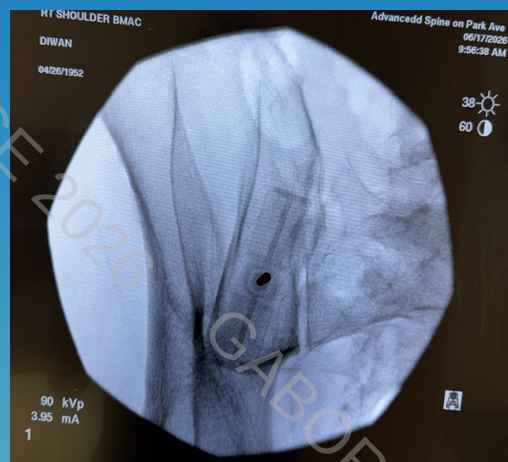
- 6 cc BMAC (60 cc BMA)
- 6 cc Plasma
- Intraarticular: 6-8 cc
- Each subchondral: 2-3 cc
- Needles: 18G for subchondral, 22 G for IA

IA + IO injections of PRP for severe hip OA

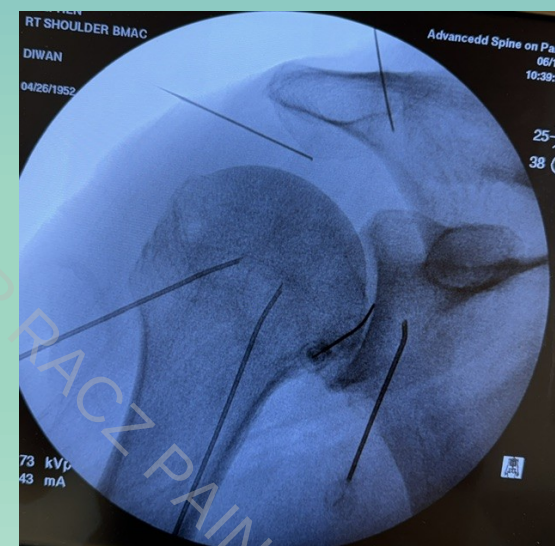
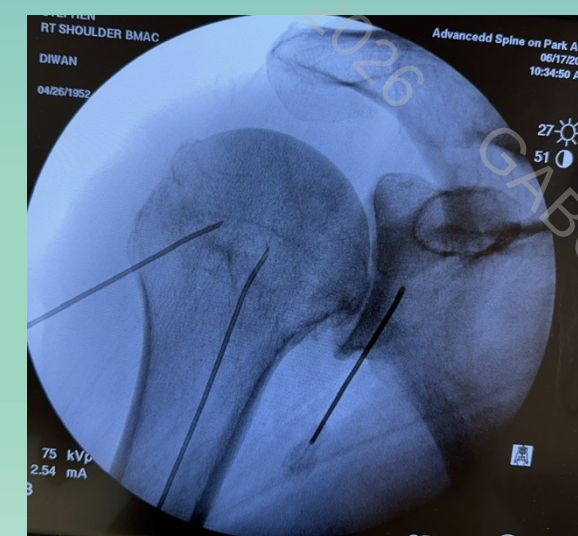
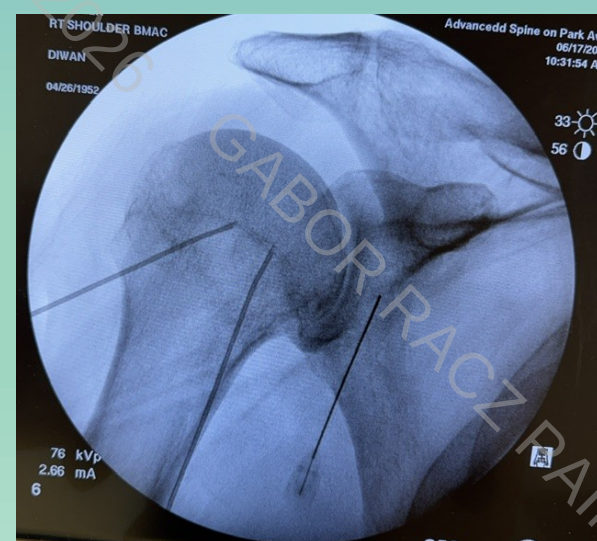
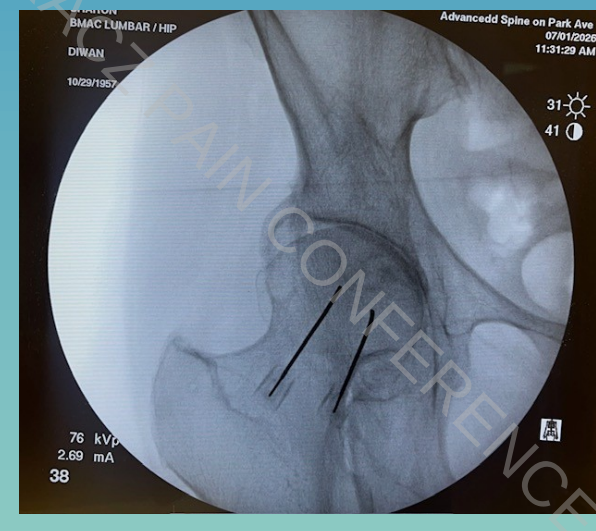
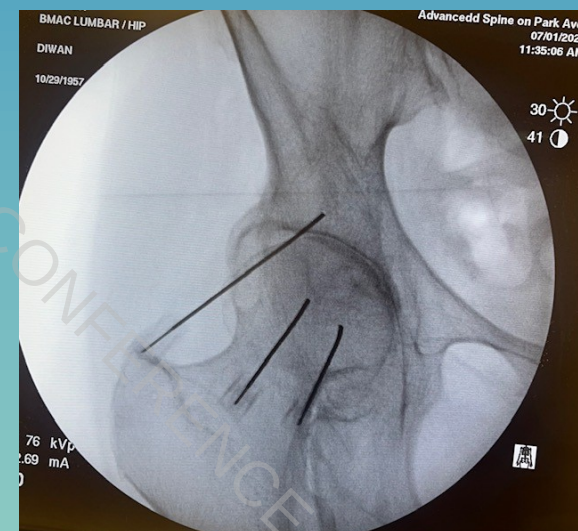
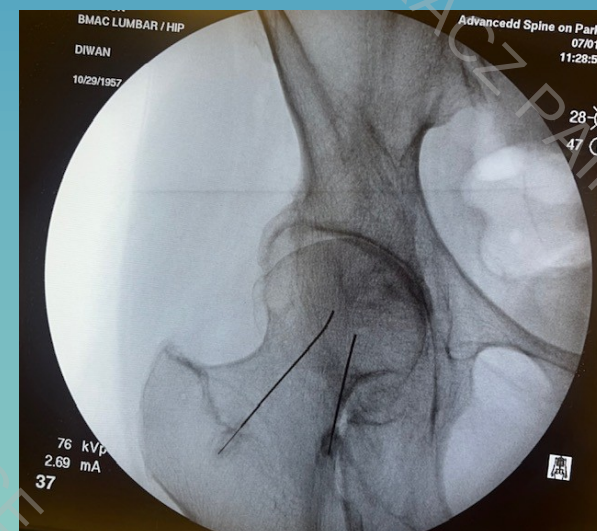
- Forty patients with HOA degree 2 and 3
- IA + IO infiltrations of PRP showed a pain reduction and improvement in functionality in severe OA
- Combining IA + IO makes the PRP reach more target tissues and joint structures involved in the development of OA



Nicolás Fiz, Diego Delgado, Ane Garate et al. *J Clin Orthop Trauma*. **2019** Dec 28; 11(Suppl 4):S585–S590



Acetabular SC + Femoral SC + IA BMAC for advanced Hip and shoulder OA



- 6 cc BMAC (60 cc BMA)
- 6 cc Plasma
- Intraarticular: 6-8 cc
- Each subchondral: 2-3 cc
- Needles: 18G sharp-tip for subchondral, 22 G for IA

Evidence: Safe and Effective

Safety

- 24 animal studies,
- All types of MSCs degeneration
- Bone-marrow-derived MSCs
- Evidence suggested
- The MSC transplant needed to assess the

Rita Lok-P

9/15/2024

Systematic Review of Cell Based Therapy for LBP



Spine

Cell-Based Therapies for lumbar discogenic low back pain - a Systematic Review and Single Arm Meta-Analysis

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Results

- Search ID's 1393 articles, of which 6 studies were eligible for this review. Studies were from 2006 to 2015 & 74 pts were included.

Safety

- No SAE's reported in the studies.
- No tumor formation observed during follow up period.

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ADVANCED SPINE ON PARK AVENUE

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Regenerative Medicine Guidelines

Regenerative Medicine Effectiveness in the Low Back Pain Guideline

Pain physician
Annu Navar
DO, Richard
MD, PhD, S
PhD, MBA,
Fellows, M
Pappolla, M
Amol Soin,
M. Aydin, D
MD, Sanjay
Vallejo, MD
P. Stitik, M
and Joshua

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low back

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Regenerative Medicine for Axial and Radicular Spine-Related Pain: A Narrative Review

Mehul J Desai, John Taylor Mansfield et al. Pain Pract. 2020 Apr;20(4):437-453

Anatomical location	MSCs	PRP	Prolotherapy
Intradiscal injections	Level I/IV All studies are for the lumbar discs, No thoracic discs One cervical studies	Level I/IV	Level III to IV
Facet Injections		Level I/IV	Level IV
Sacroiliac joint injections		Level I/IV	Level I/III
Epidural Injections		Level I/IV	Level IV

