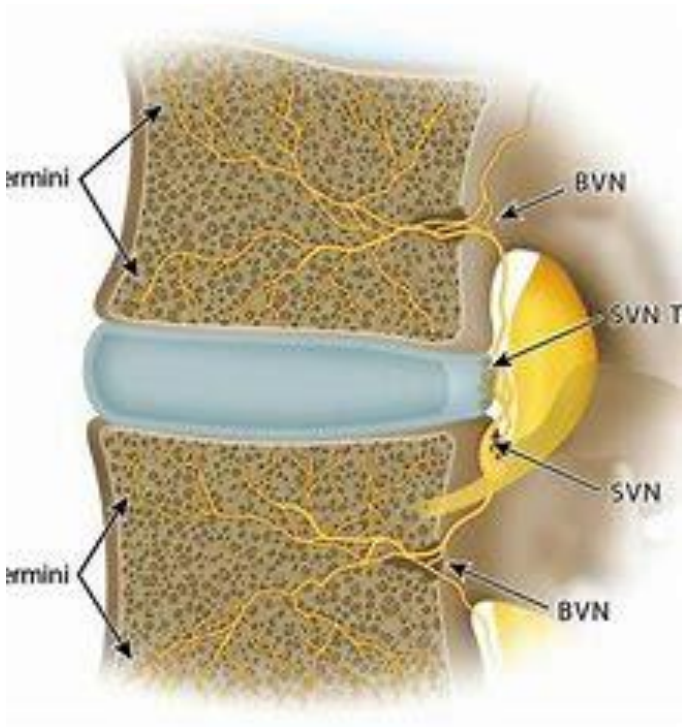
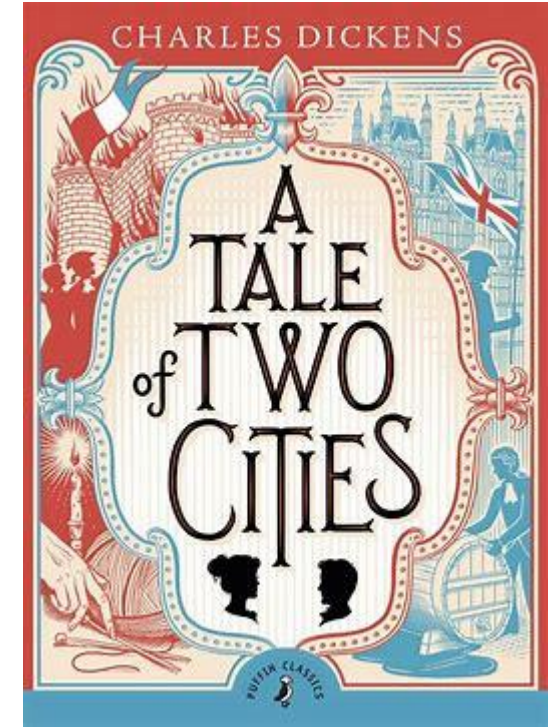




A Tale of Two Pain Conditions

Vertebrogenic and Discogenic Pain



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Objectives

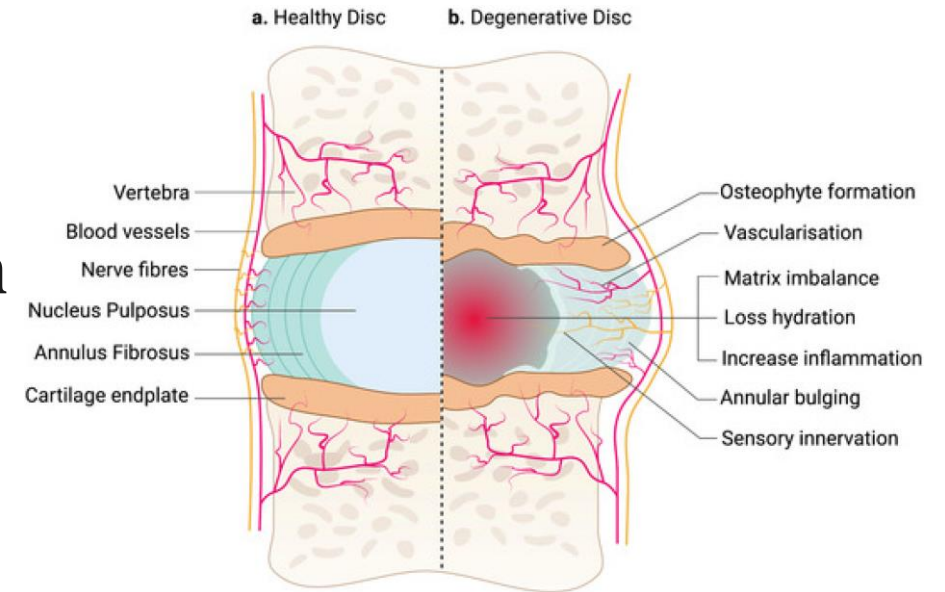
- Apprehend the pathogenesis of discogenic and vertebrogenic pain
- Assess the clinical presentation of both conditions
- Assess the imaging findings of degenerated discs and endplate defects
- Evaluate the utility of diagnostic interventions
- Appraise the evidence for therapeutic options

- Why is it important to identify the etiology?



Discogenic Pain

- Discogenic pain is caused by disc degeneration and internal disc disruption with fissures in the annulus fibrosus and associated nociception via branches of the sinuvertebral nerve .



