Treatment Options for Low Back Pain Due to Degenerative Disc Disorder (Including Research Trials)

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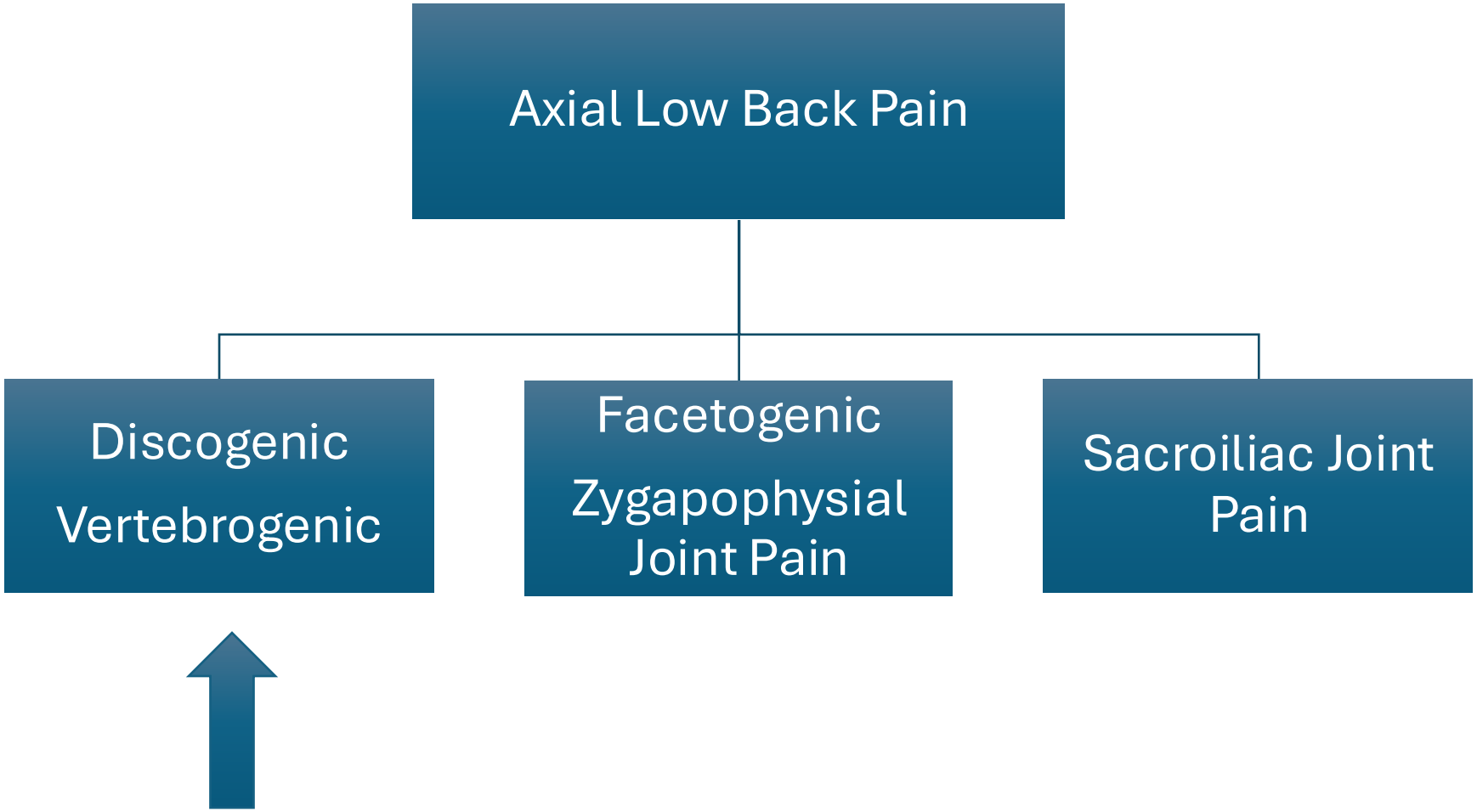
Overview of LBP Research Trials and Treatment Options

- *Sponsored Research:*
- Biorestorative: Intradiscal stem cell study – autologous BRTX-100 and platelet lysate
- Mesoblast intradiscal stem cell study - *rexlemestrocel-L+HA*
- ReGelTec: HYDRAFIL-D – intradiscal injectable polymer
- ***Payer/sponsor hybrid***
- Saluda Spinal Cord Stimulation Clinical Trial:
  - ECAP controlled-closed-loop SCS trial for trunk and extremity pain
- ***Cash or Medicare/commercial payer:***
- Vivex Biologics; VIA Disc – injectable nucleus pulposus particulate
- Intracept; BVN RFA – basivertebral nerve radiofrequency ablation
- Platelet Rich Plasma – PRP
- Comprehensive conservative care; interventional care; surgical options


Axial Low Back Pain
Discogenic
Vertebrogenic
Facetogenic
Zygapophysial
Joint Pain
Sacroiliac Joint
Pain

J. Anat. (2012) **221**, pp480–496 doi: 10.1111/j.1469-7580.2012.01521.x

REVIEW

Diversity of intervertebral disc cells: phenotype and function

Girish Pattappa, Zhen Li, Marianna Peroglio, Nadine Wismer, Mauro Alini and Sibylle Grad

AO Research Institute Davos, Davos, Switzerland

Table 2 Summary of characteristics of human IVD cells.

	NP cells	AF cells	CEP cells
Morphology	Rounded	Elongated	Rounded
Gene expression	Type II collagen, Cytokeratin-19, FOX-F1, CA12, PAX-1, Brachyury.	Type I collagen, type V collagen, tenomodulin	–
ECM proteins	Collagen type II, Aggrecan, hyaluronan	Type I collagen, Type II collagen, aggrecan, elastin	Type II collagen, aggrecan, hyaluronan