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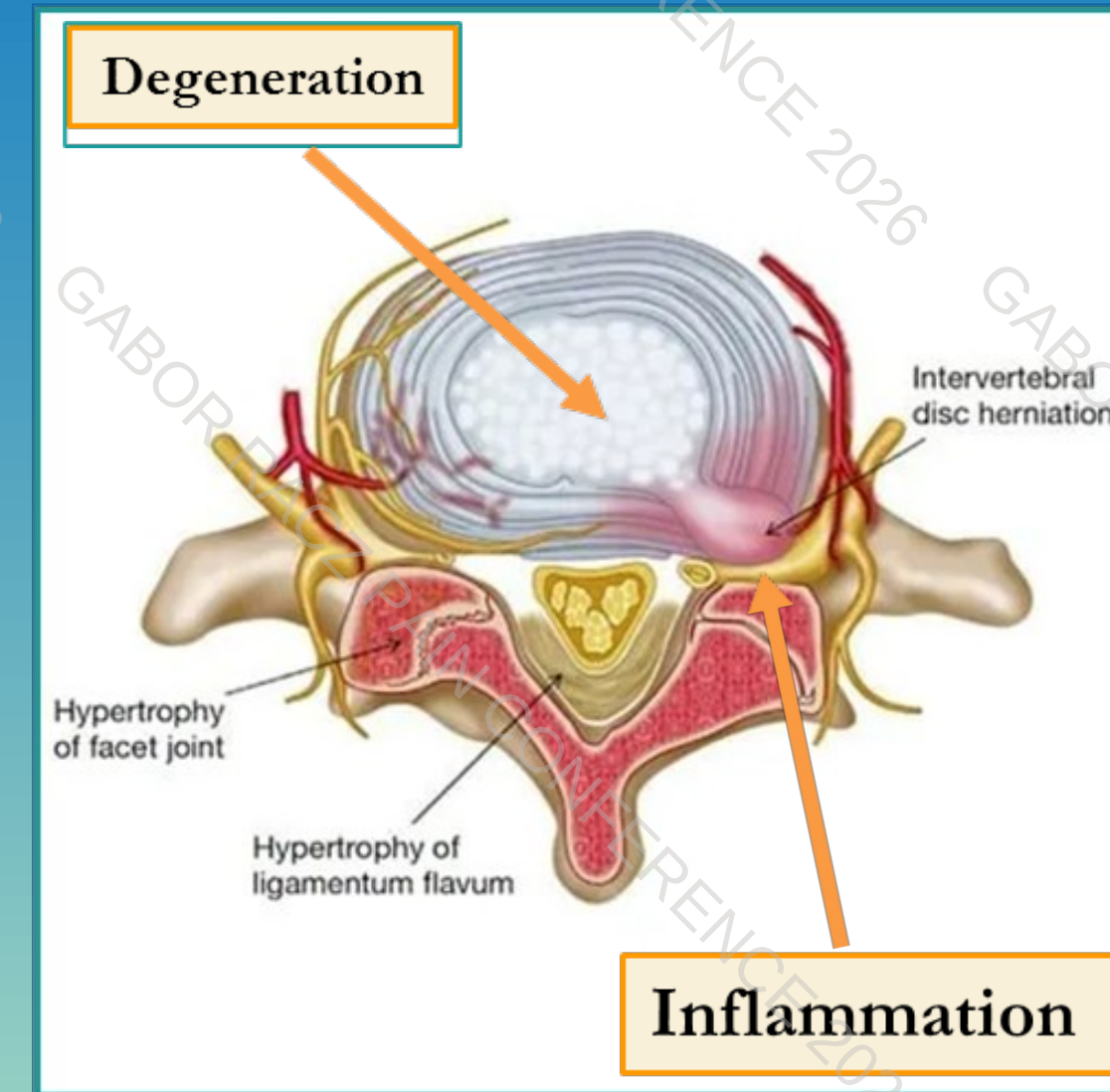
ADVANCED SPINE ON PARK AVENUE

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Inflammation is Peripheral and Disc Degeneration Central

- The degeneration progresses from the nucleus to periphery
- The inflammatory is from periphery to NP
- The effective healing occurs in the outer annulus and cartilage endplate
- Peridiscal injection for symptomatic relief
- Intradiscal Injection for disc regeneration

Implications for physical therapies for discogenic back pain. Clinical Biomechanics. (2010), Vol 25 (10); 961-971

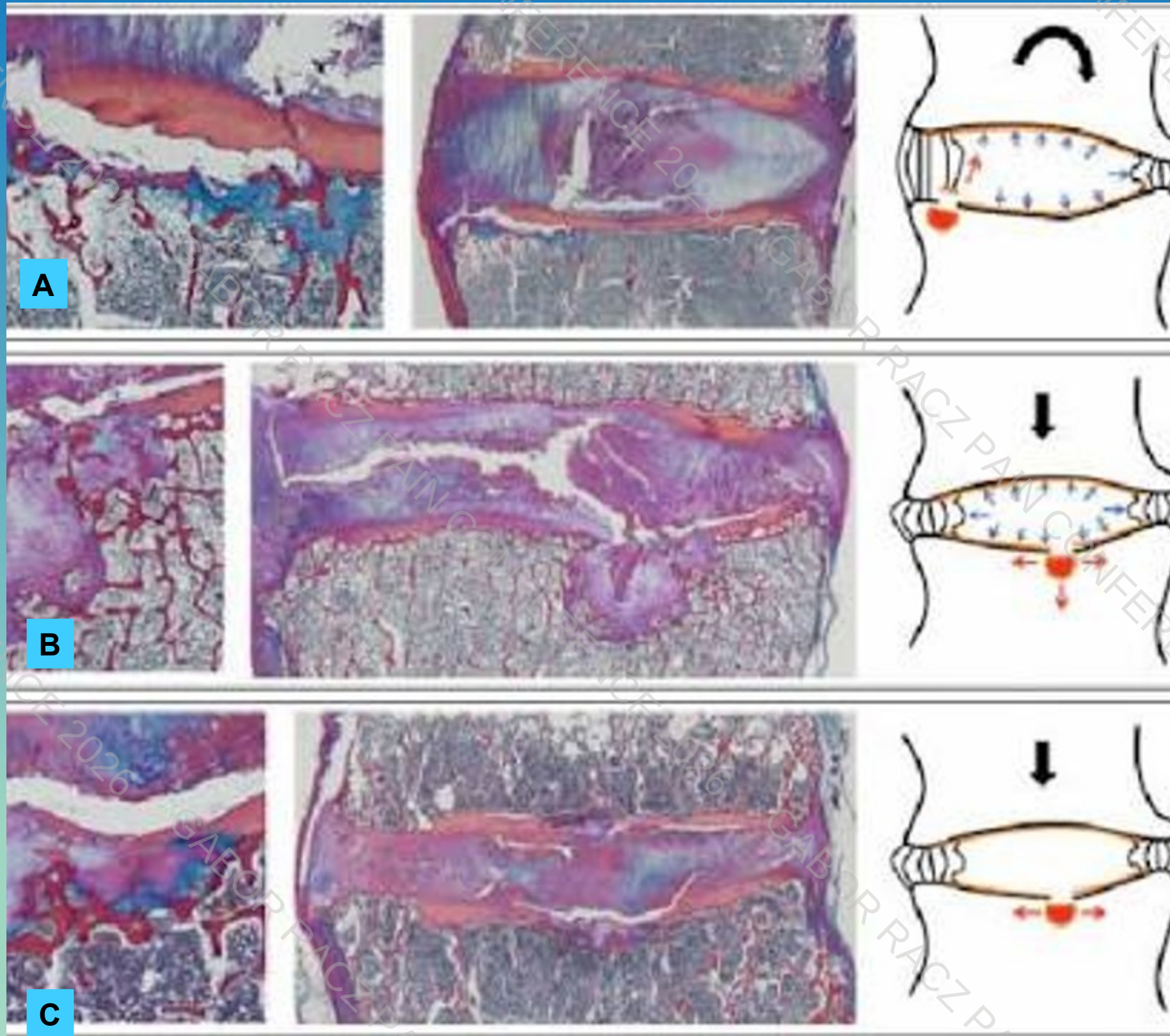


Healing of a painful disc should not be confused with reversing disc degeneration

The Role of the Vertebral Endplate in LBP

- Endplates: Interface between rigid vertebral bodies and compressible intervertebral disks
- Lumbar spine carries significant forces and discs have no blood supply
- Endplates: Strong to prevent CEP fracture and porous to facilitate nutrient diffusion
- The damaged endplates leak proinflammatory cytokines and chemokines to vertebral BM
- Damaged endplates are susceptible to chemical sensitization and mechanical stimulation
- The role of damaged innervated endplates is underappreciated because **innervated damage is poorly visualized with diagnostic imaging**

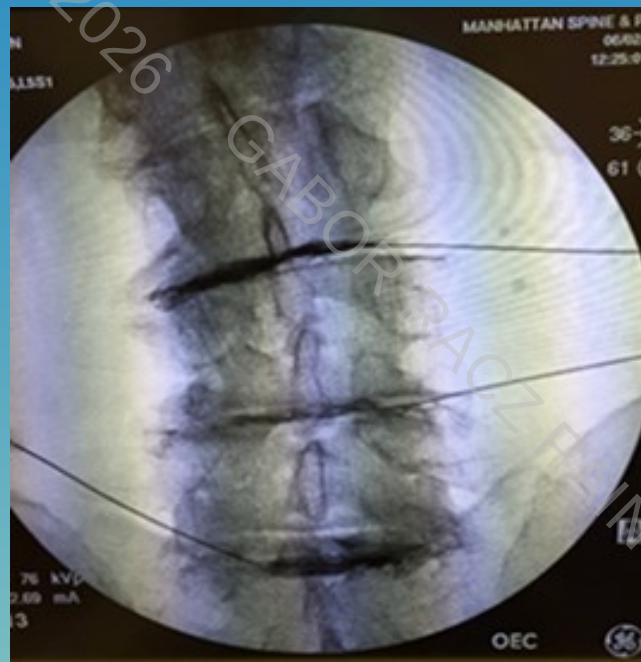
J. C. Lotz, A. J. Fields, and E. C. Liebenberg. Global Spine J 2013;3:153–164



Various endplate defects

- (A) Endplate avulsion resulting from bending motion that causes traction at the interface between the endplate and disc
- (B) Traumatic endplate fragment resulting from excessive compression with a healthy nucleus pulposus
- (C) Central endplate fracture resulting from excessive compression with a degenerate, fibrous NP

Degenerative Discs is progressive....



- **Matrix Homeostasis:** Balance between **anabolism** and **catabolism**
- **ECM** important for disc regeneration
- Disc Degeneration: Chronic matrix remodeling process
- Calcified Endplates - diminished nutrition - more degeneration
- Questionable Survival of MSCs
- As nutrition diffusion ↓ the severity of degeneration ↑

Genetic predisposition

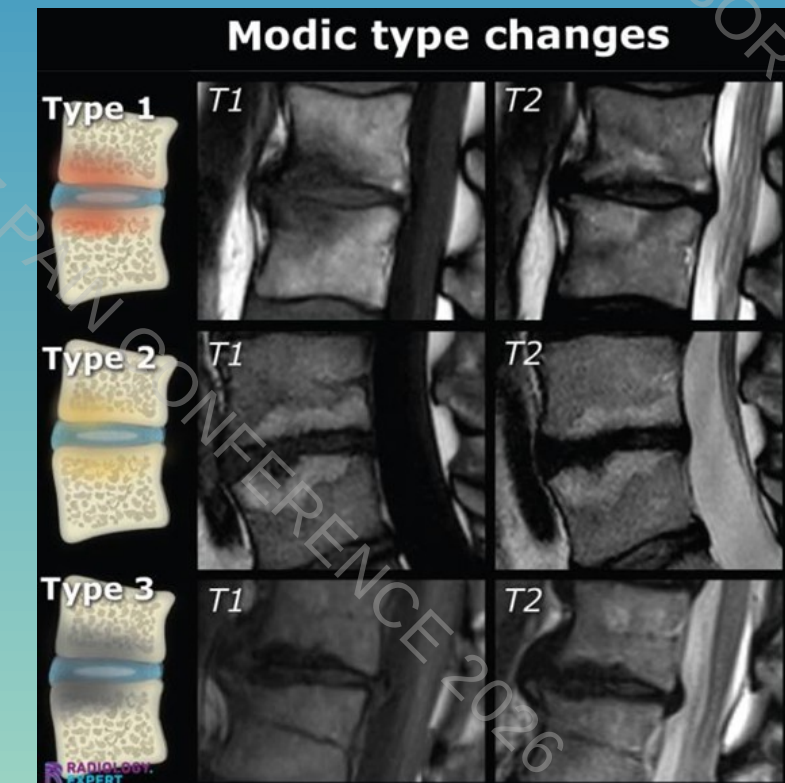
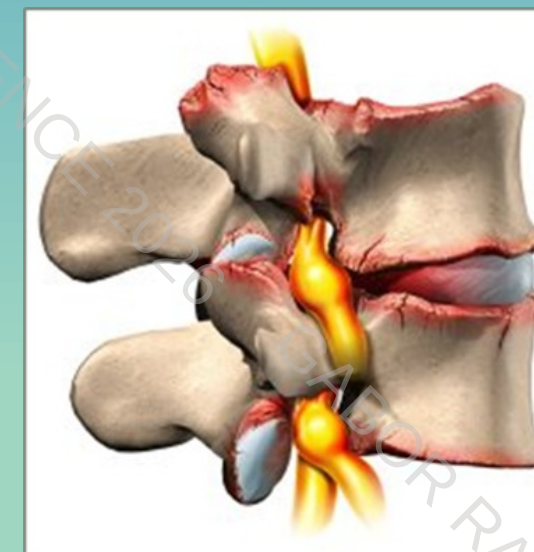
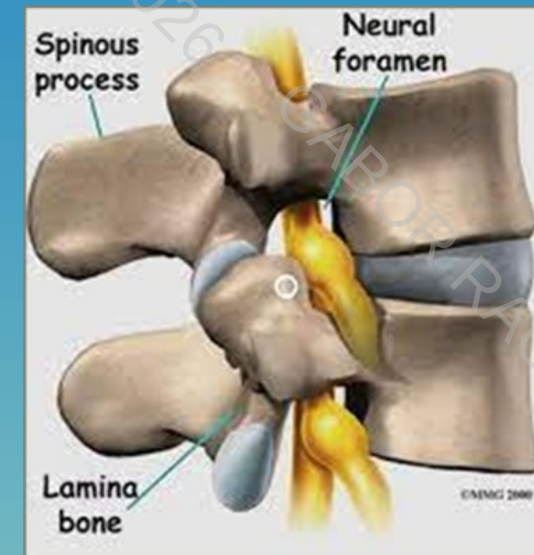
Repeated microtrauma