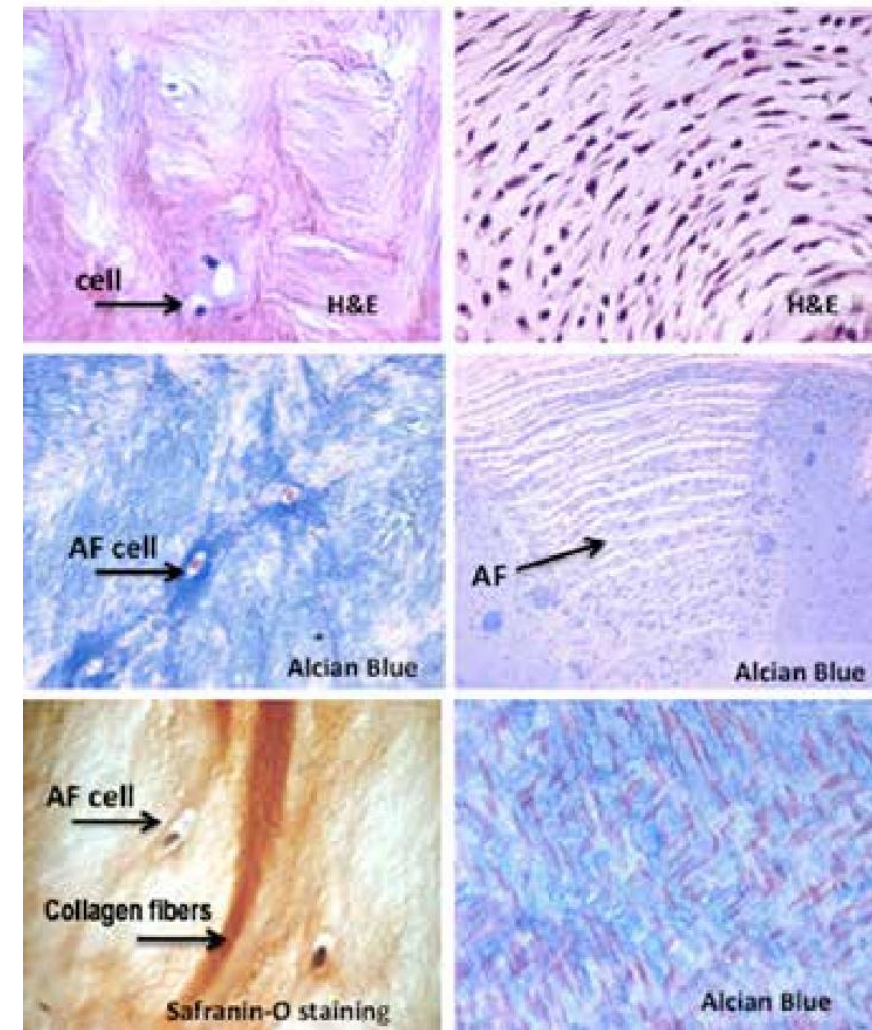
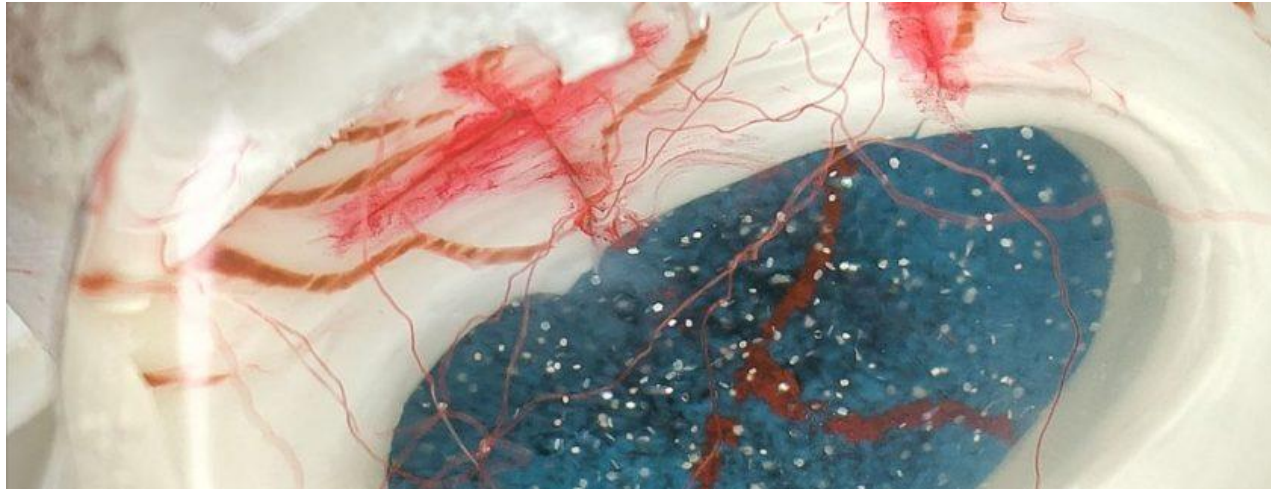
Adams MA, Dolan P. Intervertebral disc degeneration: Evidence for two distinct phenotypes. J Anat 2012;221(6):497–506.

de Schepper EIT, Damen J, van Meurs JBJ, et al. The association between lumbar disc degeneration and low back pain: The influence of age, gender, and individual radiographic features. Spine (Phila Pa 1976) 2010;35(5):531–6.

Cheung KMC, Karppinen J, Chan D, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three indiv Spine (Phila Pa 1976) 2009;34(9):934–40.

Videman T, Battié MC, Gibbons LE, Maravilla K, Manninen H, Kaprio J.. Associations between back pain history and lumbar MRI findings. Spine (Phila Pa 1976) 2003;28 8.





- It was thought that neurovascular ingrowth penetrated into annular fissures, leading to increased sensitivity and nociception via the sinuvertebral nerve .