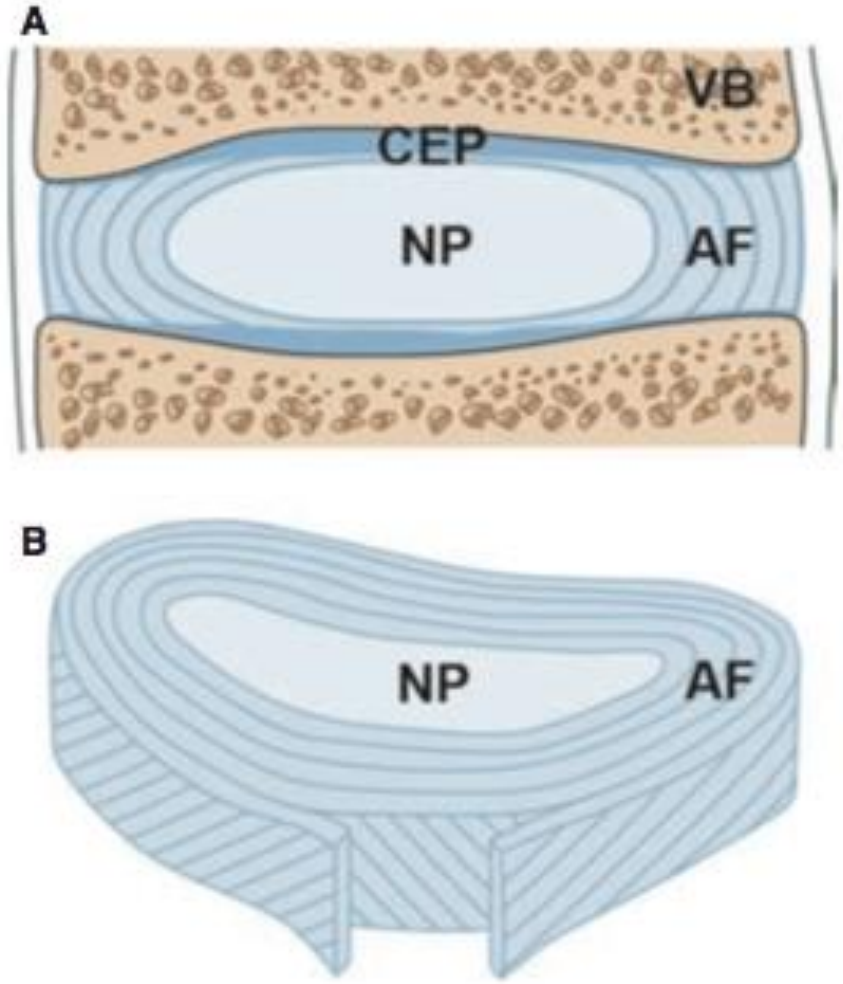
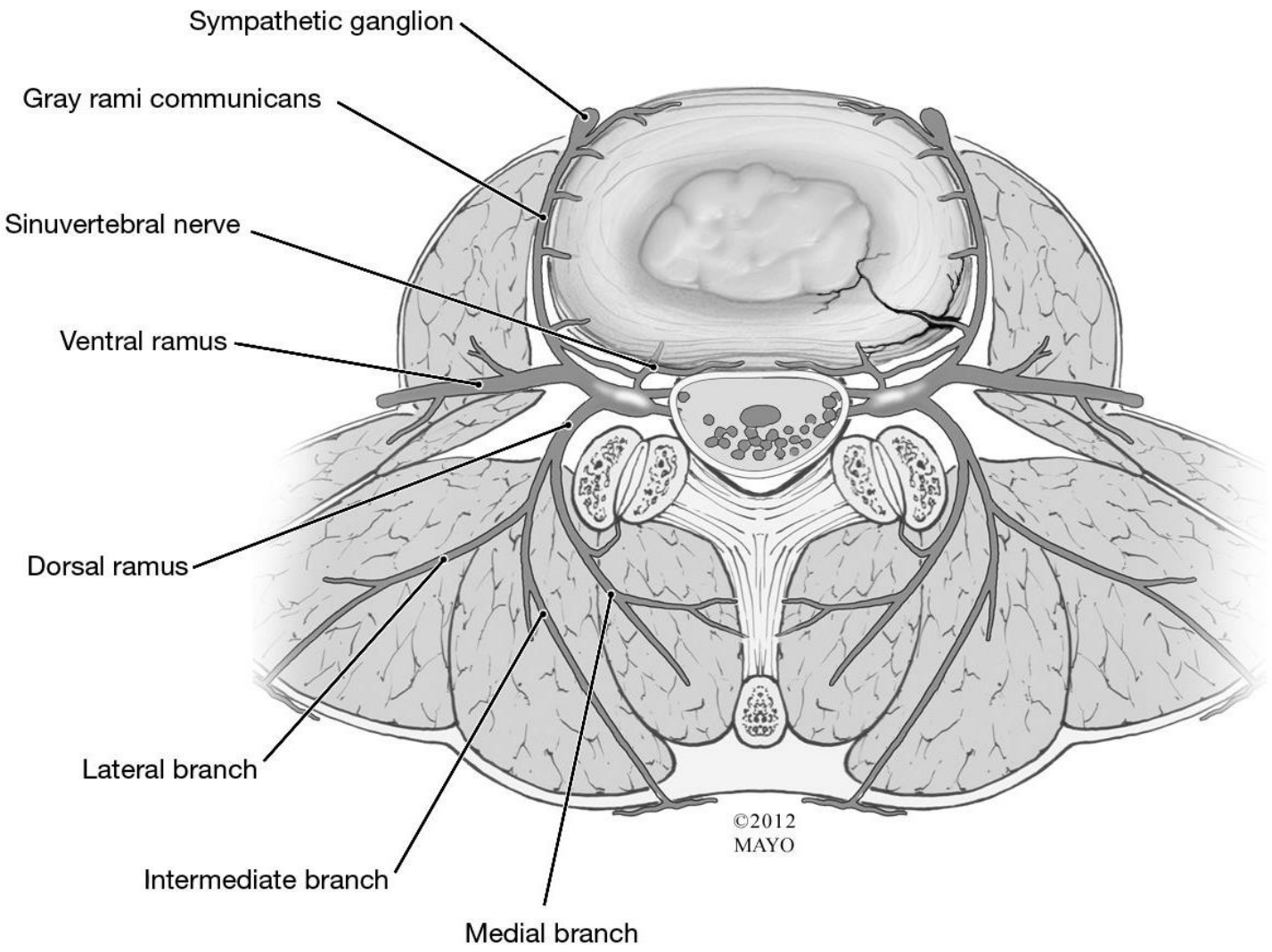


Fig. 1 Schematic representation of an intervertebral disc (IVD). The cartilaginous endplate (CEP) and the adjacent vertebrae (VB) are visualized in the sagittal section of the disc (A). The annulus fibrosus (AF) is formed by structured lamellae which encapsulate the central nucleus pulposus (NP) (B).

Discovertebral Complex: Innervation



Disc: outer 1/3 annulus

- Sinuvertebral nerve
- Grey rami
- Sympathetic plexus
- Neo-innervation

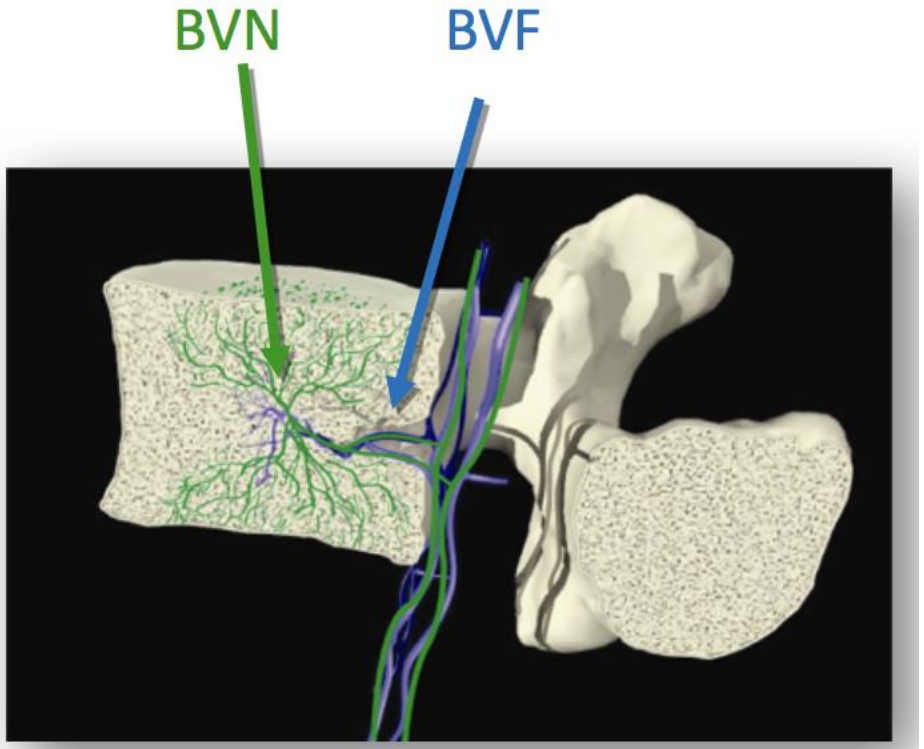
Courtesy Aaron Calodney, MD and Spine Intervention Society

Anatomy of Innervation of Endplates

Basivertebral Nerve Anatomy

- BVN enters the vertebral body via the Basivertebral Foramen
- Bifurcates at the terminus of the BVF
- Aborizes towards the endplates.

Bailey et al.