Compromised Nutrition

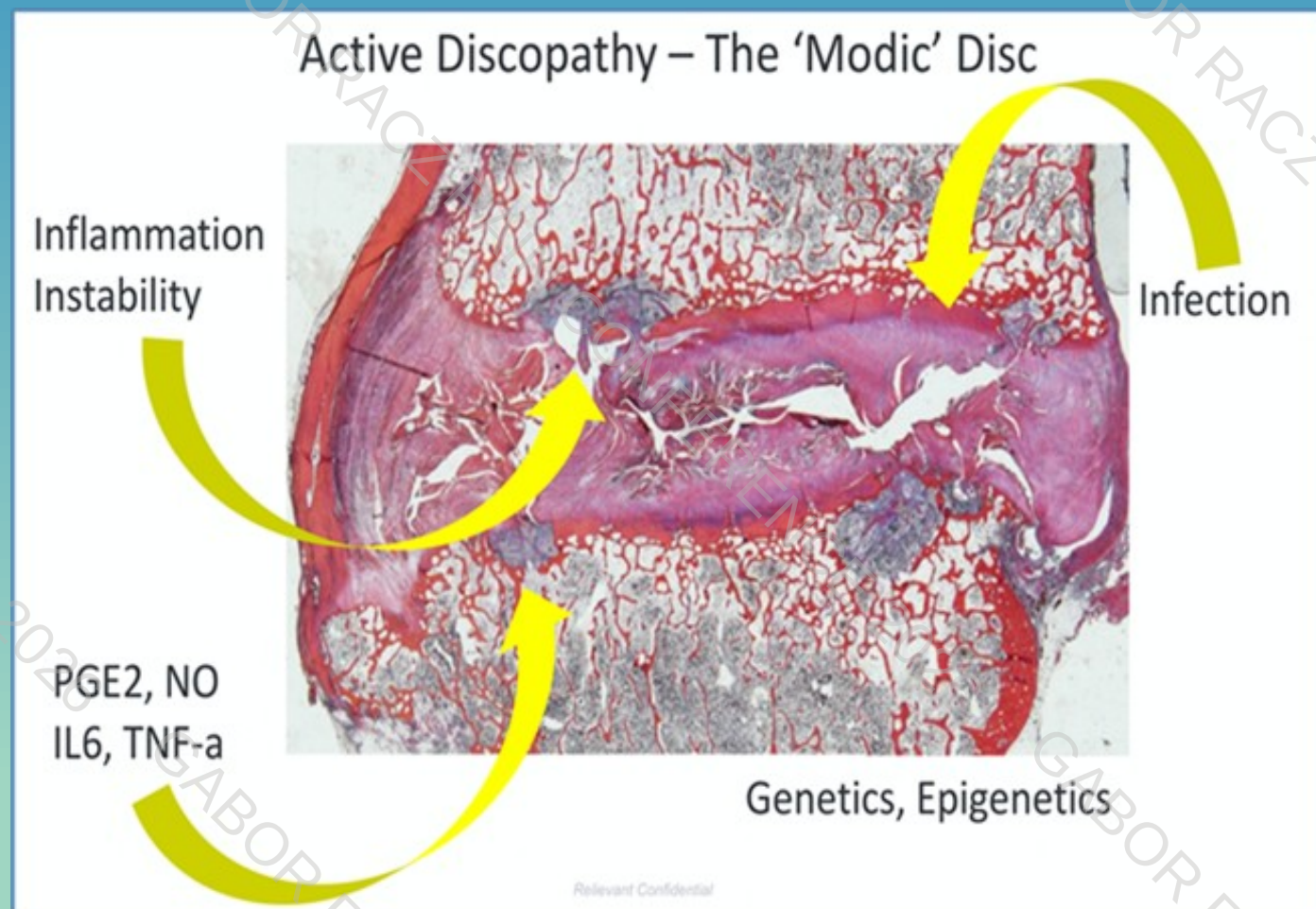


Disc Degeneration is progressive....

- Advanced degeneration CEP gets calcified and fractured causing **Modic Changes**
- The Modic 1-2 changes are dynamic markers of the degeneration of lumbar spine
- Type 1 (Fibrovascular): **inflammatory process** associated with active low back symptoms and segmental instability



Shifting Paradigm from discs to vertebra



- Endplate defects allow pro-inflammatory disc tissue to leak into the vertebral bone marrow
- Chronic endplate inflammation leads to Modic changes (MRI) and causes vertebrogenic CLBP



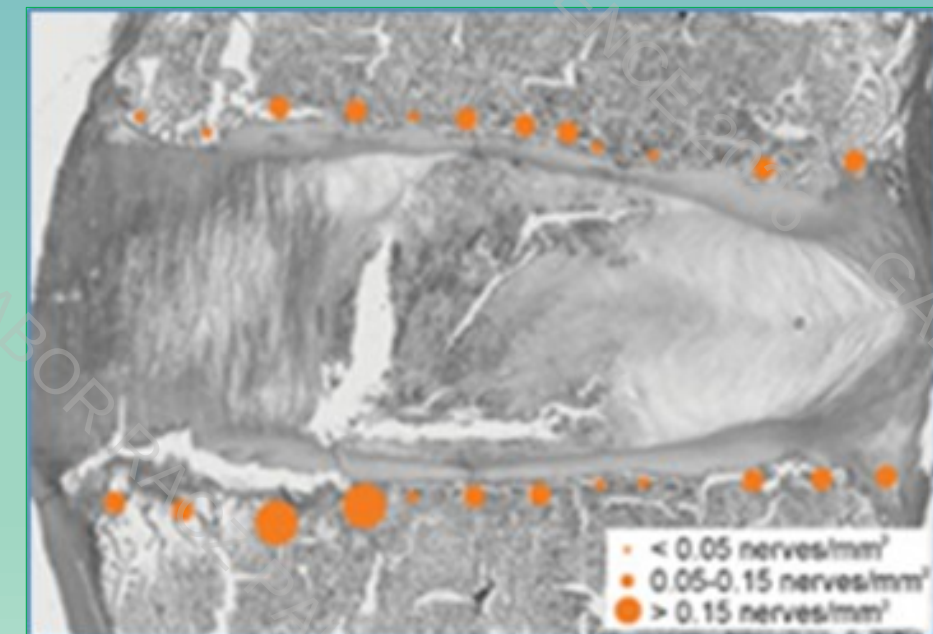
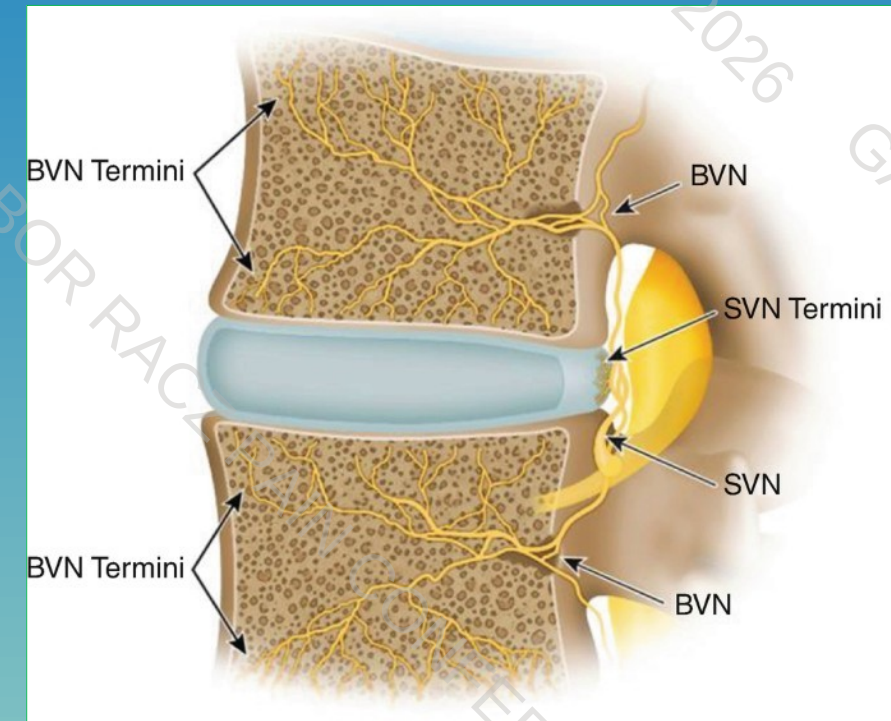
Discography Correlation to Modic Changes

- Consistent with vertebrogenic axial LBP
- High correlation with discography
- Close to 100% specificity with advanced Modic changes
- Poor outcome with conservative treatment
- Worse outcome after discectomy

European Journal of Radiology
Volume 157, December 2022, 110589

Vertebral endplates and the BVN

- BVN innervates the endplates more than discs
- The BVN nociceptors proliferates in damaged endplates
- Damaged endplates causes Modic changes, and strongly correlate with chronic axial LBP