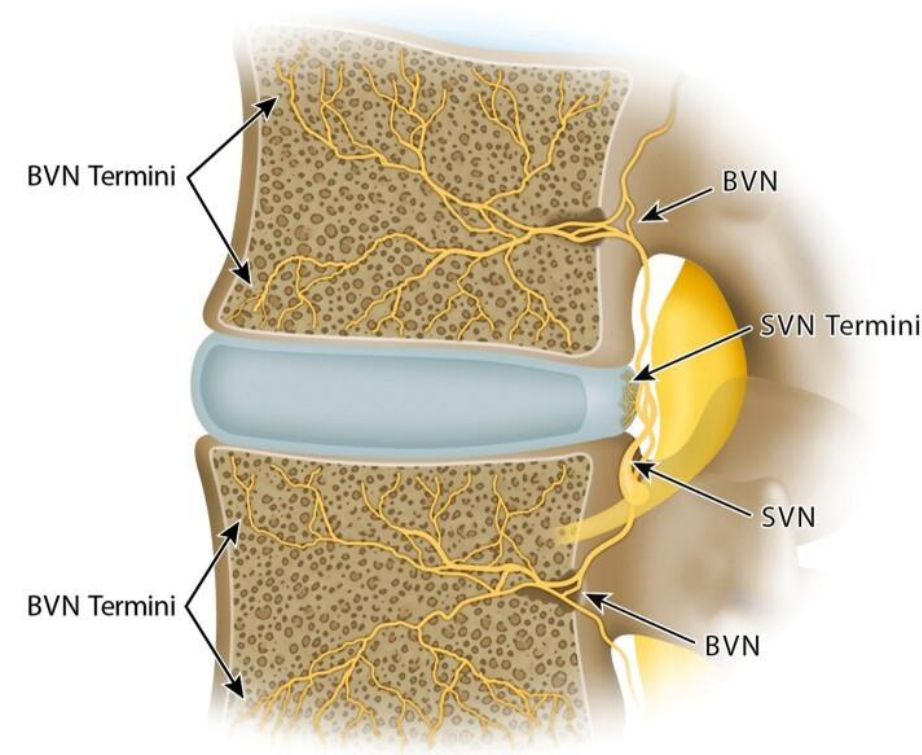
Ohtori S, Miyagi M, Inoue G.. Sensory nerve ingrowth, cytokines, and instability of discogenic low back pain: A review. Spine Surg Relat Res 2018;2(1):11–7.

Freemont AJ, Peacock TE, Goupille P, Hoyland JA, O'Brien J, Jayson MIV.. Nerve ingrowth into diseased intervertebral disc in chronic back pain. Lancet 1997;350(9072

Fields AJ, Liebenberg EC, Lotz JC.. Innervation of pathologies in the lumbar vertebral end plate and intervertebral disc. Spine J 2014;14(3):513–21.

Basivertebral Nerve

- In the late 1990s, **Heggeness et al** reported that vertebral bodies were richly vascularized and innervated by nociceptors that traced back to the basivertebral nerve.
- BVN is a branch of the sinuvertebral nerve (SVN) that enters the vertebral body through the foramen in its posterior wall, then it arborizes to innervate the vertebral endplates



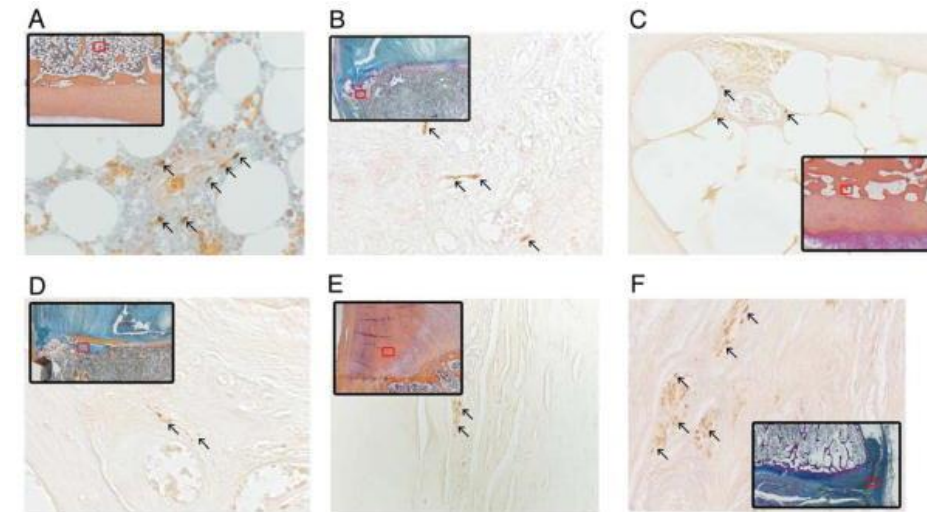
Antonacci MD, Mody DR, Heggeness MH.. Innervation of the human vertebral body. J Spinal Disord 1998;11(6):526-31.

Bailey JF, Liebenberg E, Degmetich S, Lotz JC.. Innervation patterns of PGP 9.5-positive nerve fibers within the human lumbar vertebra. J Anat 2011;218(3):263-70.



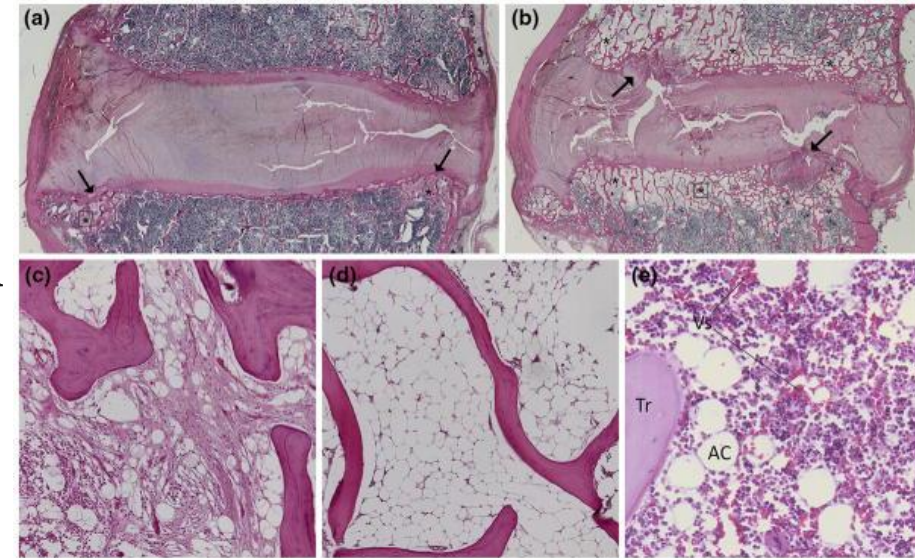
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- Histomorphology of human vertebral bodies demonstrated **endplate nociceptor densification** in areas associated with increased disc degeneration.
- Only **30%** of annular tears in degenerated discs had pathologic neural ingrowth, compared with **90%** of adjacent endplates (which were twice as densely innervated).



