International Journal of Spine Surgery, Vol. 00, No. 0, 2025, pp. 1–6
https://doi.org/10.14444/8808

Safety Evaluation of Intradiscal Delivery of Nucleus Pulposus Allograft for Lumbar Discogenic Pain

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ABSTRACT

Background: Persistent concerns remain about the deleterious pathological effects of minimally invasive transannular puncture, such as occurs during discography and therapeutic intradiscal procedures. The objective of this study was to estimate the safety profile associated with fluoroscopically guided intradiscal delivery of nucleus pulposus (NP) allograft under clinical trial and real-world conditions.

Methods: This was a retrospective pooled analysis of adverse events (AEs) and clinical complaints captured from 4 different treatment populations (n = 392) and a database of commercial cases (n = 19,392 discs treated) with lumbar discogenic pain who underwent minimally invasive intradiscal NP allograft supplementation. All AEs were graded for severity as mild, moderate, or severe, and relatedness was judged as possibly, probably, or definitely. All serious AEs were adjudicated for outcome.

Results: There were 51 total AEs reported across all 4 clinical cohorts, and 6 AEs (12%) were judged to be related to the NP allograft product and the intradiscal procedure, with an additional 4 AEs (8%) related solely to the intradiscal procedure. None of the AEs was associated with infection (ie, discitis), neurological compromise, or escalation to surgical treatment. The product-attributable serious AE incidence was 0.26% (1/392). Of the commercial cases (n = 19,392 discs treated), no clinical AEs were reported from this cohort, with only 101 device complaints (0.521%) related primarily to delivery interface or packaging integrity.

Conclusions: Intradiscal NP allograft supplementation for symptomatic degenerative disc disease demonstrates a favorable safety profile. These findings serve to temper concerns about the risk of disc complications and accelerated degeneration following transannular puncture.

Clinical Relevance: These findings validate that the NP allograft product and procedure have an exemplary safety profile. As a microinvasive, motion-preserving intervention, this procedure has the potential to bridge the therapeutic gap between conservative care and invasive spine surgery for patients suffering from discogenic back pain.

Level of Evidence: 4.

Focus Issue Article

Keywords: degenerative disc disease, nucleus pulposus, allograft, intradiscal, discogenic pain, safety, adverse events, complications

INTRODUCTION

Lumbar discogenic pain is a leading cause of chronic low back disability and is associated with persistent treatment challenges due to progressive disc degeneration.[1,2] Loss of nucleus pulposus (NP) hydration, cellular density, and extracellular matrix integrity are established pathophysiological drivers of nociception.[3,4] For patients suffering from chronic symptomatic disc disease, a large treatment gap exists between nonsurgical conservative care measures and surgical interventions. Indeed, operative procedures such as spinal fusion and disc arthroplasty permanently alter the structural anatomy of the vertebral motion segment.[5] Effective strategies to restore intradiscal homeostasis and maintain the structural and functional integrity of the intervertebral disc remain limited.[6] Minimally invasive intradiscal strategies that address degenerative mechanisms directly have therefore emerged as a clinically rational pathway.[7]

Despite the potential utility of intradiscal delivery of therapeutic agents into the NP, concerns persist regarding the safety of access to the NP via annular puncture. Preclinical work by Elliott et al[8] demonstrated radiographic and histological evidence of degeneration following needle access in an animal intervertebral disc model. Moreover, much-touted clinical research from Carragee et al noted postdiscography reductions in disc height and T2 signal, outcomes that reflect possible

iatrogenic compromise of disc structure, had a profound effect on the perceived safety of not only discography but minimally invasive intradiscal access in general.[9–11] These findings have served to implicate the procedural route itself as a contributor to degeneration.

However, more contemporary safety analyses dispute that injection alone drives structural decline. Pinto et al[12] reported no postinjection degeneration or serious complications in patients receiving fluoroscopically guided intradiscal delivery using a modern technique. A narrative review of intradiscal technique likewise found no increased rates of collapse, herniation, or neurological deterioration following biological and nonbiological disc injections.[13]

A retrospective cohort study of 200 patients undergoing lumbar total disc replacement with ≥10-year follow-up found no increased rate of reoperation for disc-related pain among levels that had previously undergone discography.[14] Across 251 injected discs and 124 noninjected levels, the reoperation rate was statistically similar (10.8% vs 8.1%, $P > 0.40$). Logistic regression confirmed that reoperation risk was driven by discogram result, specifically abnormal response, rather than the act of discography itself. These findings reinforce the procedural safety of discographic injection when performed on structurally normal discs.