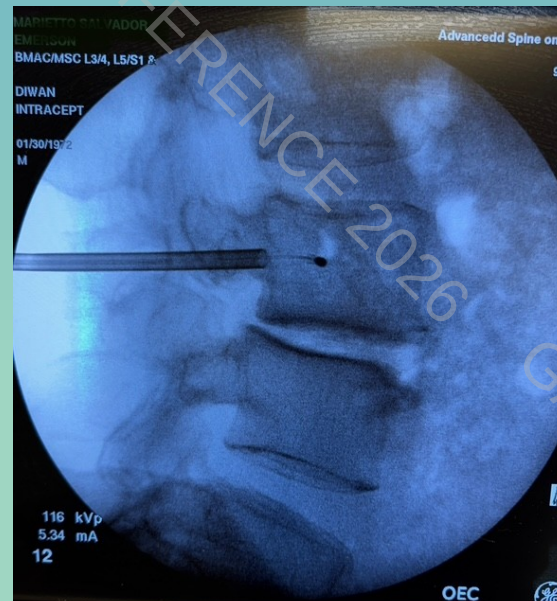
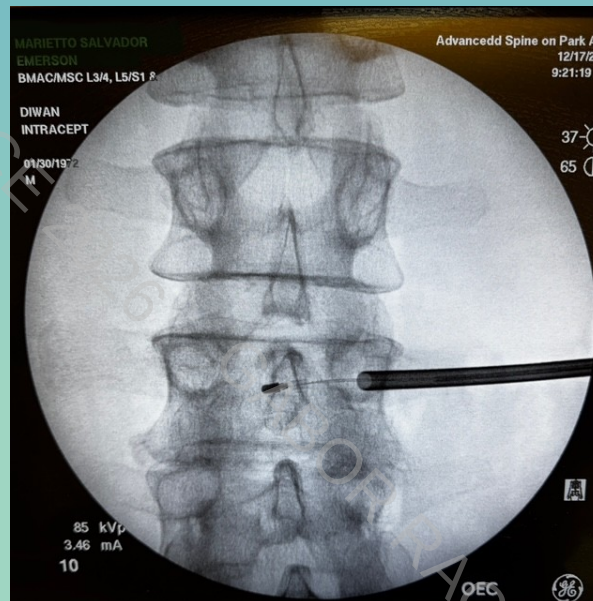


1. Bailey JF, Liebenberg E, Degmetich S, Lotz JC. *Journal of Anatomy* 2011;218(3):263-70. 2. Lotz JC, Fields AJ, et al. *Global Spine J* 2013;03:153-64. 3. Mok F et al. *The Spine Journal*; 2016

Vertebrogenic pain: Treatment options



- Conservative treatment
- Spinal injections/Antibiotics
- Intraosseous bipolar RFA of the BVN
- Extraosseous epiduroscopic RFA of SVN
- Intraosseous (Subchondral) biologics
- Surgical posterior fusion

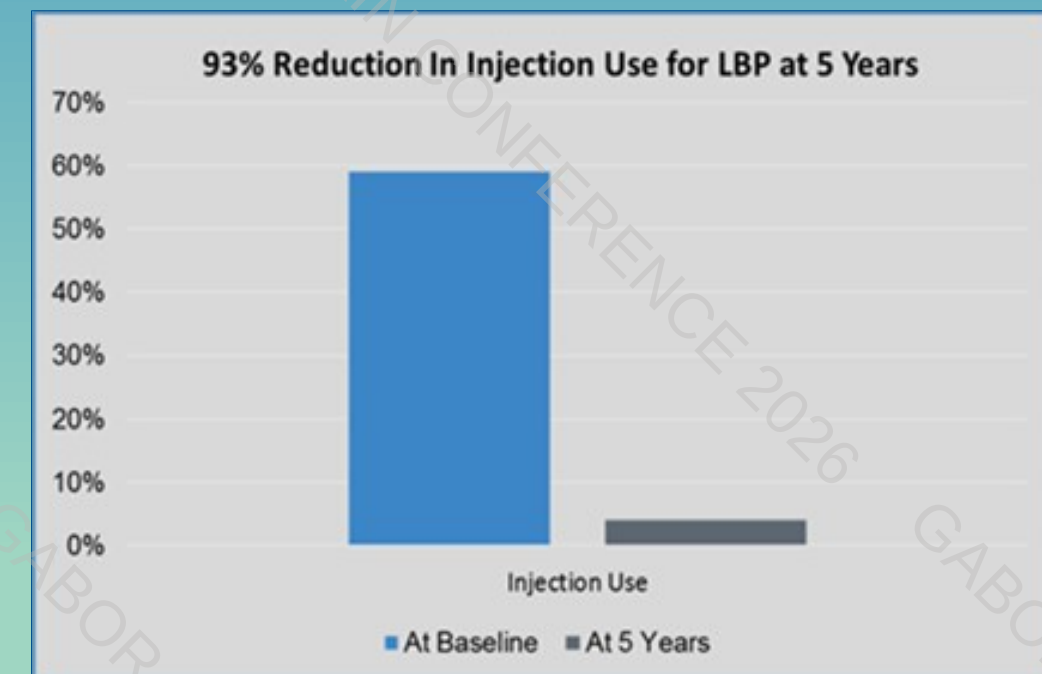
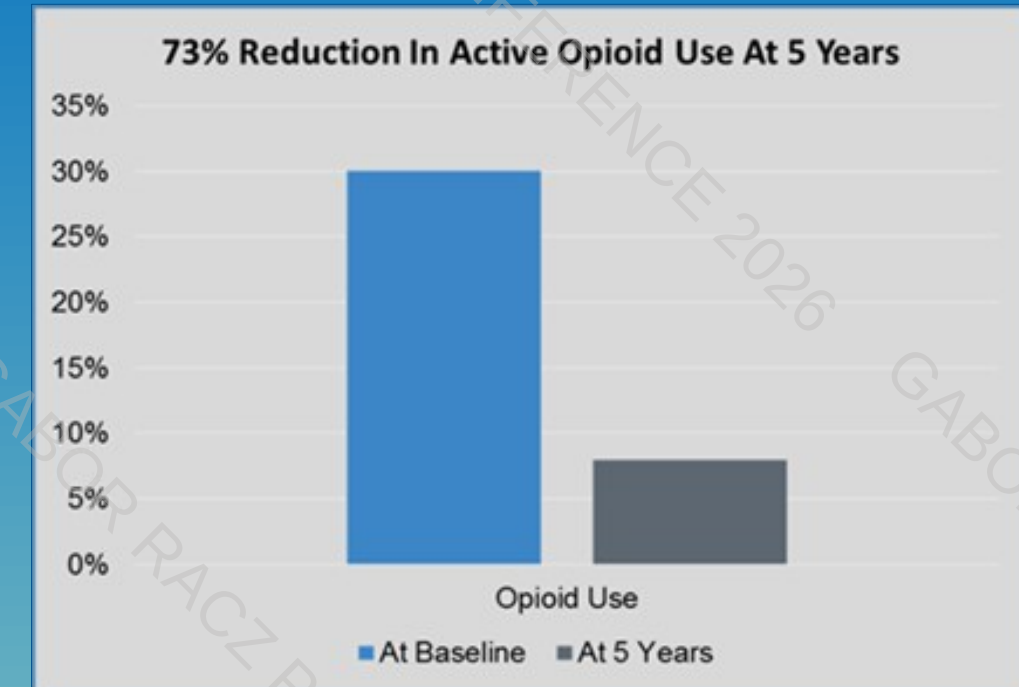


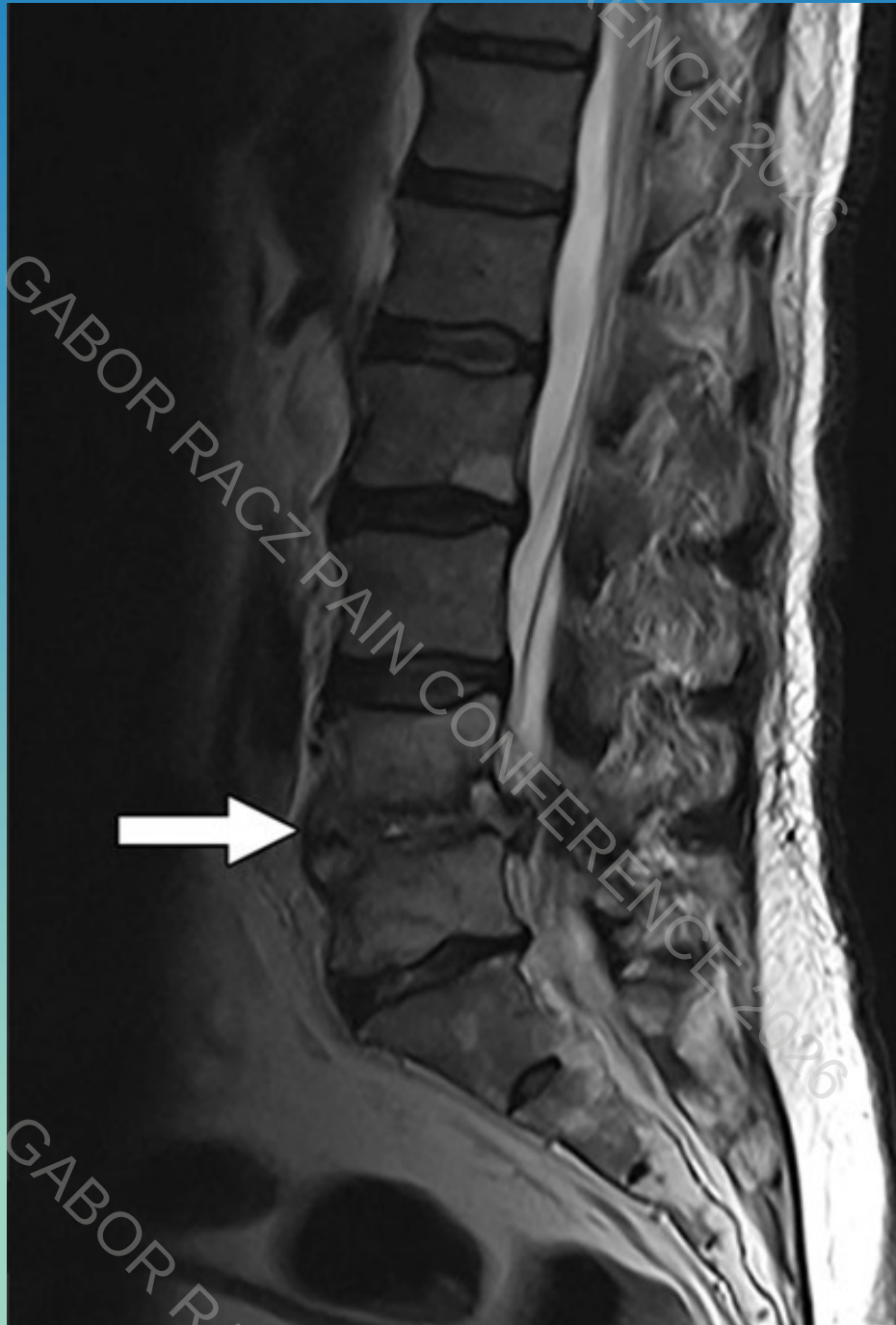
- Bipolar lesion at 80° C 15 mins for S1 lesion
- 7 Mins if perfect placement posterior 1/3rd and midway between two endplates

5-Year - Mean ODI and VAS Improvement

- Mean reduction in VAS of 4.38 points
- 6 ...but our goal is beyond
- 4 just symptomatic relief.....
- One-third (34%) of pts. pain free at 5 yrs.