Fields AJ, Liebenberg EC, Lotz JC.. Innervation of pathologies in the lumbar vertebral end plate and intervertebral disc. Spine J 2014;14(3):513–21.

- This distinction between annular and endplate innervation is likely due to differences in nerve ingrowth potential.
- For the annulus, nerve ingrowth is inhibited by :
 - Physical pressure
 - Lack of proteoglycans
- Whereas nerves can easily proliferate in fibrovascular bone marrow adjacent to sites of endplate damage.



Discovertebral Complex

- Immunohistochemical studies of the BVN have demonstrated immunoreactivity to S-100, substance-P, and PGP 9.5 further supporting the **BVN's role in nociceptive innervation**.
- Accumulated damage to the discovertebral complex may result in chemical and mechanical sensitization of **endplate nociceptors**.

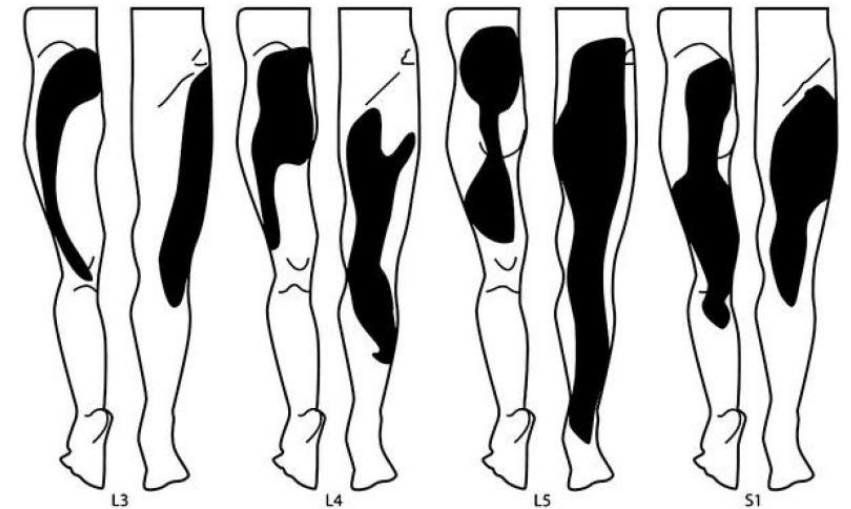
Dudli S, Fields AJ, Samartzis D, Karppinen J, Lotz JC.. Pathobiology of modic changes. Eur Spine J 2016;25(11):3723–34.

Degmetich S, Bailey JF, Liebenberg E, Lotz JC.. Neural innervation patterns in the sacral vertebral body. Eur Spine J 2016;25(6):1932–8.

Lotz JC, Fields AJ, Liebenberg EC.. The role of the vertebral end plate in low back pain. Glob Spine J 2013;3(3):153–63.

Clinical Presentation

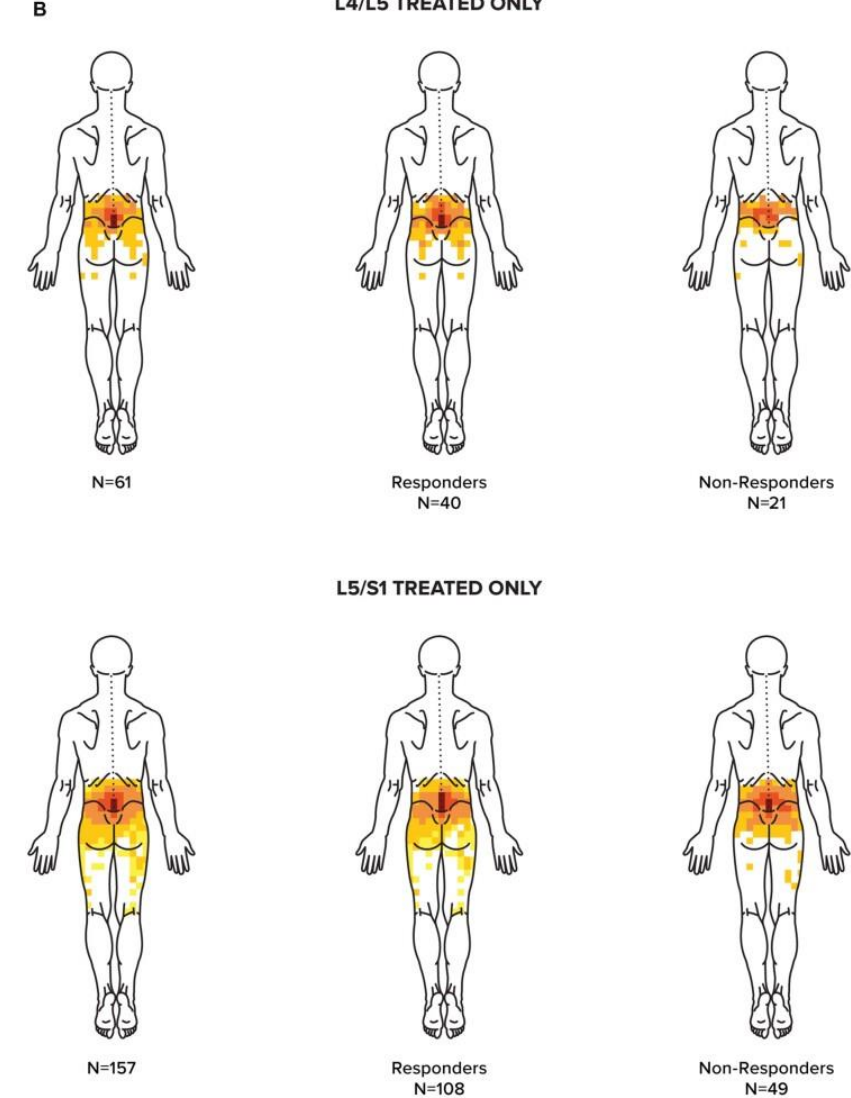
- The clinical diagnosis of lumbar discogenic disease is characterized by axial midline low back pain, sitting intolerance, pain with flexion, positive provocation with sustained hip flexion, absence of motor/sensor/reflex change.
- Although it is localized to the low back, it can also be coupled with referred pain to the lower extremities, usually above the knees in a non-dermatomal distribution.