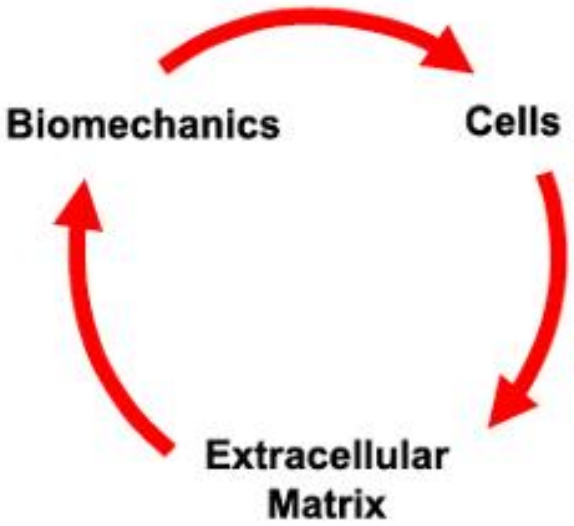


Fig. 1. Concept of the degenerative circle of intervertebral disc degeneration.

Vergroesen, et.al (2015) proposed that there is a dynamic interplay between the biomechanics, cell function, and extracellular matrix within discs. Pathology of one component may lead to breakdown or dysfunction of others and biological or mechanical augmentation may improve the state of other components.

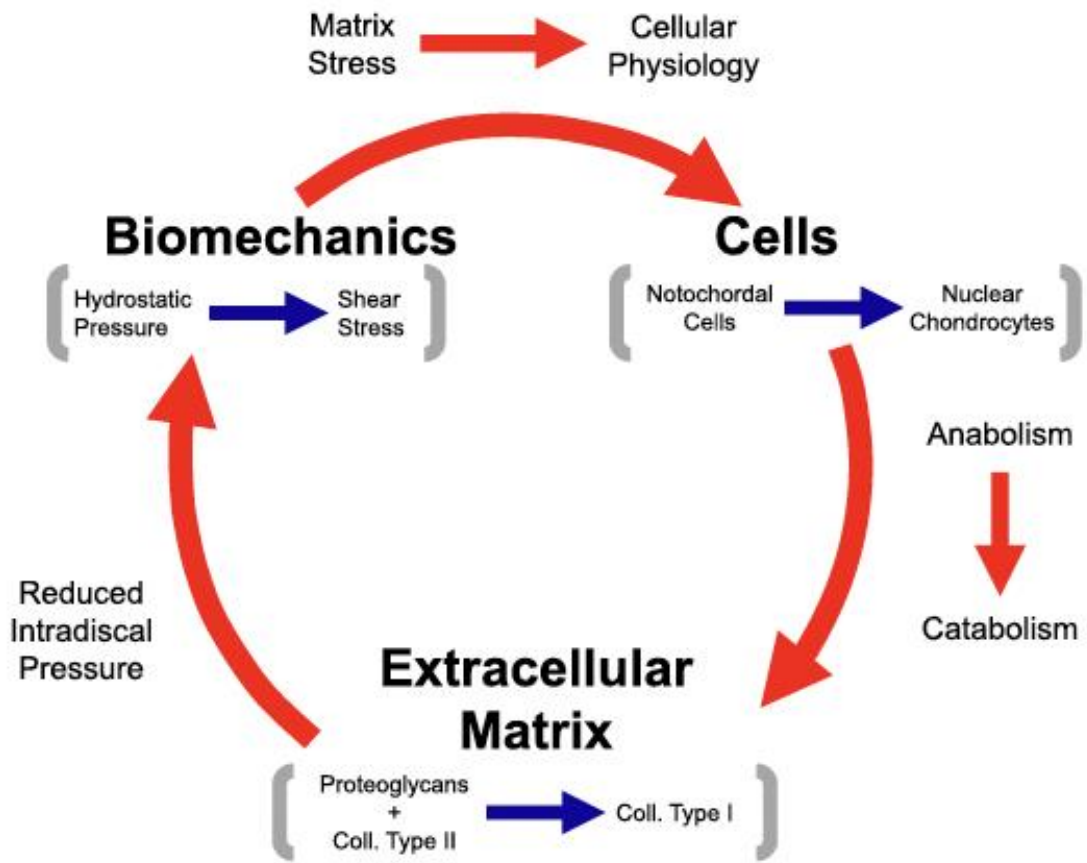


Fig. 2. The degenerative circle of intervertebral disc degeneration. Homeostasis of the intervertebral disc is dependent on the interaction of cells, extracellular matrix and biomechanical stress. If this balance is disturbed, the cells stop producing proteoglycans, this will give a reduction in hydrostatic pressure and increase shear forces on the cells. An increase of shear forces further decreases the production of proteoglycans, leading to progressive degeneration.

10.3389/fbioe.2024.1417600

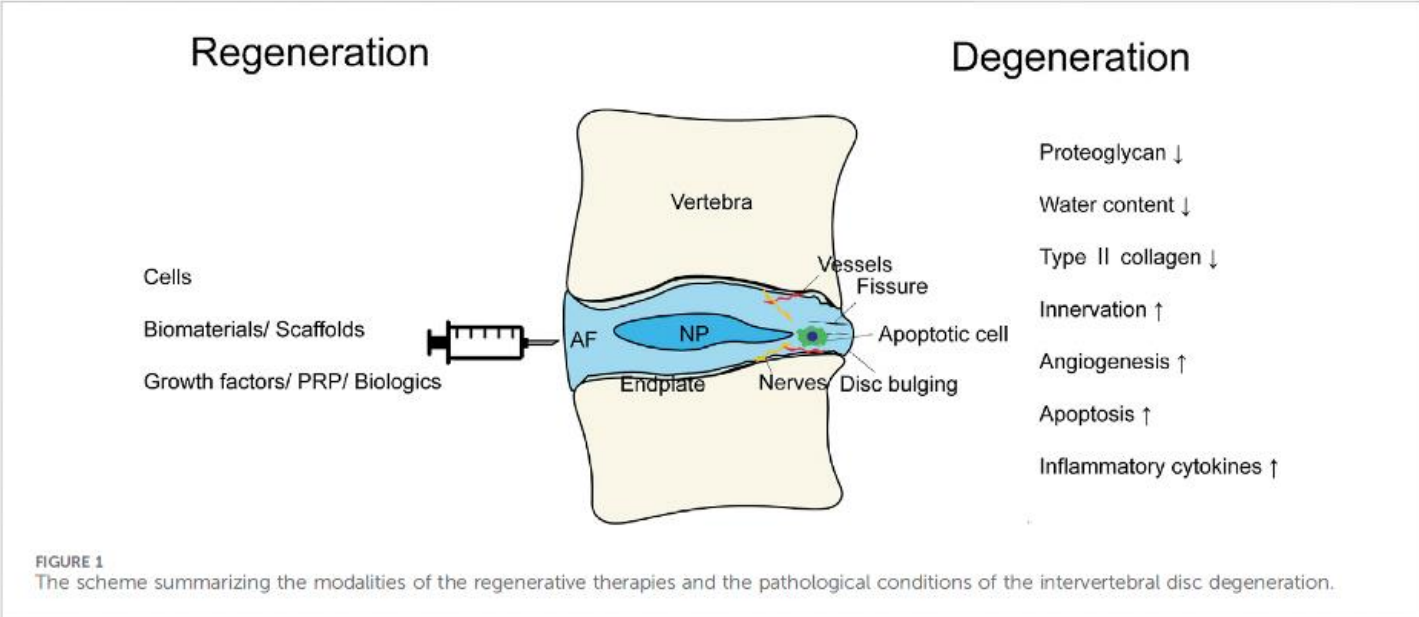


FIGURE 1
The scheme summarizing the modalities of the regenerative therapies and the pathological conditions of the intervertebral disc degeneration.

The degenerative process leads to changes in cell gene expression, a breakdown of the nucleus matrix, increased shear forces and other mechanical malfunction, and ingrowth and sensitization of nerve fibers. This often leads to a painful condition. Research into the effects of injection of cells, growth factors, structural supports (e.g. polymer injection), and other strategies is ongoing.