International J Spine Surgery, Vol. 13, No. 2, 2019, pp. 1-10





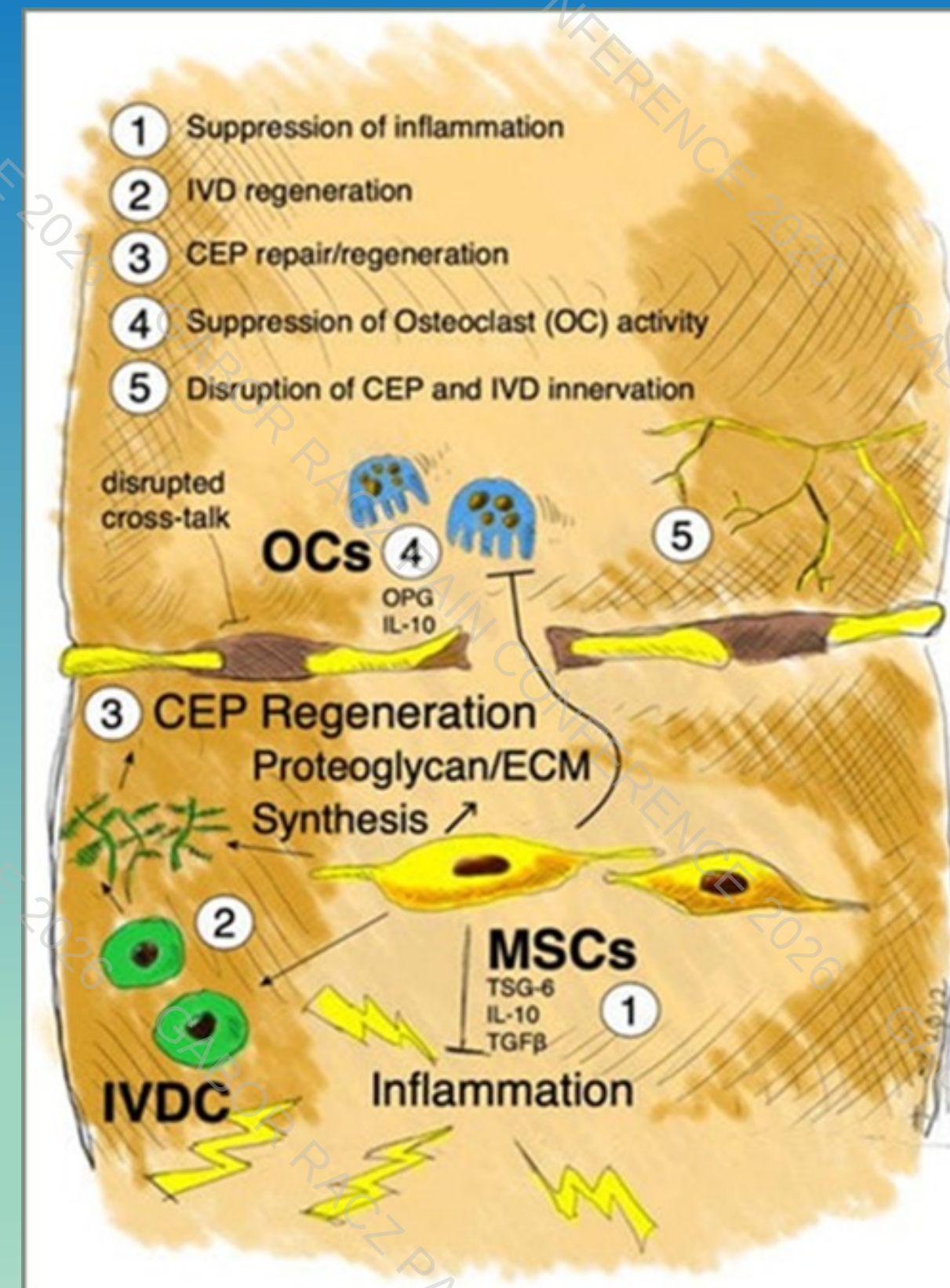
Segmental instability

- After RFA of BVN for the Modic Changes: Pt has **excellent symptomatic relief**
- However, advanced disc degeneration continues, and and progressive destruction of the endplates leading to **Segmental Instability**

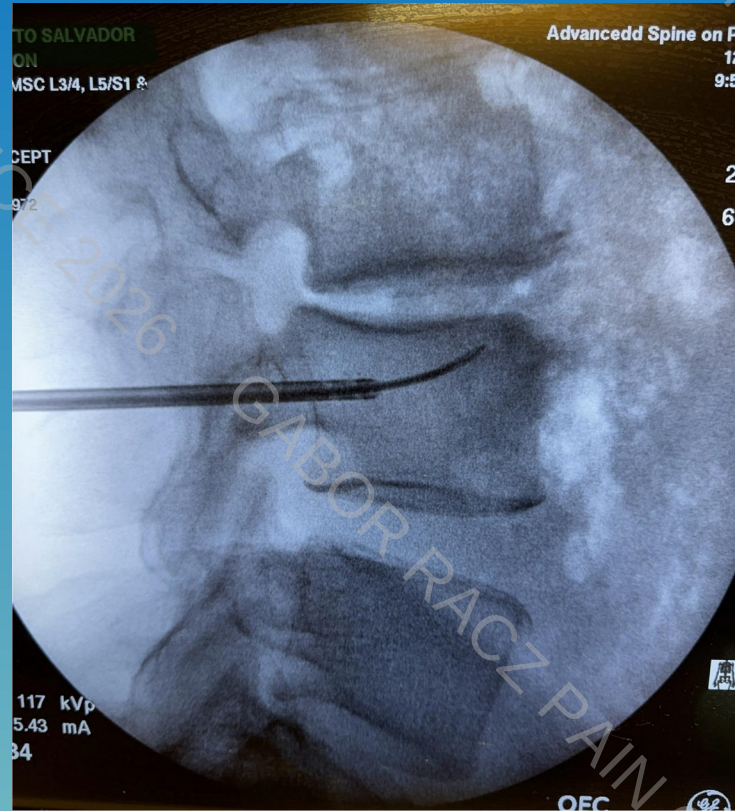
MSCs for Degenerated Discs with Modic Changes

- MSCs is a safe with Immunomodulatory and Anti-inflammatory properties
- MSCs:
 - Suppress osteoclast activity
 - Stop inflammatory leakage
 - Heal the endplate
 - Regenerate the disc
- Regeneration of endplate will **prevent segmental instability** and **improve the nutrition of disc**

Nick Herger, et al. *Int. J. Mol. Sci.* 2022, 23, 2721

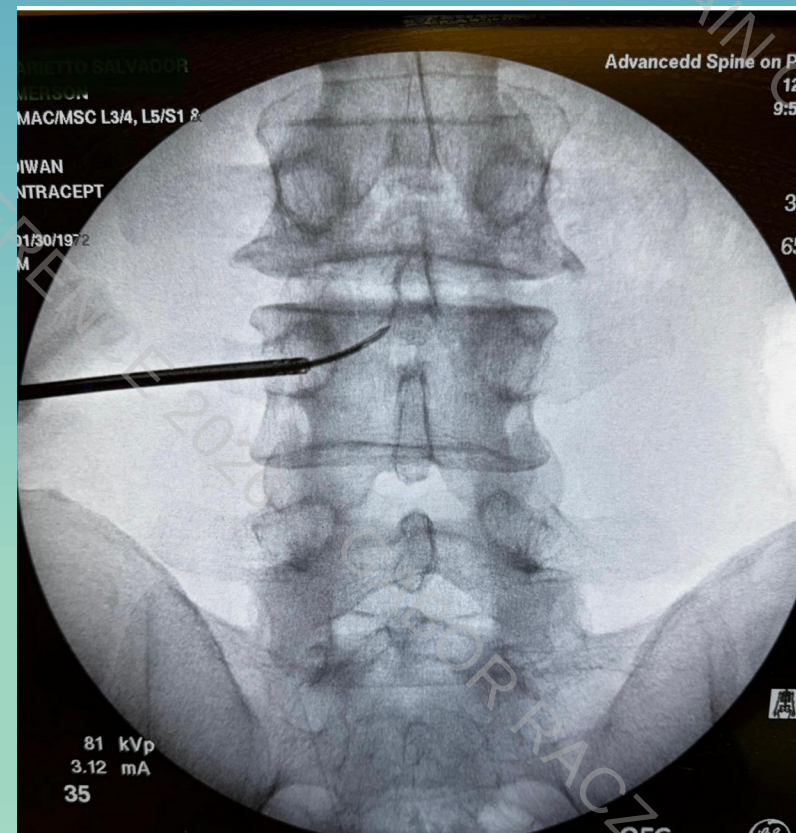


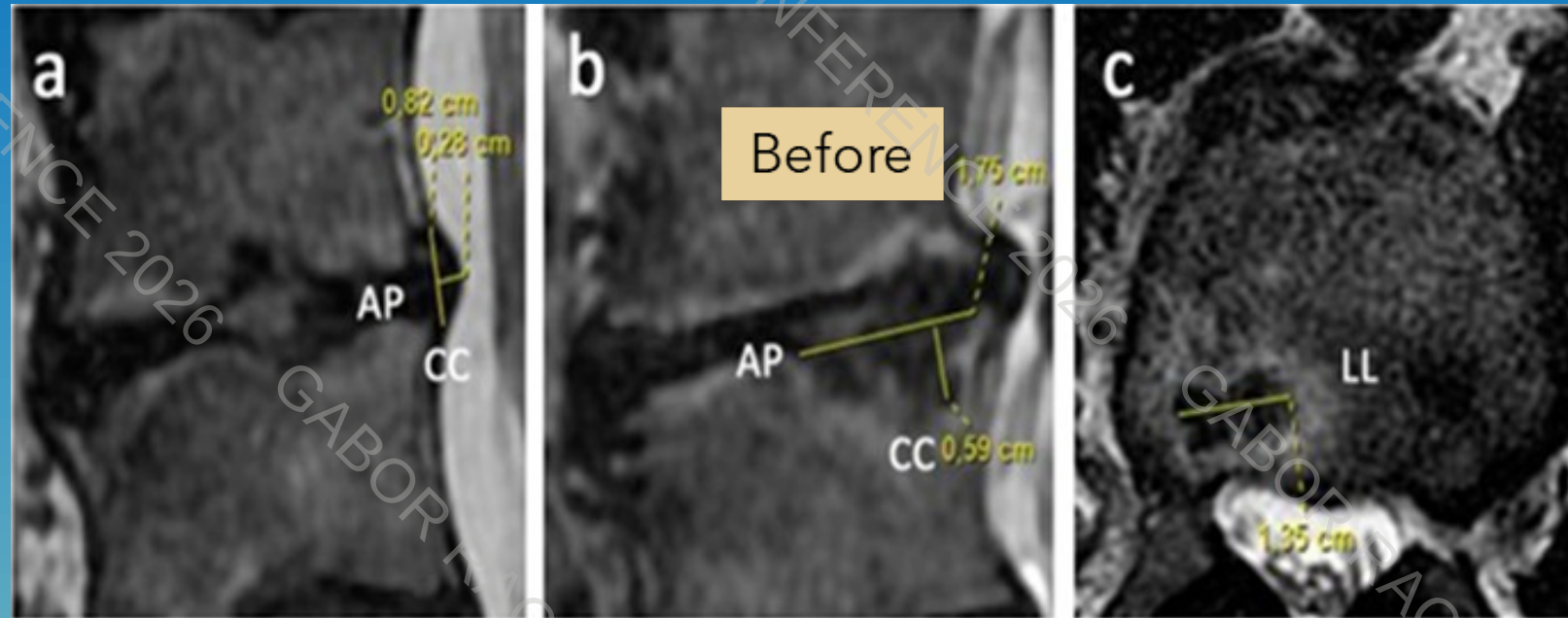
- Suppress osteoclast activity



Why subchondral biologics?