Bogduk N. On the definitions and physiology of back pain, referred pain, and radicular pain. *Pain*. 2009;147:17–19. doi: 10.1016/j.pain.2009.08.020. [DOI] [PubMed] [Google Scholar]
DePalma M.J., Ketchum J.M., Trussell B.S., Saullo T.R., Slipman C.W. Does the Location of Low Back Pain Predict Its Source? *PMR*. 2011;3:33–39. doi: 10.1016/j.pmrj.2010.09.006. [DOI] [PubMed] [Google Scholar]
O'Neill C.W., Kurgansky M.E., Derby R., Ryan D.P. Disc Stimulation and Patterns of Referred Pain. *Spine*. 2002;27:2776–2781. doi: 10.1097/00007632-200212150-00007. [DOI] [PubMed] [Google Scholar]
Stynes S., Konstantinou K., Dunn K.M. Classification of patients with low back-related leg pain: A systematic review. *BMC Musculoskelet. Disord*. 2016;17:1–19. doi: 10.1186/s12891-016-1074-z. [DOI] [PMC free article] [PubMed] [Google Scholar]
Stynes S., Konstantinou K., Dunn K.M., Lewis M., Hay E.M. Reliability among clinicians diagnosing low back-related leg pain. *Eur. Spine J*. 2015;25:2734–2740. doi: 10.1007/s00586-015-4359-2. [DOI] [PubMed] [Google Scholar]

Clinical Presentation

- In studies that use a treatment response to BVN RFA as a proxy for a “true” diagnosis of vertebrogenic pain, vertebrogenic pain at the L3–S1 levels appears to present as **mid-line low lumbar pain** with minimal cephalad referral but potentially some referral to the paraspinal and/or gluteal regions .



McCormick ZL, Sperry BA, , Boody BS, et al, . Pain location and exacerbating activities associated with treatment success following basivertebral nerve ablation: An aggregated cohort study of multicenter prospective clinical trial data. Pain Med 2022



Clinical Presentation

- Analysis of pain patterns of those successfully treated with BVN RFA showed that **no patients reported pain below the knee**, suggesting that pain referral from endplates does not produce more distal radiation .
- However, this pattern could also be **artifactual** since many candidates for BVN RFA might have been excluded if they had significant symptoms concerning for radicular pain.

McCormick ZL, Sperry BA, , Boody BS, et al, . Pain location and exacerbating activities associated with treatment success following basivertebral nerve ablation: An aggregated cohort study of multicenter prospective clinical trial data. Pain Med 2022

Clinical Presentation

- It is possible that patients with vertebrogenic pain experience **referral into the lower leg**, but this should only be entertained after exclusion of other potential sources of lower leg pain.
- This pain pattern mirrors what was previously described as axial “discogenic” back pain

Clinical Presentation

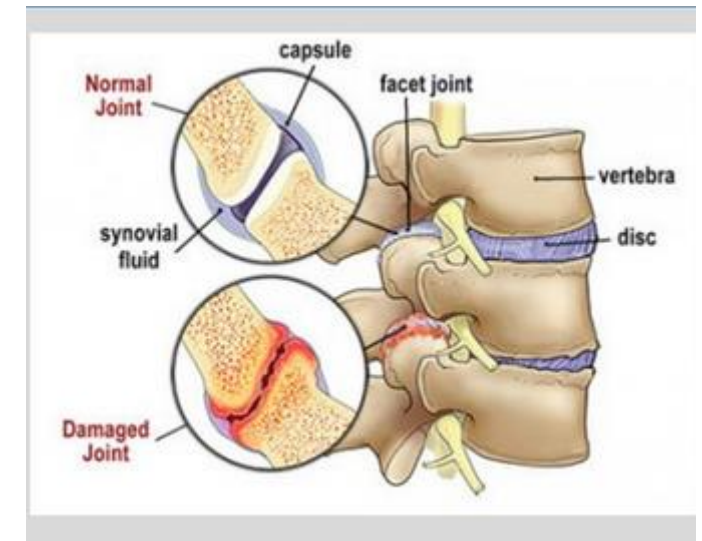
- Compared to CLBP controls, patients with CLBP and **Modic type 1** changes (MC1) are more likely to report night pain, prolonged morning stiffness, and pain greatest in the morning .
- Patients with presumed vertebrogenic LBP frequently report pain exacerbation with activity and absence of pain exacerbation during lumbar extension.

Bailly F, Maigne J-Y, Genevay S, et al. Inflammatory pain pattern and pain with lumbar extension associated with Modic 1 changes on MRI: A prospective case-control study of 120 patients. Eur Spine J 2014;23(3):47.