The current study evaluates adverse events (AEs) and safety outcomes following intradiscal administration of VIA Disc NP, a human NP allograft, in patients with chronic lumbar discogenic pain associated with degenerative disc disease (DDD). Clinical complaints, procedural complications, and postinjection events were tracked across a pooled cohort. The objective was to determine whether fluoroscopy-guided NP allograft injection compromises patient safety or treatment tolerability under clinical trial and real-world conditions.

METHODS

This retrospective pooled analysis evaluated AEs and clinical complaints across 4 different treatment populations and a database of cases performed in the commercial setting, respectively. All patients were treated with a single intradiscal administration of NP allograft (VIA Disc NP, Vivex Biologics, Inc., Miami, FL, USA) according to the manufacturer's instructions for use.

The objective of the present analysis was to evaluate whether minimally invasive intradiscal administration of NP allograft via a 20-gauge cannula that passes through the annulus and into the center of the NP results in adverse procedural outcomes or product-related safety concerns in both clinical trial and real-world use.

The analysis of AEs included

- **Pilot study 1** ($n = 28$): patients aged 19–70 years.
- **Pilot study 2** ($n = 21$): patients aged ≥65 years.
- **Ongoing prospective registry** ($n = 291$): commercially treated patients.
- **Ongoing randomized clinical trial** ($n = 52$).

These studies formed a composite early-phase safety dataset used for pooled analysis ($n = 392$).

All AEs were evaluated by the clinical site investigator and an independent medical monitor and categorized using Medical Dictionary for Regulatory Activities preferred terms and graded for severity as mild, moderate, or severe. Relatedness was assessed for both the NP allograft and the intradiscal injection procedure as possibly, probably, or definitely. All serious adverse events (SAEs) were adjudicated for outcome and monitored in accordance with Good Clinical Practice guidelines. Documentation was submitted to the overseeing institutional review board for each site.

Clinical complaints were tracked separately from 19,392 intradiscal NP allograft procedures performed in the commercial setting from 2021 through April 2025. These reports were categorized by complaint type, including delivery system failure, mechanism of action error, contamination, and product integrity. Complaints were stratified by calendar year and tabulated by frequency to detect deviations in structural preservation and injection reproducibility.

The prevalence of AEs was calculated for the pooled dataset and separately by study. Subgroup analyses were performed to report incidence stratified by severity, causality, and outcome. Clinical complaint rates were computed overall and by year. Aggregated data were used to support trend tracking and evaluate postprocedural tolerability across stratified categories to support ongoing surveillance initiatives.

The observational components of this analysis were consistent with post-market surveillance guidance and derived from studies registered in accordance with institutional review board protocol approvals. The Table summarizes a range of practical considerations and procedural best practices for intradiscal NP allograft delivery.

RESULTS

There were 16 AEs reported in the pilot study involving patients aged 19–70 years, 7 AEs in the pilot study involving patients aged ≥65 years, 15 AEs in the registry, and 13 AEs in the randomized trial with mean lengths

Table. Practical considerations for intradiscal NP allograft injection (lumbar).