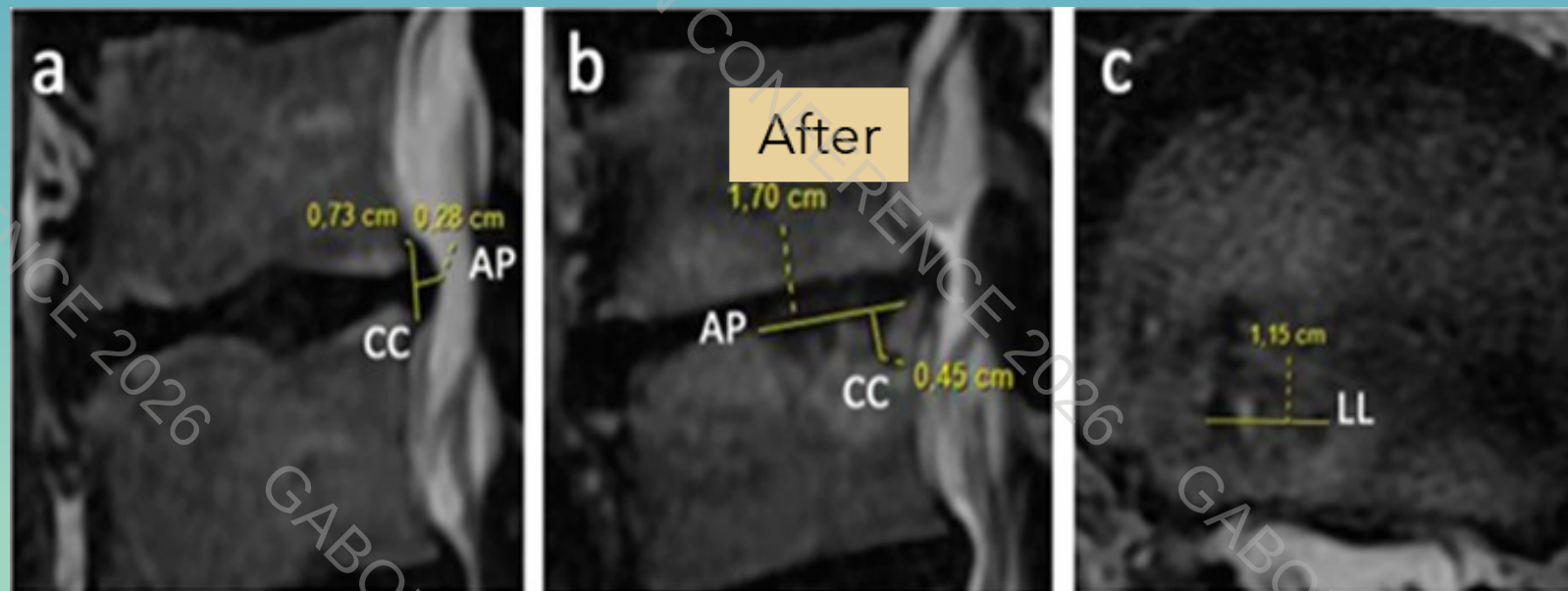
- To **heal the damaged cartilage endplates (CEP)**
- To **prevent segmental instability**
- To **improves the nutrients diffusion**
- To **Expedites the regeneration of the discs**





IO + ID PRGF for DDD and endplate lesions – a case report

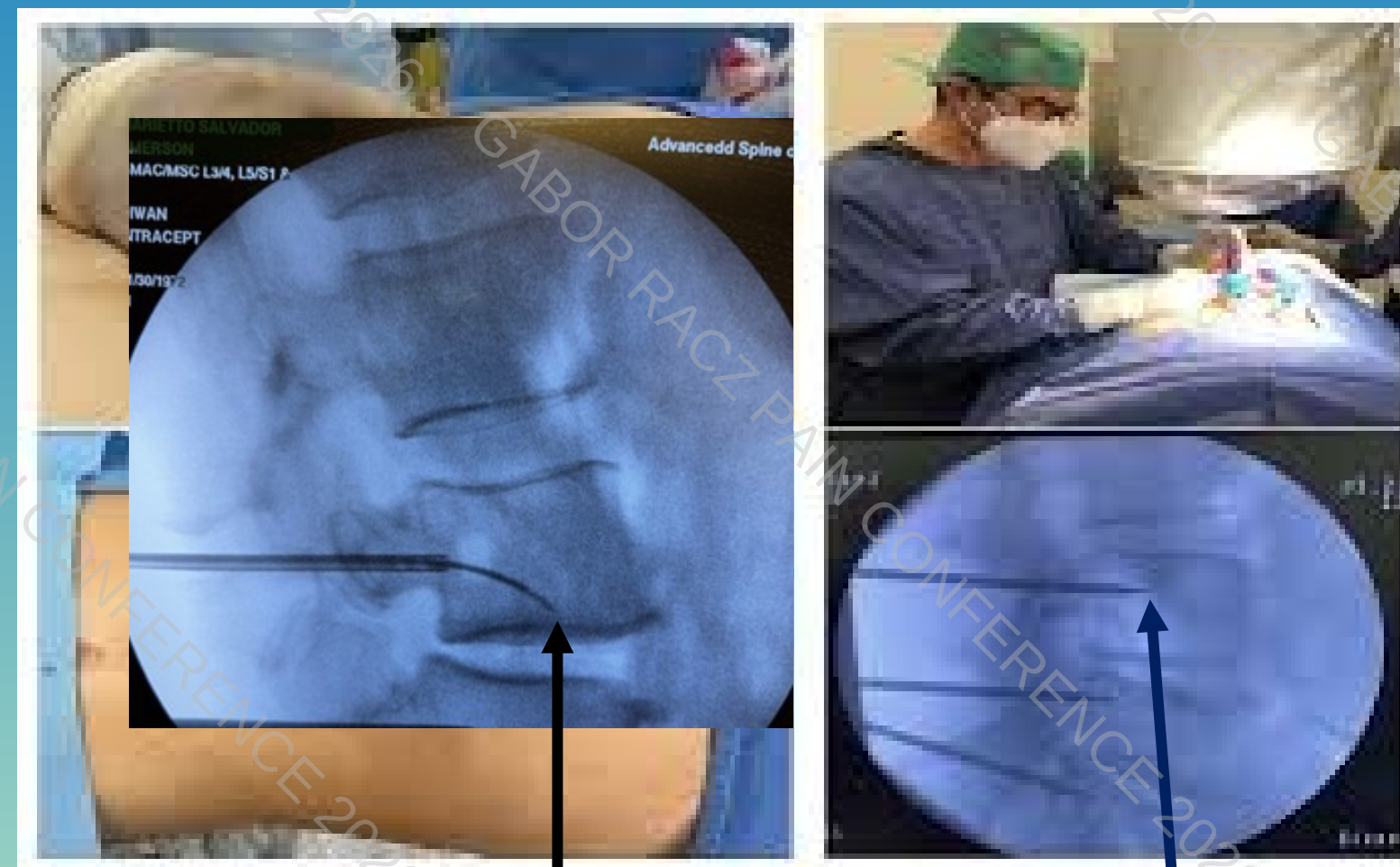
- Significant improvement in MC on MRI imaging, partial regression of protruded disc and resorption of Schmörl's nodes (6 mo. F/U)
- Intradiscal + intraosseous PRP infiltrations to treat protruded discs herniations with a successful outcome



Fernando Kirchner, et al. J Orthop Surg Res. 2020; 15: 72

IO PRP for Chronic LBP Retrospective Study

- Retrospective analysis 57 pts, F/U 9 mo.
- 56.7% had MODIC changes on MRI
- 84.2% reported severe pain (VAS 8-10), 42% received intraosseous-PRP
- 96.5% patients experienced improvement



This is Subchondral

This is Intraosseous

César Amescua-García et al. Journal of Drug Delivery & Therapeutics. 2024; 14(4):165-169

- MRI Consistent with advanced DDD and MC
- Chronic vertebrogenic and discogenic axial low back pain, with/without radicular pain
- Failed all conventional treatment options
- Recommended multilevel fusion surgery

- With or without RFA of BVN
- Subchondral Injections for endplates destruction
- Intradiscal injection for DDD
- Peridiscal injections for discogenic pain





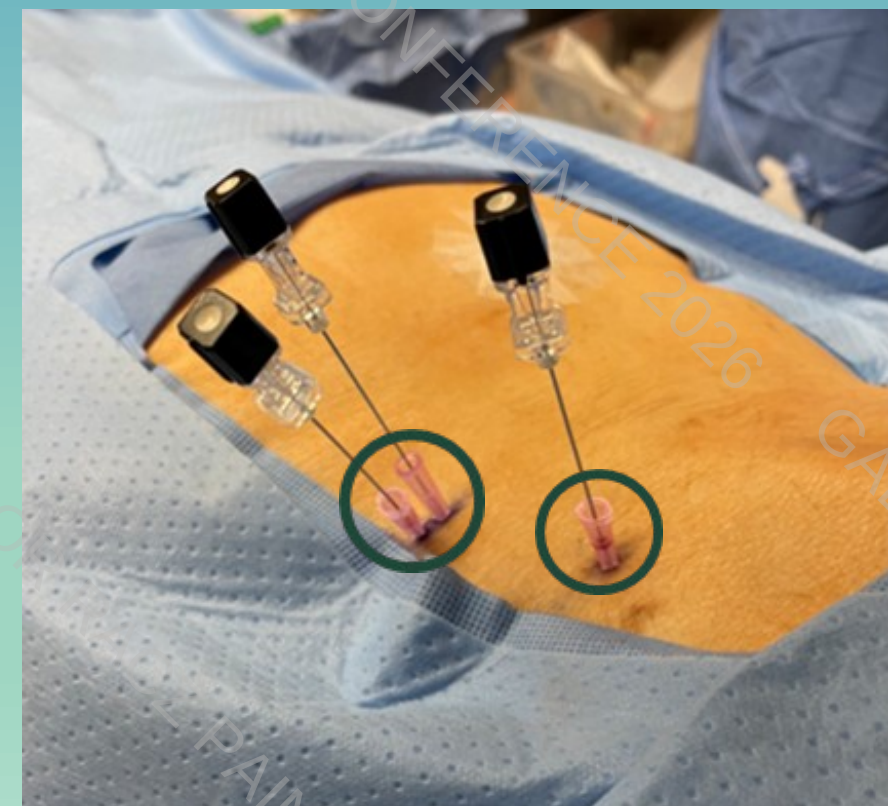
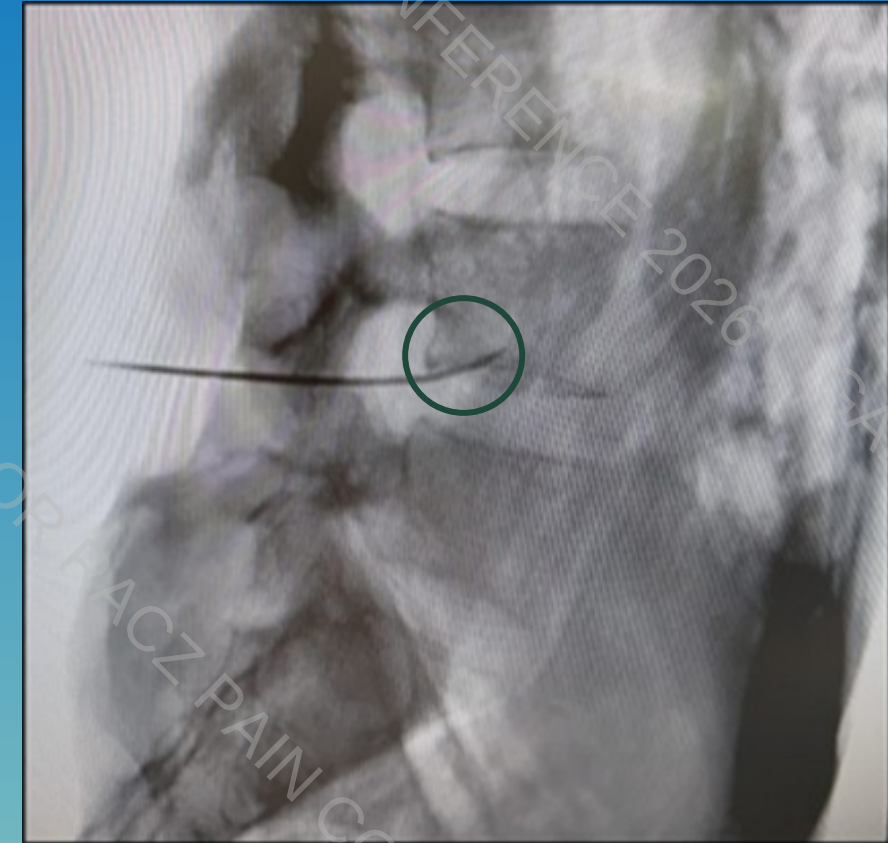
Transpedicular Approach