Clinical Presentation

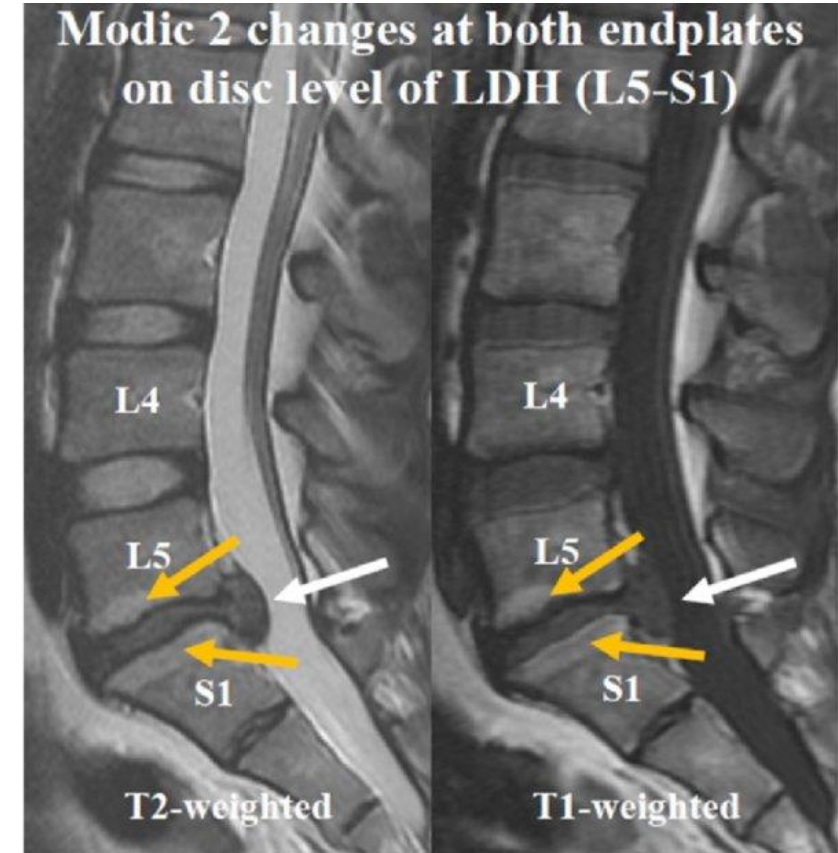
- Coexisting facet joint-related pain, with nociception via the medial branch nerves is also possible, particularly given the frequency of disc **height loss** in patients with vertebrogenic and discogenic pain, which results in **greater facet joint loading** at the spinal motion segment.



Yong-Hing K, Kirkaldy-Willis WH.. The pathophysiology of degenerative disease of the lumbar spine. Orthop Clin North Am 1983;14(3):491–504.

Imaging

- Modic type 1 changes (MC1) and endplate defects commonly co-occur in patients with **lumbar disc herniation and associated radiculopathy**.
- In patients with **Lumbar Spine Stenosis**, endplate defects are a stronger predictor of axial LBP intensity than the severity of the spinal stenosis



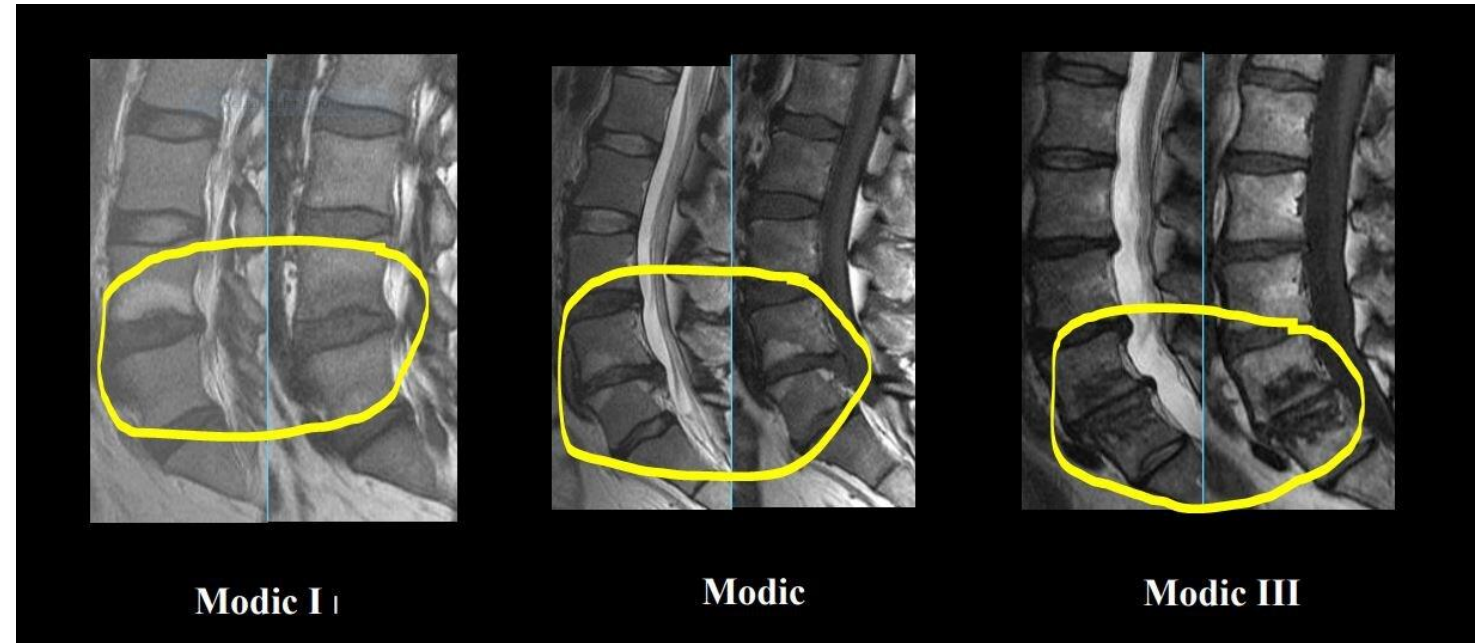
Jensen TS, Kjaer P, Korsholm L, et al. Predictors of new vertebral endplate signal (Modic) changes in the general population. Eur Spine J 2010;19(1):129–35.

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Minetama M, Kawakami M, Teraguchi M, et al. Endplate defects, not the severity of spinal stenosis, contribute to low back pain in patients with lumbar spinal stenosis. Spine J 2021;22(3):370–8.