Consideration	Key Points (NP allograft specific)
Target/indication	• Symptomatic lumbar discogenic pain with degenerative disc disease candidates; intact annulus without substantial annulus disruption. • Not for disc herniation with radiculopathy or outer annular compromise (risk of pressure-exacerbated fissure). • Based on study framing and Delphi algorithm.
Access and gauge	• Trans-Kambin posterolateral approach under fluoroscopy to the center of the NP. • 20-gauge cannula recommended (per study protocol/IFU).
Imaging guidance	• Fluoroscopy: mandatory for level confirmation, trajectory, and end-plate alignment. • CT only if complex anatomy requires it; ultrasonography not suitable for deep lumbar NP targeting.
Handling characteristics (cannula/length/tips)	• Typical cannula/needle working lengths 3.5–5 in; ≥6 in may be required in obesity/deep targets. • Use a stylet to minimize tissue coring; maintain coaxial control to avoid annular scuffing.
Injectate preparation and delivery	• Prepare and deliver per manufacturer IFU (NP allograft mix and delivery interface). • Advance cannula just into central NP; slow, steady injection; stop if unexpected resistance or pain spike. • Maintain closed system sterility; purge air per IFU to minimize clogging.
Procedural safety guardrails	• Maintain strict sterility (skin prep, drape, and sterile field). • Confirm intradiscal position using biplanar fluoroscopy before injection. • Avoid high-pressure injection; no disc pressurization beyond patient tolerance. • Utilize preprocedure intravenous antibiotics.
Contraindications/precautions	• Active local/systemic infection; untreated coagulopathy/anticoagulation without periprocedural plan; allergy to product components. • Structural exclusions: large radial fissures to periphery, extrusion/sequestration, and significant deformity/scoliosis preventing safe access.
Complication profile (observed)	• Across pooled clinical cohorts (n = 392): 51 AEs total; 6 related to product and procedure, 4 procedure only; no discitis, no neurological compromise, no surgical escalation. • SAEs: 11 total; 1 related to product and procedure (product-attributable SAE [0.26%]). All resolved without residual deficit.
Field performance (commercial)	• 19,392 discs treated (2021–April 2025): 0 clinical adverse events reported in this complaints database. • 101 device/handling complaints (0.521%), primarily delivery interface or packaging integrity (eg, mix clogging, mixing-system issues). • No patient harm; issues resolved under Corrective and Preventive Action/Supplier Corrective Action Request.
Postprocedure care	• Routine observation; reinforce activity modification briefly. • Monitor for delayed pain escalation, fever, new radicular signs (low suspicion based on dataset).
Evidence/level	• Retrospective pooled safety analysis (level 4). • Within GRADE logic, favorable safety, low complexity, and a clear therapeutic gap can justify stronger practice recommendations despite level-of-evidence constraints.

Abbreviations: AE, adverse event; CT, computed tomography; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; IFU, instructions for use; NP, nucleus pulposus; SAE, serious adverse event.

of follow-up of 23.4, 5.7, 4.2, and 2.2 months, respectively. In the study of patients aged 19–70, 5 AEs (31%) were classified as mild, 10 AEs (63%) as moderate, and 1 AE (6%) as severe. Five AEs (71%) were classified as mild, and 2 AEs (29%) were moderate in the study of patients aged ≥65 years. Among registry patients, there were 6 mild AEs (40%), 5 moderate AEs (33%), and 4 severe AEs (27%). Finally, in the ongoing randomized trial, 3 AEs (23%) were classified as mild, 8 AEs (62%) as moderate, and 2 AEs (15%) as severe. Of the 51 total AEs reported across all 4 cohorts, 6 AEs (12%) were judged to be related to the NP allograft product and the intradiscal procedure, with an additional 4 AEs (8%) related solely to the intradiscal procedure.

The underlying medical complications associated with both the NP allograft product and the intradiscal procedure consisted of 2 separate patients with low back pain and post procedural pain, as well as single instances of back muscle spasms and thigh pain. The degree of relatedness was judged as "possibly" for 4 of these 6 events for both product and procedure, with 1 event showing definitive relatedness to the product and the procedure, and 1 event with mixed relatedness as "definitely" for the product and "possibly" for the procedure. For the 4 isolated procedure-related AEs, 2 were judged "possibly" and 1 each of "probably" and "definitely" relatedness.

There were 11 SAEs, with 1 related to the allograft product and the intradiscal procedure and 1 related solely to the procedure. All SAEs were adjudicated by the clinical site investigators and the trial medical monitor, and none were associated with infection (ie, discitis), neurological compromise, or escalation to surgical treatment.

Across 19,392 intradiscal NP allograft procedures undertaken commercially from 2021 through 2025, a