PREDICTOR VARIABLES FOR IDENTIFYING DISCOGENIC LOW BACK PAIN

PHYSICAL

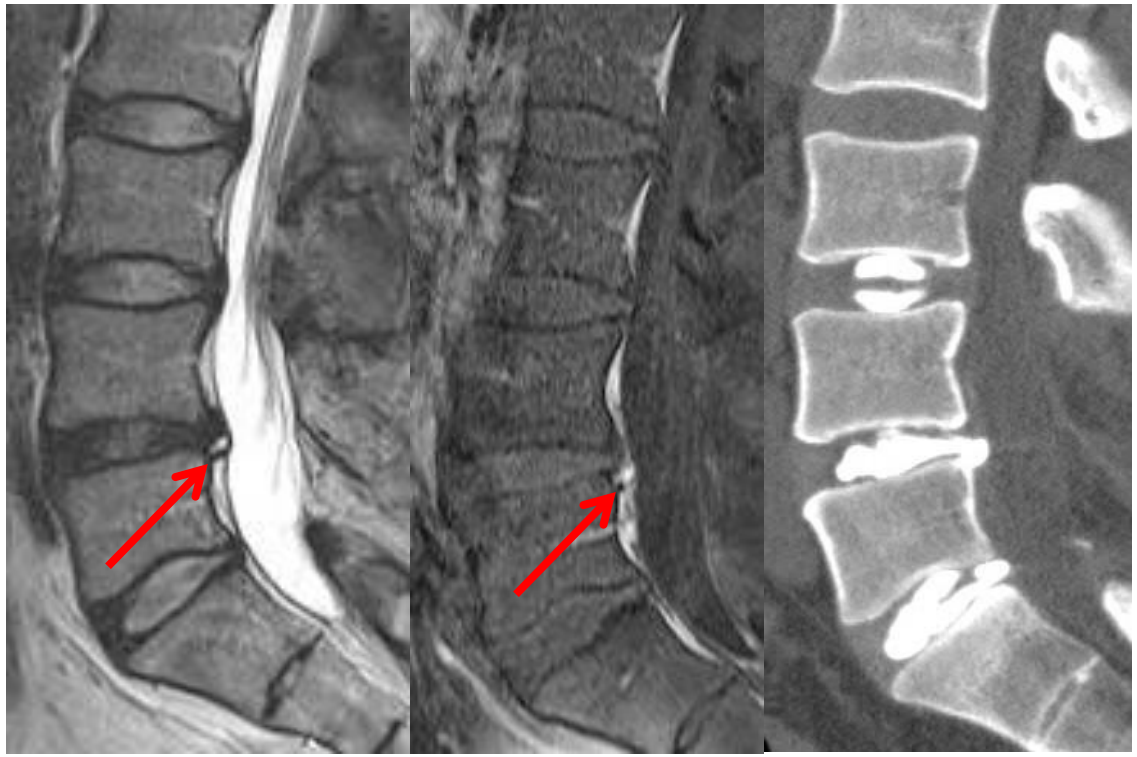
- Midline Low Back Pain (with or without leg pain)[2]
- Pain with Forward Flexion[3]
- Sitting Intolerance[2]
- Positive Sustained Hip Flexion Maneuver (in certain patients)[4]

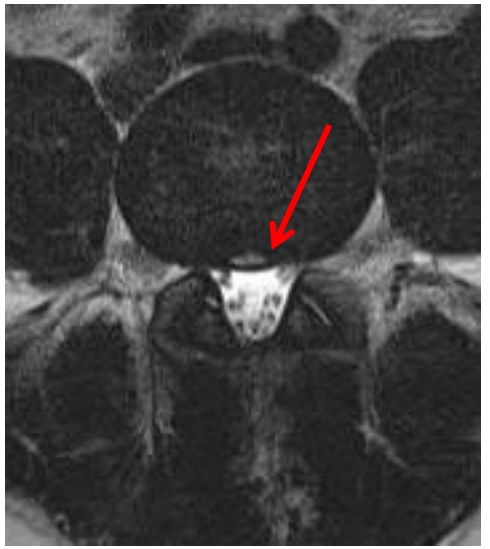
IMAGING

- Mild to Moderate Disc Degeneration[1]
- Contained Disc Protrusions
- HIZ Lesions[5]
- Modic Changes of Type II or Less[5]

1. *Griffith, J. F., Wang, Y. X., Antonio, G. E., Choi, K. C., Yu, A., Ahuja, A. T., & Leung, P. C. (2007). Modified Pfirrmann grading system for lumbar intervertebral disc degeneration. Spine, 32(24), E708–E712. https://doi.org/10.1097/BRS.0b013e31815a59a0*
2. *Young S, Aprill C, Laslett M. Correlation of clinical examination characteristics with three sources of chronic low back pai n. Spine J. 2003;3(6):460-465. doi:10.1016/s1529-9430(03)00151-7*
3. *Nachemson A. (1975). Towards a better understanding of low-back pain: a review of the mechanics of the lumbar disc. Rheumatology and rehabilitation, 14(3),129–143. https://doi.org/10.1093/rheumatology/14.Us.*
4. *DePalma M, Ketchum J, Queler E, Ruchala M, Powell D, Kouchouch A, Trussell B. Does sustained hip flexion, pelvic rock, or location of low back pain predict the etiology of low back pain? An interim analysis of 170 consecutive low back pain cases.*
5. *Bogduk N, Aprill C, Derby R. Lumbar discogenic pain: state-of-the-art review. Pain Med. 2013;14(6):813-836. doi:10.1111/pme.12082*

High Intensity Zone (HIZ): Strongly predicts a painful disc

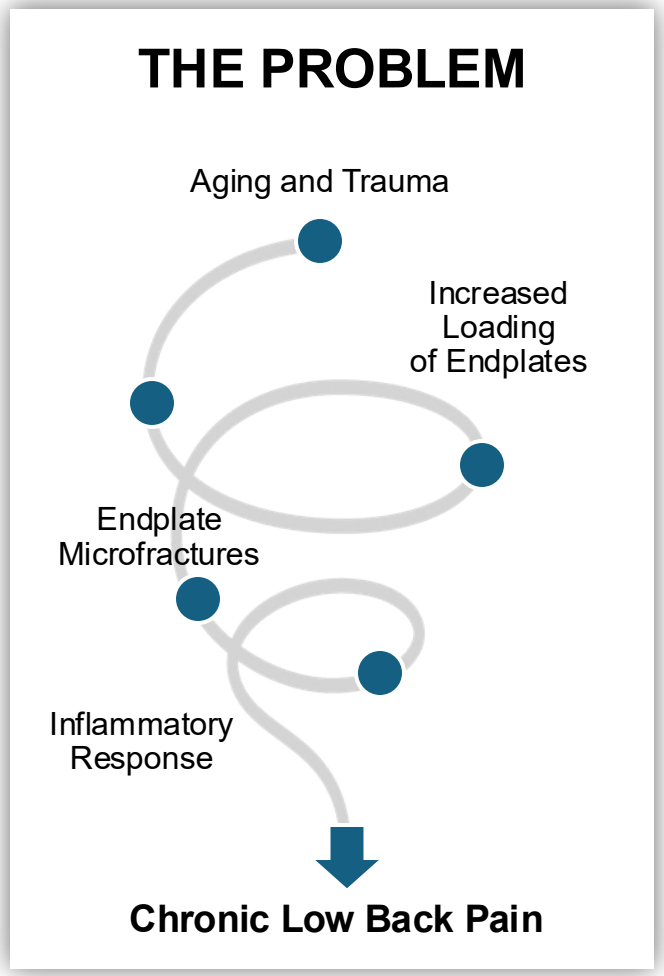




Courtesy IPSIS

Pooled data: + LR ≈ 4 If prevalence of IDD is 46%, LR of 4 provides 73% confidence of a painful disc at provocation discography