Imaging



- A correlation between vertebral endplate pathology on MRI and LBP was first suggested in **1988 by Modic et al.** who found MRI changes adjacent to vertebral endplates defects in individuals with chronic LBP
- Inflammation and bone marrow changes surrounding endplate defects are visible as Modic changes (MC) on MRI.
- Type 1 Modic changes are associated with **bone marrow edema and hypervascularity** of the vertebral body displayed as decreased signal intensity on T1-weighted images, and increased signal intensity on T2-weighted images.
- Type 2 Modic changes (MC2) are associated with **fatty replacement of the red bone marrow** in the vertebral body and display as increased signal intensity on T1-weighted images and on T2-weighted images

Modic Changes and Back Pain

- Although MC lesions may be observed in up to 12.1% of asymptomatic individuals, there remains an overall strong association between their presence and CLBP .
- Weishaupt et al. reported 88–100% specificity to CLBP in individuals depending on the extent of MC1 and MC2.
- Kuisma et al. found a 2.28 odds ratio for the presence of Modic changes at L5-S1 in individuals with CLBP.
- This association is particularly strong for MC1; a meta-analysis found an **odds ratio of 4.01** for the presence of MC1 and CLBP, while only **3% of asymptomatic** subjects exhibited MC1.

Kuisma M, Karppinen J, Niinimäki J, et al. Modic changes in endplates of lumbar vertebral bodies: Prevalence and association with low back and sciatic pain among middle-aged male workers. Spine (Phila Pa 1976) 2007;32(10):1116–22.

Brinjikji W, Diehn FE, Jarvik JG, et al. MRI findings of disc degeneration are more prevalent in adults with low back pain than in asymptomatic controls: A systematic review and meta-analysis. Am J Neuroradiol 2015;36(12):2394–9.

Lawan A, Crites Videman J, Battié MC.. The association between vertebral endplate structural defects and back pain: A systematic review and meta-analysis. E Spine J 2021;30(9):2531–48.

McCormick ZL, Conger A, Hirsch J, et al. Magnetic resonance imaging characteristics associated with a success treatment outcome after basivertebral nerve ablation: An aggregated cohort study of multicenter prospective clinical trial data. Pain Med 2022.



Imaging for Degenerated Discs



I II III IV V

	I	II	III	IV	V
Anterior AF	84.3	62.3	63.9	51.1	53.1
NP	138	113.8	76	50.7	54.7
Posterior AF	80.2	61.1	59.3	51.9	52.3

Grade	Structure	Distinction of nucleus and annulus	Signal Intensity	Height of intervertebral disc
I	Homogenous, bright white	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
II	Inhomogenous with or without horizontal bands	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
III	Inhomogenous, grey	Unclear	Intermediate	Normal to slightly decreased
IV	Inhomogenous, grey to black	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Inhomogenous, black	Lost	Hypointense	Collapsed disc space

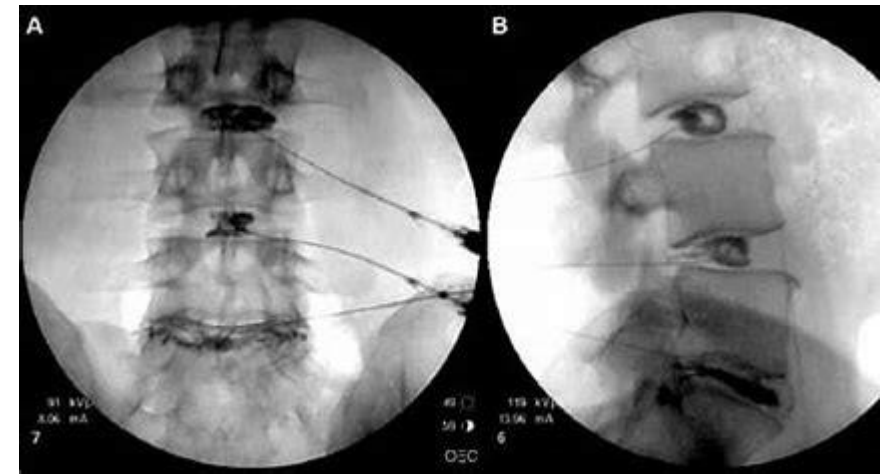
*Adapted from Pfirrmann et al. (2001) (8)



Interventional Diagnosis

- Given the complex and overlapping pain patterns of various structures, clinicians have often utilized diagnostic/prognostic injections.
- BVN block?
- Transpedicular
- Anesthetizing the track
- Sedation
- High success rate with BVN?

Interventional Diagnosis



- Discography?
- **Disc pressurization** can potentially provoke nociception transmitted by both the annulus and the sinuvertebral nerve as well as the endplate and the basivertebral nerve, as pressurization results in stretch of annulus fibrosis fibers as well as endplate deflection.
- The probability of reproducing patient symptoms during **provocation discography** is significantly greater in patients with endplate damage.

McCormick ZL, DeFrancesch F, Loomba V, Moradian M, Bathina R, Rappard G.. Diagnostic value, prognostic value, and safety of provocation discography. Pain Med 2018;19(1):3–8.

Wolfer LR, Derby R, Lee J-E, Lee S-H.. Systematic review of lumbar provocation discography in asymptomatic subjects with a meta-analysis of false-positive rates. Pain Physician 2008;4;11(4):513–38.

Heggeness MH, Doherty BJ.. Discography causes end plate deflection. Spine (Phila Pa 1976) 1993;18(8):1050–3.

Bartynski WS, Agarwal V, Khan AS, Bandos AI.. Motion characteristics of the functional spinal unit during lumbar disc injection (discography) including comparison between normal and degenerative levels. Pain Med 2021;22(8):1735–42.



Interventional Diagnosis

- By definition, discs with internal derangement responsible for clinically meaningful CLBP produce such pain at <50 psi.
- Positive and negative responses to **intradiscal anesthetic injection** (i.e., functional anesthetic discography (FAD) or “discoblock”) are strongly correlated with the respective presence and absence of MC1 and MC2.

Yoganandan N, Larson SJ, Pintar FA, Gallagher M, Reinartz J, Droese K.. Intravertebral pressure changes caused by spinal microtrauma. Neurosurgery 1994;35(3):415–21; discussion 421.

Putzier M, Streitparth F, Hartwig T, Perka CF, Hoff EK, Strube P.. Can discoblock replace discography for identifying painful degenerated discs? Eur J Radiol 2013;82(9):1463–70.