- Transpedicular approach: Similar to RFA of BVN
- Jamshidi access canula for TP approach:
- Trajectory planning:
 - 2 to 8 (right) and 10 to 4 (left) for inferior endplate
 - 4 to 10 (right) and 8 to 2 (left) for superior endplate
- 16 - 18 G curved tip needle directed towards CEP

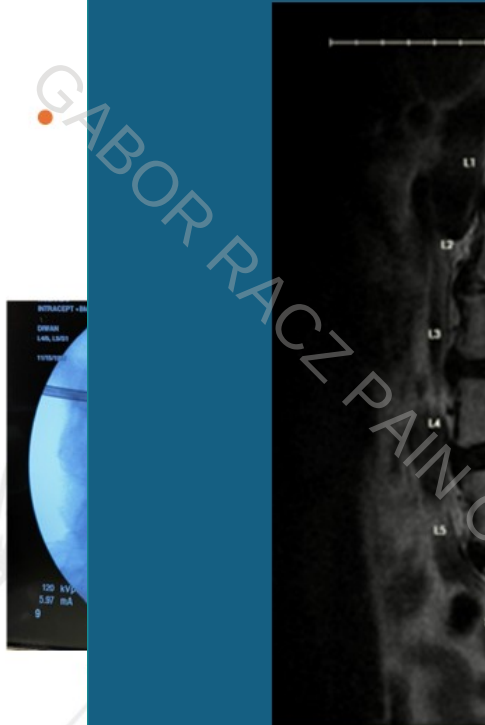


Transdiscal approach

- The procedural steps same as discography
- 22G, 6-8" curved tip needle
- Always use Needle-in-Needle technique
- Dual antibiotics intravenous prophylaxis (Cefazolin + Gentamycin)
- No intradiscal antibiotic
- Advantages: One needle can be used for Subchondral, Intradiscal and Peridiscal injections
- Disadvantage: Calcified endplates are difficult to inject

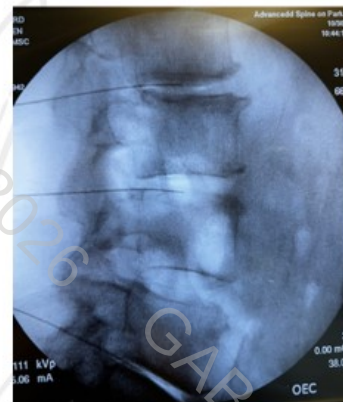


- Case 1: 72/M with Axial CLBP



ADVA

- Case 3: 81/M with Chronic Axial LBP with Radicular Pain
- MRI: Advanced DDD + MC
- Intradiscal + IO BMAC
- F/U: 4 months. 80% pain relief with improved ROM



IO + ID BMAC/MSCs

ADVANCED SPINE ON PARK AVENUE



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Combined Intradiscal, Peridiscal, and Subchondral Bone Marrow Aspirate Concentrate Injections for Vertebrogenic and Discogenic Low Back Pain with Modic I and II: A Retrospective Pilot Study Case Series

Running Title: Subchondral, Peridiscal and Intradiscal BMAC for Vertebrogenic Pain

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Case series – 13 patients

Baseline demographic and clinical characteristics of the study population

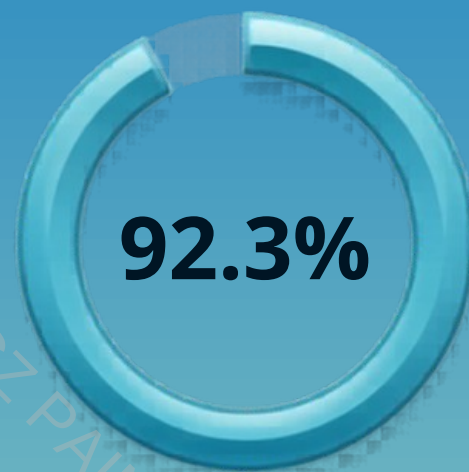
Patient ID	Age (years)	Sex	Primary diagnosis*
DAJ0000005	68	M	Vertebrogenic LBP; lumbar spondylolysis; lumbar disc disorders
SHMA0000006	66	F	Vertebrogenic LBP; disc degeneration; lumbar spondylosis
BEST0000002	82	M	Vertebrogenic LBP; disc degeneration
PER0000011	72	M	Lumbar disc degeneration; lumbar spondylolysis
OCFR0000001	48	M	Lumbar disc degeneration; lumbar spondylolysis
OCFR0000001	77	F	Vertebrogenic LBP; lumbar disc degeneration
RACA0000002	77	M	Vertebrogenic LBP; lumbar spondylolysis; disc degeneration
KAJA07AF448A	27	M	Vertebrogenic LBP; lumbar spondylolysis; disc disorders
MASH07BEEC94	66	F	Vertebrogenic LBP; disc degeneration; post-laminectomy syndrome
ARJE0000001	35	F	Vertebrogenic LBP; thoracolumbar disc degeneration
DEAL07C47AED	45	F	Vertebrogenic LBP; lumbar spondylosis; disc disorders
MAEM07CA4B06	53	M	Vertebrogenic LBP; lumbar spondylolysis; disc disorders
P1_SLO	35	M	Lumbar disc disorders with radiculopathy
P2_SLO	53	F	Lumbar disc disorders with radiculopathy

Abbreviations: VAS, Visual Analog Scale; BVN-RFA, basivertebral nerve radiofrequency ablation

Clinical outcomes and patient-reported results following treatment							
Patient ID	Follow-up duration	Byn-rfa	Post-treatment pain (VAS)	Pain reduction (%)	Functional improvement†	Patient satisfaction	Would recommend
DAJO000005	8 months	No	0	100%	80% improvement; major gains in mobility and QoL	Very satisfied	Yes
SHMA000006	12 months	Yes	4	60%	Increased ROM and daily functionality	Satisfied	Yes
BEST000002	12 months	No	0	100%	Was Able to walk 1 mile and exercise; no further injections	Very satisfied	Yes
PERO000011	14 months	Yes	1	88.9%	Resumed regular exercise; improved sleep and QoL	Very satisfied	Yes
OCFR000001	16 months	No	0	100%	Normalized ROM, sleep, and QoL	Very satisfied	Yes
RACA000002	10 months	No	5	50%	Reduced pain with activity; improved ROM and sleep	Satisfied	N/A
KAJA07AF448A	8 months	No	2	66.7%	Improved ROM and ability to perform strenuous tasks	Satisfied	Yes
MASH07BEEC94	6 months	No	3	62.5%	Pain almost resolved in treated area	Satisfied	Yes
ARJE000001	5 months	Yes	4	50%	Moderate functional improvement	Neutral	Yes
DEAL07C47AED	8 months	No	2	60%	Significant improvement reported	Satisfied	Yes
MAEM07CA4B06	4 months	Yes	3	62.5%	Increased ROM and daily functionality	Satisfied	Yes
P1_SLO	9 months	No	3	50%	Moderate functional improvement	Neutral	Yes
P2_SLO	6 months	No	3	57.1%	Reduced pain with activity; improved ROM	Satisfied	Yes
†Functional improvement was assessed based on patient-reported changes in mobility, daily activities, sleep, and overall quality of life. Abbreviations: VAS = Visual Analog Scale, ROM = range of motion, QoL = quality of life Table 3. Individual pain intensity before and after combined intradiscal and subchondral biologic treatment							

Restoring Functional Capacity Safely

Patient Satisfaction



Satisfied or Very Satisfied



Would recommend the procedure to family/friends

Functional Gains



Enhanced mobility



Increased walking tolerance



Restored sleep quality



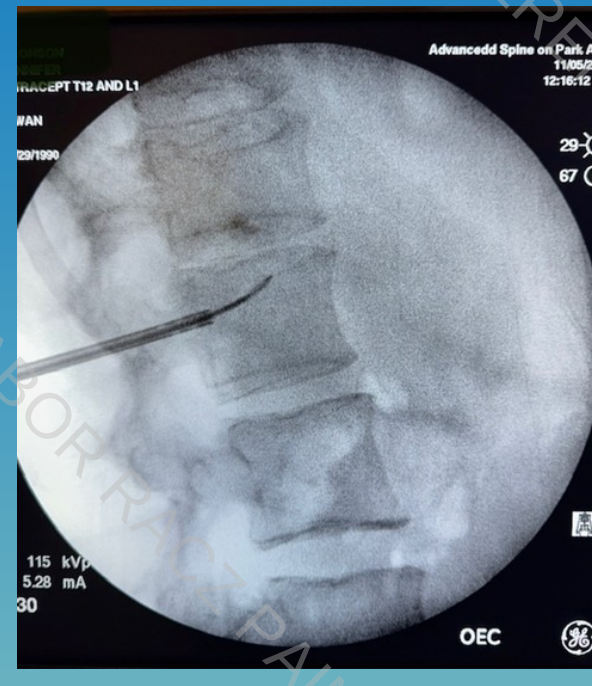
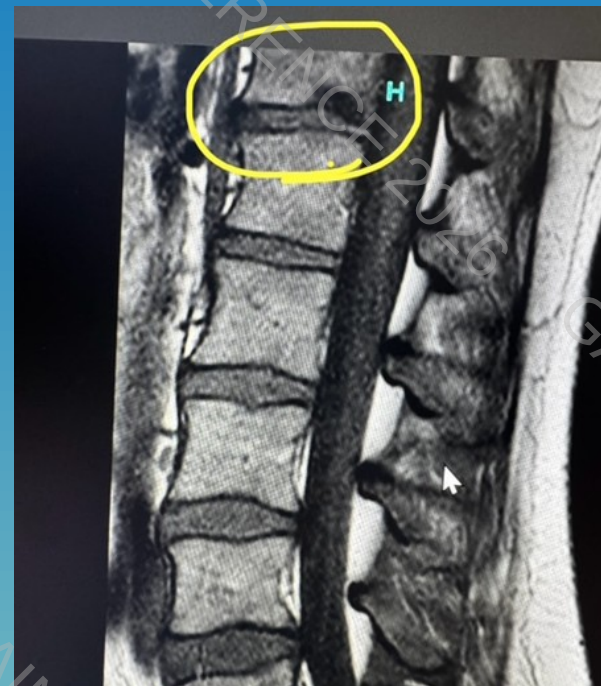
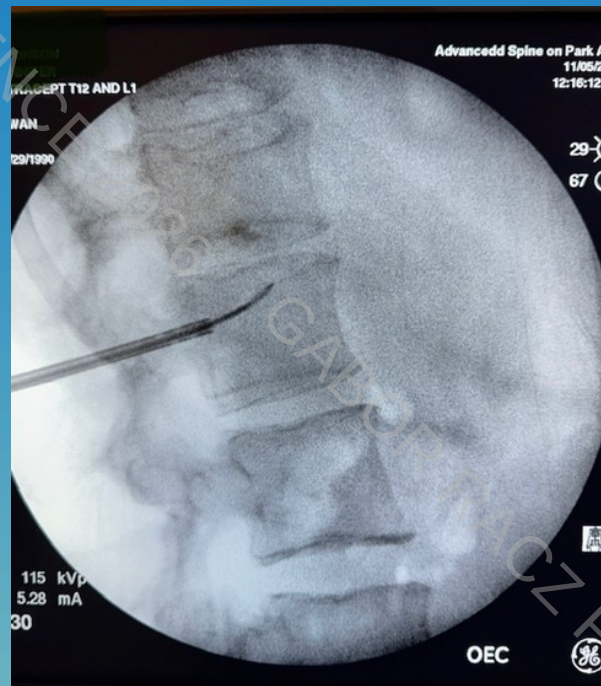
Return to exercise