Modic Changes

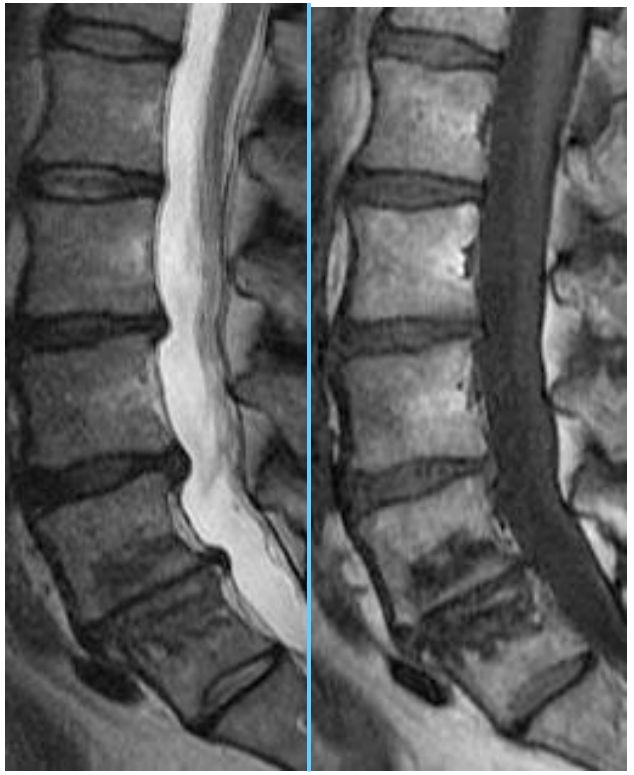


- Identifiable in routine MRI
- Represent inflammatory response to endplate fracture
- Changes in T1 and T2 views
- MC are highly specific for CLBP[1]
- LBP patients with MC report a greater frequency and duration of LBP episodes[2-5]
- LBP severity correlates with MC lesion size[6]

Endplate Inflammatory Change
Modic Classification

Modic I

Modic II



Modic III

End Plate Inflammatory Change

- **Modic Changes:** endplate signal change
  - **Modic I**: Vascularized granulation tissue
  - **Modic II:** Fatty infiltration
  - **Modic III:** Sclerotic change

- **Modic I > II represent an inflammatory state:** increased levels of TNF α reactive cells, & cellular products.

Courtesy Aaron Calodney, MD

Clinical Diagnosis of Lumbar Discogenic Pain

- Painful with increased intradiscal pressure
  - Sitting
  - Bend/lift
  - Valsalva
- Midline disc may hurt with extension
- May include instability symptoms of catch/shift/crepitus, pain with arising from flexion and transitional movements

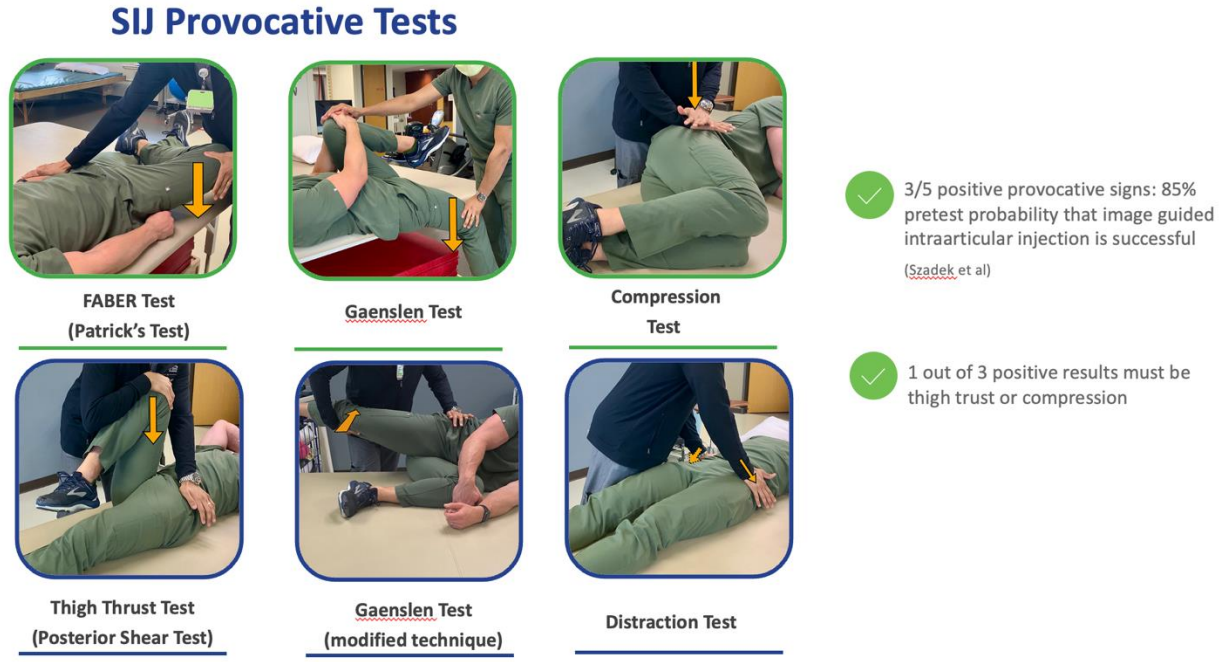
Differentiating Axial LBP Source

Structure	Image	History (P=pain)	Exam
Disc	MRI: HIZ, Modic Changes	P arising from sit, midline; P w bend, lift, Valsalva	Centralization (McKenzie), flexion
LZJ (facet joint)	DDD/DJD common (not predictive)	P standing, better walking, sitting; age > 52	P w combined extension / rotation (absent = negative predictor)
SIJ	Not predictive or sensitive/specific but rule out fracture, stress response, tumor, inflammation	P arising from sit, P unilateral at or below PSIS	Fortin finger (pt. points to SIJ as P location; Gillet test; 3 of 5 positive: pelvic distraction, compression, FABER, thigh thrust, Gaenslen's (or sacral spring test)

- SIJ pain , as determined by a targeted physical exam. The following tests should be performed
  - Distraction
  - Compression
  - Thigh thrust
  - Sacral thrust
  - Gaenslen's
    - Subjects who present with ALL of the following symptoms should be considered positive for SIJ pain

      - Maximal tenderness at or below L5
      - Tenderness over the posterior superior iliac spine/sacral salcus
      - Three positive SIJ provocation tests (Laslett's tests)
    - Should the results of the targeted examination prove inconclusive, the investigator should perform a diagnostic injection of anesthetic to the SI joint to determine presence of SI joint pain. If the anesthetic injection relieves more than 50% of the subject's pain, the presence of SI joint pain is confirmed.

Mesoblast exclusion of SIJ pain
Replace FABER with sacral thrust



Source: Buchanan P, Vodapally S, Lee DW, Hagedorn JM, Bovinet C, Strand N, Sayed D, Deer T. Successful Diagnosis of Sacroiliac Joint Dysfunction. *J Pain Res.* 2021;14:3135-3143 https://doi.org/10.2147/JPR.S327351

Research Trials – Intradiscal Therapies (Injectables)

- BioRestorative – BRTX-100 (autologous stem cells and PRP lysate)
  - A Single Dose of BRTX 100 for Patients With Chronic Lumbar Disc Disease (cLDD) (https://clinicaltrials.gov/study/NCT04042844)
- Mesoblast – Rexlemestrocel-L (donor mesenchymal precursor cells and hyaluronic acid)
  - Study Details | Efficacy and Safety of Rexlemestrocel-L Combined With HA* in Participants With Moderate to Severe Chronic Low Back Pain | ClinicalTrials.gov (https://clinicaltrials.gov/study/NCT06325566)
- ReGelTec – HYDRAFIL-D (structural polymer)
  - HYDRAFIL-D: HYDRogel Augmentation for Intervertebral Lumbar Discs | ClinicalTrials.gov (https://clinicaltrials.gov/study/NCT0601155)