Alamin TF, Kim MJ, Agarwal V.. Provocative lumbar discography versus functional anesthetic discography: A comparison of the results of two different diagnostic techniques in 52 patients with chronic low back pain. Spine J 2011;11(8):756–65.



Rule out Diagnosis

- The diagnosis of vertebrogenic LBP should be strongly suspected when MRI demonstrates the presence of Modic 1 or 2 changes, with or without endplate defects.
- Clinicians are encouraged to apply evidenced based diagnostic tools to evaluate for alternative or comorbid spinal pain generators when suspected; this may include lumbar MBBs and/or intra-articular SIJ injections to evaluate for alternative causes of LBP depending on the clinical presentation.
- Included in the LCD.

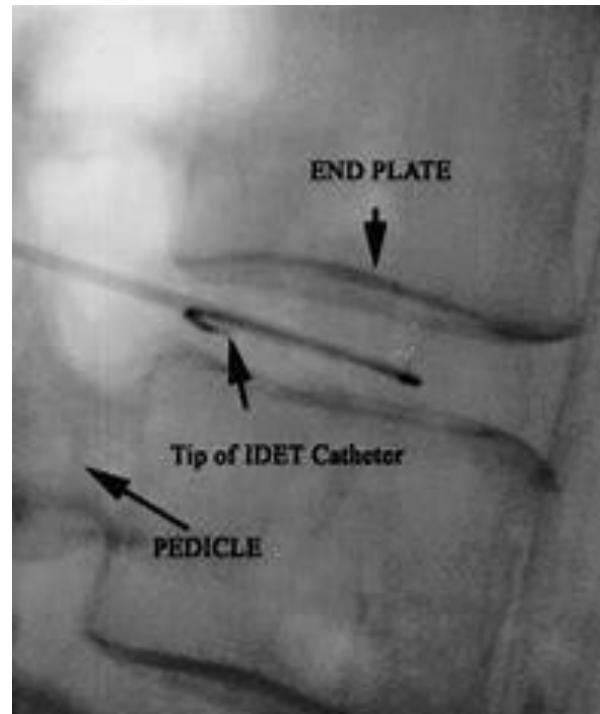
Treatment

- The current evidence supporting intraosseous BVN RFA:
- Two large RCTs comparing BVN RFA to sham and “standard care” and from four single group cohort studies, all demonstrating similar benefits.
- Each study used transpedicular access and bipolar RFA to target the BVN terminus at motion segments from L3 to S1 with MC1 and/or MC2.
- Single-arm meta-analysis of outcomes after intraosseous BVN RFA demonstrates that 64% (95% confidence interval [CI] 43–82%) and 75% (95% CI 63–85%) of participants report $\geq 50\%$ pain reduction and ≥ 15 -point Oswestry Disability Index (ODI) improvement at 12 months.
- These improvements appear durable in the two studies that reported outcomes at **2 years and 5 years**.

De Vivo AE, D'Agostino G, D'Anna G, et al. Intra-osseous basivertebral nerve radiofrequency ablation (BVA) for the treatment of vertebrogenic chronic low back pain. *Neuroradiology* 2021;63(5):809–15. [DOI] [PubMed] [Google Scholar]
Truumees E, Macadaeg K, Pena E, et al. A prospective, open-label, single-arm, multi-center study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain. *Eur Spine J* 2019;28(7):1594–602. [DOI] [PubMed] [Google Scholar]
Khalil JG, Smuck M, Koreckij T, et al. A prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain. *Spine J* 2019;19(10):1620–32. [DOI] [PubMed] [Google Scholar]
Fischchenko IV, Garmish AR, Kravchuk LD, Saponenko AI, Clinic CM. Radiofrequency ablation of the basivertebral nerve in the treatment of chronic low back pain: Analysis of a small clinical series. *Hir Pozvonochnika* 2021;18(3):61–7. [Google Scholar]
70. Markman JD, Rhyne AL, Sasso RC, et al. Association between opioid use and patient-reported outcomes in a randomized trial evaluating basivertebral nerve ablation for the relief of chronic low back pain. *Neurosurgery* 2019;86(3):343–7. [DOI] [PubMed] [Google Scholar]
FISCHGRUND JS, RHYNE A, FRANK J, et al. Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 2-year results from a prospective randomized double-blind sham-controlled multicenter study. *Int J Spine Surg* 2019;13(2):110–9. [DOI] [PMC free article] [PubMed] [Google Scholar]
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Fischgrund JS, Rhyne A, Frank J, Sasso R, et al. Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: A prospective randomized double-blind sham-controlled multi-center study. *Eur Spine J* 2018;27(5):1146–56. [DOI] [PubMed] [Google Scholar]
Koreckij T, Kreiner S, Khalil JG, Smuck M, Markman J, Garfin S. North American Spine Society Journal (NASS) Prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 24-Month treatment arm results. *North Am Spine Soc J* 2021;8(October):100089. [DOI] [PMC free article] [PubMed] [Google Scholar]
Smuck M, Khalil J, Barrette K, et al. Prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 12-Month results. *Reg Anesth Pain Med* 2021;46(8):683–93. [DOI] [PMC free article] [PubMed] [Google Scholar]
Macadaeg K, Truumees E, Boody B, et al. A prospective, single arm study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 12-Month results. *N Am Spine Soc J* 2020;3(September):100030. [DOI] [PMC free article] [PubMed] [Google Scholar]

Intradiscal Therapies

- Clinical Trials
- Poor Evidence
- Ablative
 - IDET
 - Biaculooplasty
- Regenerative
 - Allograft
 - Stem cells



Pilot Study

e Nucleus Pulposus Allograft Supplementation in Patients with Lumbar Discogenic Pain: Initial 6-month Outcomes from a Prospective Clinical Pilot Study

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Conclusion

- The neural growth indicates the important role of endplates in nociception
- There is a significant overlapping in the clinical presentation of both entities
- There is no gold standard diagnostic tools to aid the diagnosis
- There is robust evidence for I-BVN RFA.
- There is growing interest in regenerative medicine to treat discogenic pain