Safety Profile



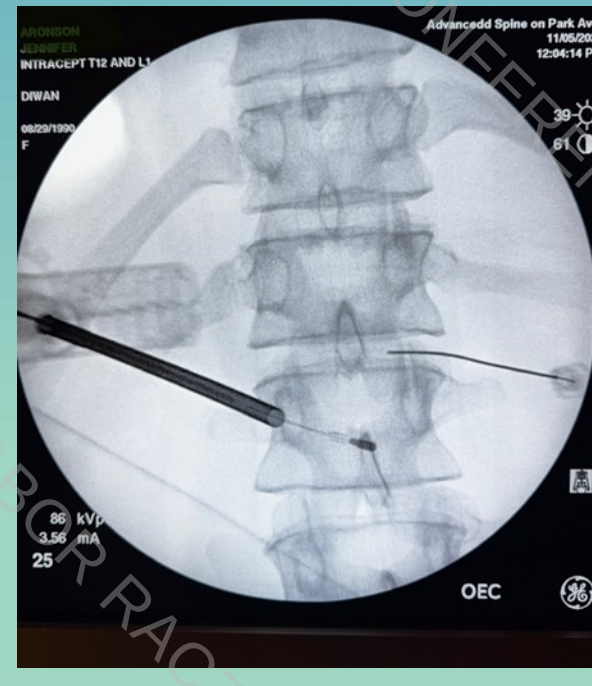
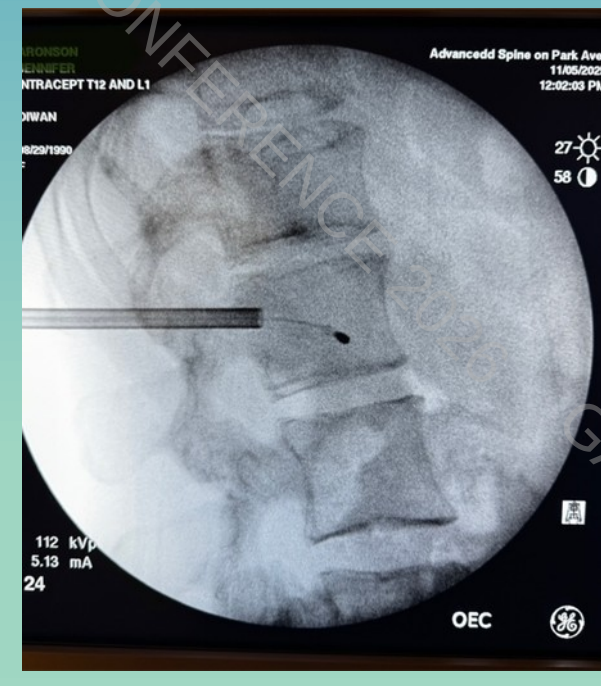
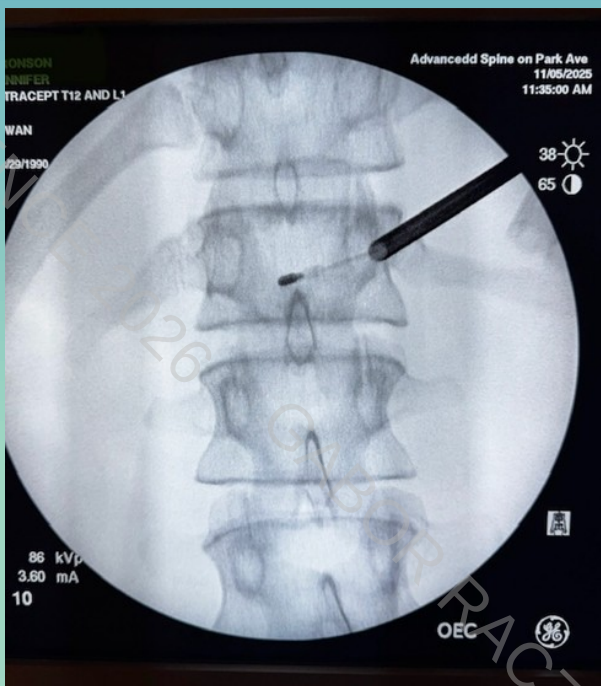
No major complications.
Mild, transient harvest-site and injection site soreness resolved spontaneously within 48 hours.

- Mean VAS dropped from 7.3 to 2.1 (Absolute reduction of 5.2 points)
- Zero Non-Responders: 100% of patients achieved $\geq 50\%$ pain reduction
- 38.5% of patients achieved $\geq 80\%$ pain reduction



T12-L1 RFA of BVN + SC at T12 and L1 CEPs + ID + PD BMAC

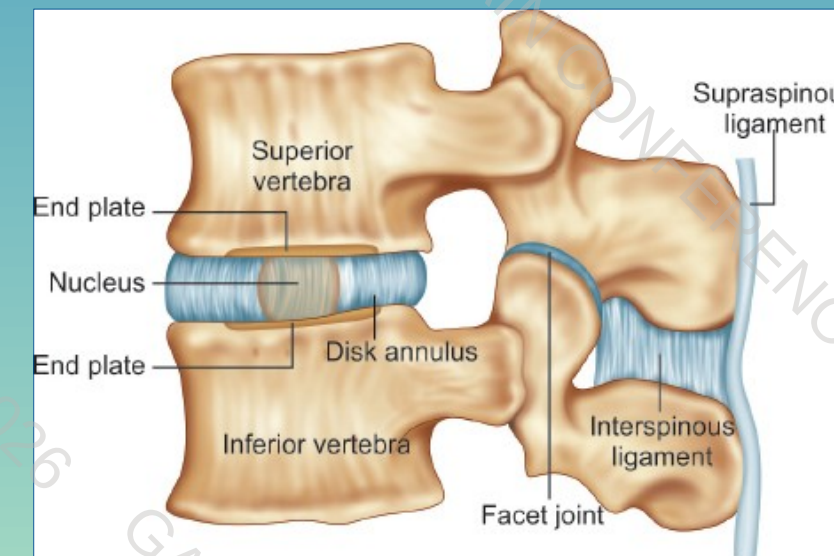
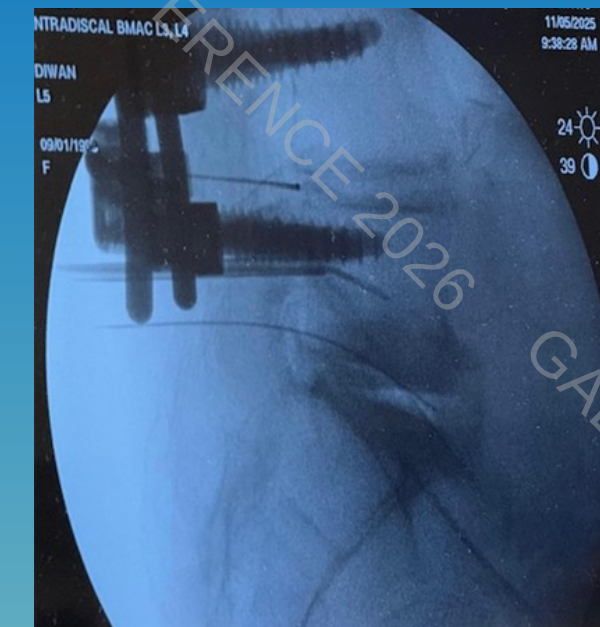
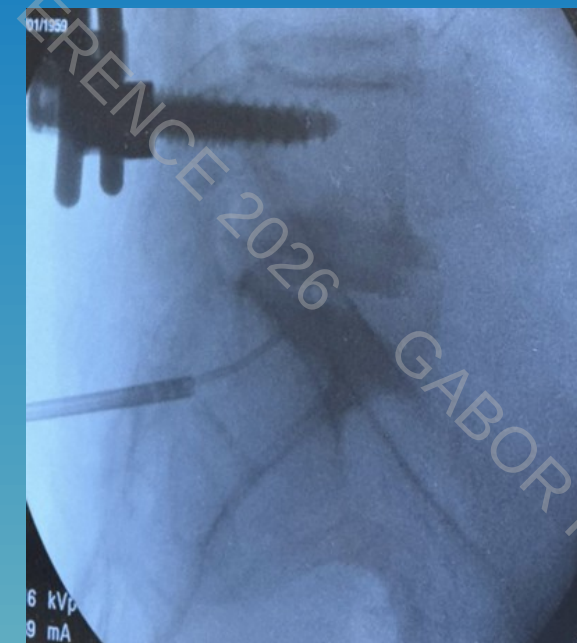
- 35 Y/F with severe thoracolumbar pain
- Failed spinal procedures
- Insurance denied coverage for RFA of BVN procedure
- In-office Intrasept procedure at T12 and L1 levels



Functional Spinal Unit Approach for Orthobiologics Injections for Low Back Pain

- The **FSU**, the smallest structural unit of the spine, consists of 2 vertebrae, an IVD, facet joints, and associated supporting ligaments
- Orthobiologic treatments offer a promising disease-modifying approach by addressing the entire FSU rather than isolated pain generators

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R Navani, J Fábio Lana, MD, and S Diwan, MD.
Pain Physician 2025; 28:S145-S156*



Multilevel BMAC Injections at SC + ID + PD + Facets + Epidural space + Multifidus muscle

Heterogenous studies and flaws

- Heterogeneous studies:
 - Require large sample size
 - more complex data analysis
 - harder to draw conclusions
- Effect of BAMC at Gr-2 DDD in a Young pt. vs. older pt. with Gr-5 DDD
- Poorly specified study goals: Regeneration of the DD vs. symptomatic improvements, or both
- **Biologics must be delivered to target tissue precisely** to expedite regeneration and maximize the outcome :
 - Intradiscal injection for reversal of degenerarion symptomatic relief for Modic 1 & 2 changes
 - Peridiscal injections for
 - Subchondral injection
- Lack of standardized for biologics injection **location**, injection **volume**, **cellular count**, centrifuge protocol, and injections techniques



Stay tuned.
We are collecting data....

**Thank You for
your attention!!**

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