BioRestorative Receives FDA Fast Track Designation for BRTX-100 Chronic Lumbar Disc Disease Program

February 20, 2025 08:30 ET | Source: BioRestorative Therapies, Inc

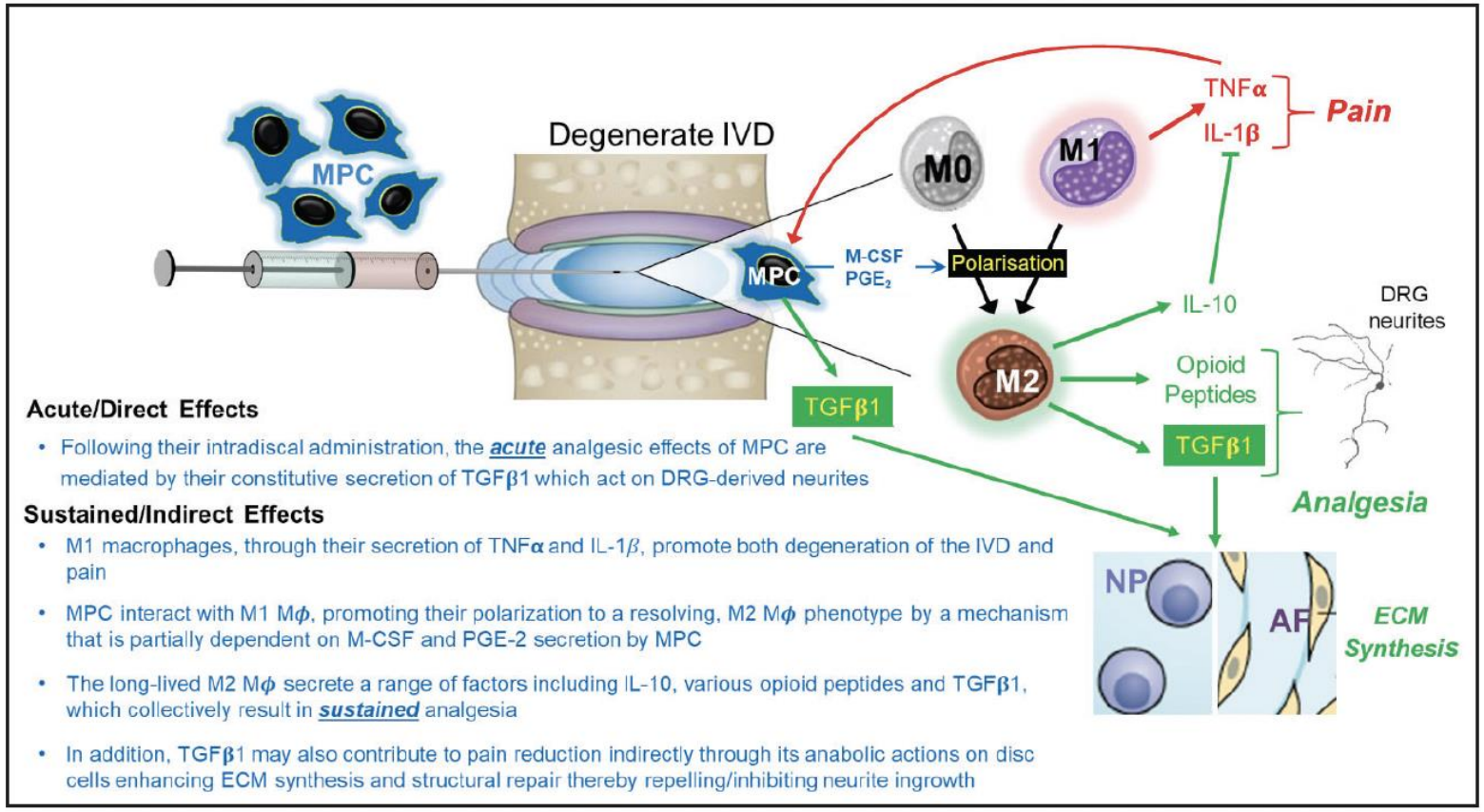
Follow

BioRestorative Therapies

- A Phase 2, Double-Blind, Saline-Controlled, Randomized Study to Evaluate the Safety and Preliminary Efficacy of a Single Dose **Intradiscal Injection of BRTX-100 for Patients with Chronic Lumbar Disc Disease (cLDD)**. (Injection of Stem Cells into Painful Lumbar Discs)
-
- Sponsored by BioRestorative Therapies, Inc.
-
- Principal Investigator: J. Scott Bainbridge, MD, Enrollment June 2022- Present.
- Contact: Josephine Steinbrecher, Research Administrator, DBPS Research, LLC
- 303-327-5511; ext. 319; josephine@denverpaininstitute.com
-
- Link to Stem Cell Injection for Low Back Pain Study Site
-
- https://clinicaltrials.gov/study/NCT04042844
-
- Stem Cell Injections Into Painful Lumbar Discs Study Information .pdf

Mesoblast Clinical Trial

Figure 2: Rexlemestrocel-L (MPC) Hypothesized Mechanism of Action



Mesoblast

- Phase 3 study to treat lumbar degenerative disc disease (DDD). The study is looking to evaluate the efficacy of donor stem cells plus hyaluronic acid (HA) injected into painful lumbar discs.
-
- The primary purpose of this study is to evaluate the efficacy of rexlemestrocel-L+HA compared to control in reducing low back pain at 12 months post-treatment and safety of a single injection of rexlemestrocel-L+HA injected into a lumbar intervertebral disc compared to control through 12 months post-treatment.
-
- Principal Investigator- Gary Ghiselli, MD
- Sub-Investigators- J. Scott Bainbridge, MD (injectionist), Drew Trainor, DO, Susan Estes, NP-C, and Michelle Hogue, FNP-BC
- Contact: Josephine Steinbrecher, Research Administrator, DBPS Research, LLC
- 303-327-5511; ext. 319; josephine@denverpaininstitute.com
-
- Study Details | Efficacy and Safety of Rexlemestrocel-L Combined With HA* in Participants With Moderate to Severe Chronic Low Back Pain | ClinicalTrials.gov
-
- Mesoblast Low Back Pain Research Brochure PDF

HYDRAFIL® - Injectable Gel Implant for Degenerated Discs

Researchers are conducting this study to evaluate the safety and effectiveness of a new investigational spinal implant called **HYDRAFIL** for the treatment of lumbar (low back) degenerative disc disease. **HYDRAFIL** is intended to treat one (1) or two (2) lumbar disc levels.

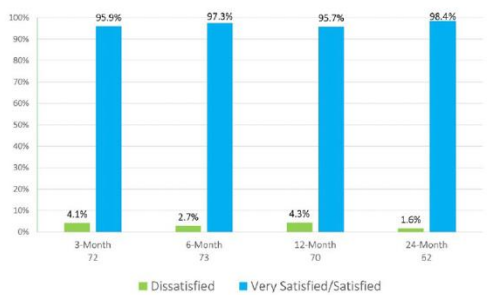
HYDRAFIL is a hydrated polymer gel (hydrogel) that mimics the natural properties of the nucleus inside an intervertebral disc in the spine. It is designed to be an injectable, soft, space-filling, disc augmentation technology.

- **Permanent implant device -** motion preserving biomechanical properties
- **Minimally invasive procedure -** quick, percutaneous injection administered via a 17-gauge needle
- **Short recovery time -** patients are walking within two hours following injection
- **Early clinical results -** show satisfaction and significant improvements in pain and function

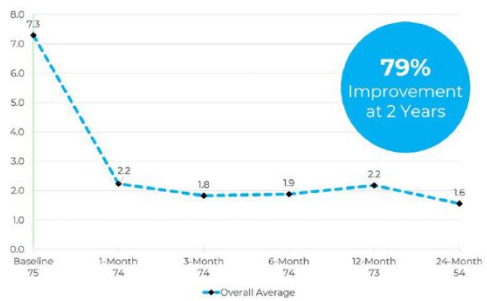
Preliminary 2-Year OUS Early Feasibility Study Results (N=75)[1]

[1] Data on file at ReGelTec, Inc.

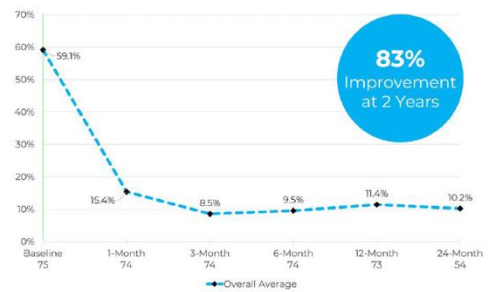
ReGelTec



Patient Satisfaction Following Treatment



Low Back Pain Improvement Over Time



Function Improvement Over Time

ReGelTec / HYDRAFIL-D

- This pivotal study is designed to evaluate the safety and effectiveness of the ReGelTec HYDRAFIL System in subjects with axial chronic low back pain (CLBP) due to degenerative disc disease (DDD) who continue to have severe back pain and dysfunction after at least six (6) months of conservative care.
-
- Principal Investigator- J. Scott Bainbridge, MD
- Sub-Investigators- Drew Trainor, DO, Susan Estes, NP-C, and Michelle Hogue, FNP-BC
- Contact: Josephine Steinbrecher, Research Administrator, DBPS Research, LLC
- 303-327-5511; ext. 319; josephine@denverpaininstitute.com
-
-
- Study Details | HYDRAFIL-D: HYDRogel Augmentation for Intervertebral Lumbar Discs | ClinicalTrials.gov
-
- ReGelTec HYDRAFIL-D Research Study for Low Back Pain Brochure PDF

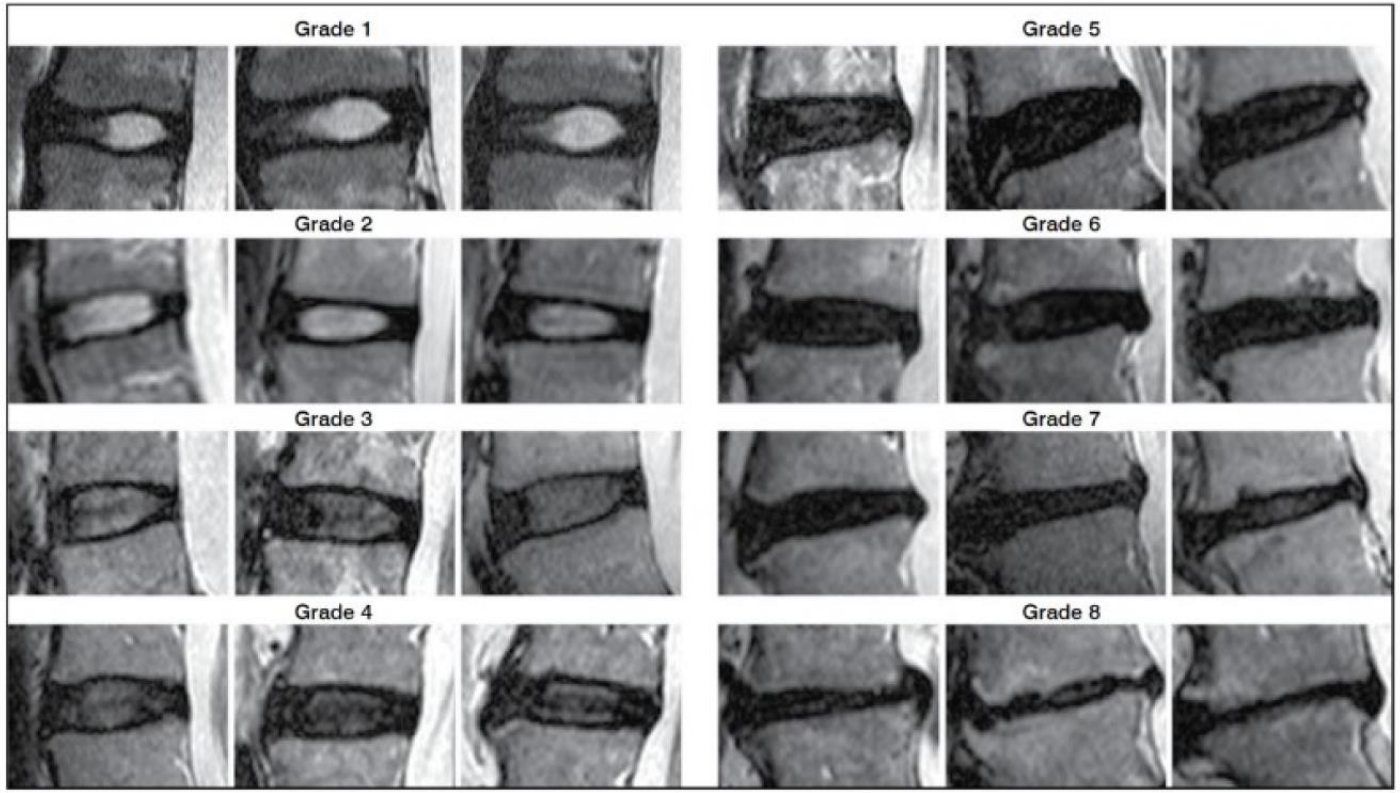
Clinical Research Trials at DBPS Research / The Denver Spine & Pain Institute for the treatment of lumbar degenerative disc disease with LBP

Contact Josephine at 303-327-5511, ext. 19
Josephine@denverpaininstitute.com

	BioRestorative	Mesoblast	ReGelTec
Treatment – intradiscal injection	Stem (MSC) cells, platelet lysate BRTX-100	Stem (MPC) cells Rexlemestrocel-L, HA	Hydrogel augmentation HYDRAFIL-D
Source	Patient bone marrow and blood-autologous	Human donor - allogeneic	Polymers
Inclusion	18-60yo, 1 disc, mP 2-7 (1 if HIZ or protrusion, <50% disc loss	18+yo, 1 disc, mP 3-7, <30% disc loss, < 60 mo pain	22-85yo, 1-2 discs, mP 4-8
PROM	VAS 40-80, ODI 30-90	VAS 40-90, ODI 20-90	VAS 50+, ODI 40+
Screening injections	Discography, MBB	Disco, MBB, SIJ	Discography
Exclusion	Cobb>20, Modic 3, spondy, MME>30, BMI 41, protrusion 5mm or extrusion	Cobb >15, >60 mo pain, spondy grade2, disc extrusion >2x disc height, Modic 3, osteoporosis, MME >75,	Cobb>20, Modic 3, spondy grade 2, MME>60, BMI 36, osteoporosis, extrusion, wide fissure protrusion
Design, randomization (R), control	RCT, double-blind, 2:1 R; sham – needle near disc, no injection	RCT, double-blind, 1:1 R; sham – needle near disc, 2cc saline injected	RCT, 2:1 R, CM control, sham procedure skin puncture
Payment, oversight, IRB	Sponsor, FDA, IRB	Sponsor, FDA, IRB; 2 year crossover	Sponsor, FDA, IRB

RCT = randomized, controlled trial; mP = modified Pfirrmann; All have failed 6 months CM; Facet/SIJ pain ruled out; study screening includes imaging and select diagnostics.

Figure and Table 8.1. Modified Pfirrmann Grading System for Lumbar Disc Degeneration



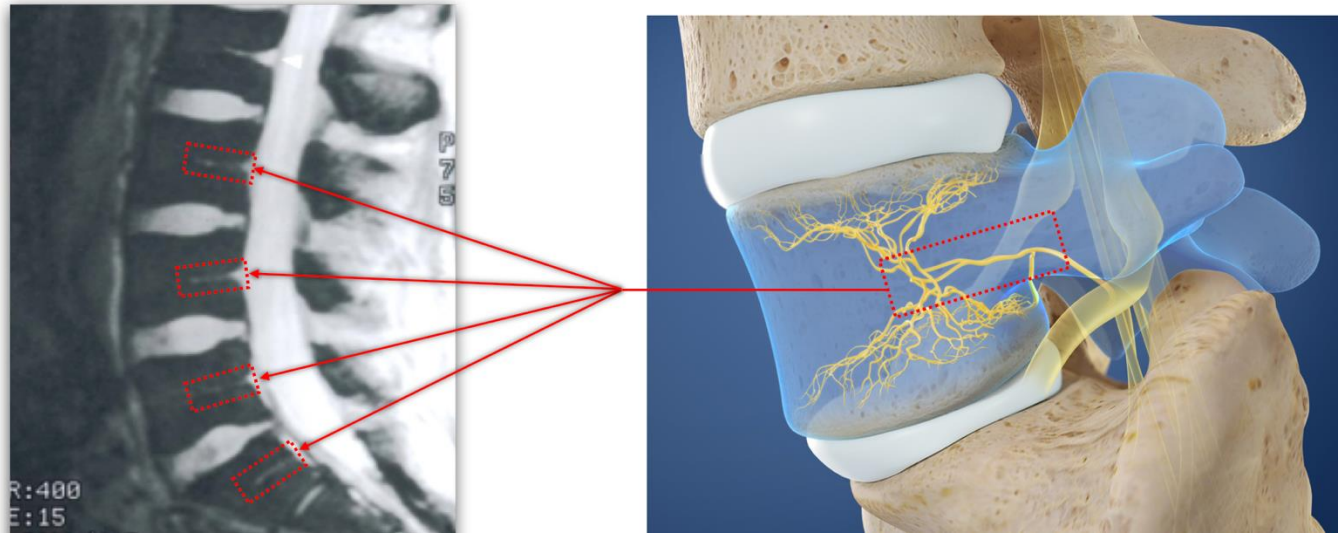
Grade*	Signal From Nucleus and Inner Fibers of Annulus	Distinction Between Inner and Outer Fibers of Annulus at Posterior Aspect of Disc	Height of Disc
1	Uniformly hyperintense, equal to CSF	Distinct	Normal
2	Hyperintense (>presacral fat and <CSF) ± hypointense intranuclear cleft	Distinct	Normal
3	Hyperintense through <presacral fat	Distinct	Normal
4	Mildly hyperintense (slightly >outer fibers of annulus)	Indistinct	Normal
5	Hypointense (= outer fibers of annulus)	Indistinct	Normal
6	Hypointense	Indistinct	<30% reduction in disc height
7	Hypointense	Indistinct	30%-60% reduction in disc height
8	Hypointense	Indistinct	>60% reduction in disc height

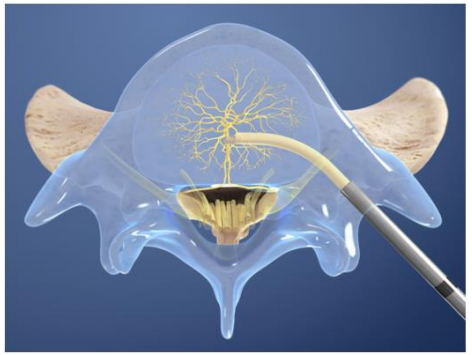
Commercial and Cash Pay Options (Treatment of LBP Due to DDD)

- Basivertebral Nerve Ablation (Intracept)
- Via Disc (intradiscal injection of particulate nucleus pulposus)
- PRP – platelet rich plasma (with A2M and other plasma proteins)

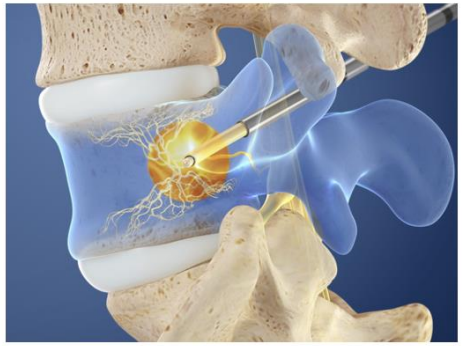
Basivertebral Nerve Ablation – Treatment of Vertebrogenic / Endplate Pain

The Basivertebral Foramen (BVF) and the BVF Terminus are routinely seen on lumbar MR image





2. Create the Channel



4. Ablate the BVN

- Example MRI demonstrating post-op lesions
- Note ideal location of each lesion

Basivertebral Nerve Ablation Summary

Study / Year	Design / Population	Key Outcomes	Long-Term Results & Clinical Significance
SMART Trial (Fischgrund et al.)	Level 1 sham-controlled randomized clinical trial with crossover to single arm at 3 months.	• ODI reduction: 25% (clinically meaningful; MCID = 10 points) • 12 mo: 64% ≥ 50% pain reduction; 29% pain-free	• 24 mo follow-up: ODI improved 28.5 points; 72% ≥ 50% pain reduction; 31% pain-free. • Opioid use ↓ 62%, steroid injections nearly eliminated. • Durable, clinically significant benefit vs sham through 2 years.
INTRACEPT Trial (Smuck et al.)	Level 1 prospective randomized control trial comparing BVN ablation vs standard care; n = 140.	• BVN ablation group had significantly greater reduction in both ODI and VAS scores vs standard care. • Benefits at all time points through 12 months.	• Confirms reproducibility across independent cohort. • Validates superiority over conservative therapy within 1 year.
McCormick et al. Long-Term Pooled Analysis (2022)	Pooled 3 prospective trials (mean follow-up 5.6 years).	• VAS reduction: mean 4.3 points. • ODI reduction: mean 28 points. • 32% pain-free, 72.7% overall improvement. • 65% discontinued opioids, 58% fewer injections.	• 13% required further treatment at index level; 6% underwent lumbar fusion. • No serious device- or procedure-related adverse events through 5 years. • Confirms durable, long-term efficacy and safety.

Summary of Evidence Strength – BVN RFA (Intracept)

- Multiple Level 1 RCTs (SMART and INTRACEPT) demonstrate statistically significant and clinically meaningful improvements in disability (ODI) and pain (VAS) versus sham or standard care.
- Durability of benefit shown up to 5–6 years with sustained functional improvement, decreased opioid dependence, and reduced need for injections or surgery.
- ODI improvements consistently exceed MCID (≥ 10 points), confirming real-world functional recovery.
- Safety profile: No serious device- or procedure-related adverse events reported through long-term follow-up.

ViaDisc NP – Injected Donor Nucleus Pulposus

- Vivex Biologics, Inc. (Vivex.com) (https://viadiscnp.com)
  - Supplemental Nucleus Pulposus Allograft in Patients with Lumbar Discogenic Pain: Evaluation of Clinical Outcomes and Quality of Life in Medicare Beneficiaries (6 months)
  - Azeem et al. 2025
  - Age65+; n=21; 82% with significant reduction in pain, 65% reached 3/10 or less; 68% with significant improvement in function
  - Durability of Supplemental Nucleus Pulposus Allograft in Patients with Lumbar Discogenic Pain (24 months)
  - Costandi et al. 2025
  - Mean age 44; n=28; 64% with significant reduction in pain; 73% with significant improvement in function

PRP and Plasma Protein Concentrate (A2M, etc.) Intradiscal Injection

- There have been recent advancements in our knowledge of the regenerative/anabolic and anti-inflammatory effects of PRP and key plasma proteins and how to optimally concentrate them
- Lumbar Intradiskal Platelet-Rich Plasma (PRP) Injections: A Prospective, Double-Blind, Randomized Controlled Study
  - Tuakli-Wosornu et al. 2016
  - N=47 (29 treatment, 18 control); 8 weeks; Significant drop in pain and improvement in function over control; 56% treatment and 18% control satisfied with outcome at 8 weeks

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