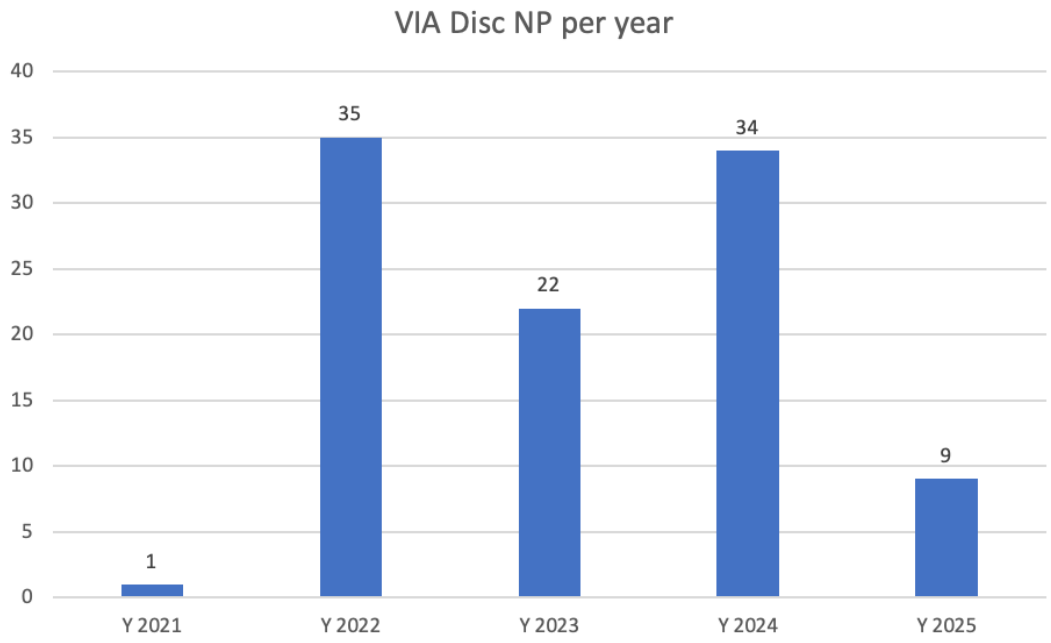

Figure. Frequency of site-reported complaints following 19,392 nucleus pulposus (NP) allograft procedures from 2021 to 2025 (as of May 31, 2025) in the clinical practice setting.

total of 101 complaints were recorded, yielding a complaint rate of 0.521%. The most frequent complaint reason was "mix clogged in needle (delivery failure)" (n = 44), followed by "mixing system malfunction" events (n = 22), and "mixing system cap fell off" (n = 21). Other categories included "contamination" (n = 3), "expired product" (n = 2), and a range of isolated incidents such as "incorrect order No.," "wrong kit," or "seal compromised" (n = 1 each). Mixing system malfunction refers to when the NP allograft product has escaped the green mixing device and is in the outer package.

Complaint frequency varied by year as illustrated in the Figure: 1 in 2021, 35 in 2022, 22 in 2023, 34 in 2024, and 9 in 2025 (as of May 31, 2025). Trends over time showed no escalation or spread in severity. Most complaints were linked to the delivery interface or packaging integrity. All entries were resolved under internal Corrective and Preventive Action and SCAR Supplier Corrective Action Request procedures, and no cases involved patient harm or regulatory escalation.

DISCUSSION

Supplementation of symptomatic lumbar discs with NP allograft demonstrates a safety profile that compares favorably with both historical controls and emerging injectable alternatives. Integrated surveillance across 4 clinical cohorts identified 51 total AEs; only 6 events (12%) were judged to be product related, and just 1 was a serious AE, yielding a product-attributable SAE incidence of 0.26% (1/392) at ≤24 months.

None of the product or procedure-related AEs exhibited clinical signs of discitis, nerve injury, hematoma, or epidural extension—complications typically associated with annular trauma. This absence of puncture-mediated morbidity aligns with the matched-cohort study of McCormick et al[15] showing no accelerated disc degeneration, internal disc disruption, or disc herniation after 7 years of follow-up in patients with symptomatic DDD undergoing low-pressure discography. These convergent findings reinforce that a 20-gauge transannular approach results in negligible structural harm when executed under contemporary technique.[12,15]

All product- or procedure-associated AEs resolved without residual deficit or sequelae, yielding a 100% recovery rate by the final study visit. This outcome indicates that the intradiscal introduction of NP allograft neither perpetuates inflammatory cascades nor provokes delayed neurovascular compromise, features that are critical for intradiscal durability.

The therapeutic rationale underlying puncture safety is further strengthened by the hypothesis that replenishing the degenerating disc with metabolically competent, "healthy" extracellular matrix obviates the microenvironmental triggers of Carragee-style needle-induced degeneration.[9] The injected NP matrix may

promote rehydration, redistribute mechanical loads, and inhibit nociceptive ingrowth—mechanisms that plausibly buffer against puncture-related catabolism.

Another important finding of our study is that site-reported complaints following 19,392 NP allograft procedures performed in clinical practice over the past 5 years yielded a low overall complaint rate of 0.521%. All entries involved packaging integrity or delivery system obstruction; no clinical complaints or patient injuries were reported, underscoring both manufacturing reliability and procedural reproducibility at scale.

Polymeric hydrogels are also under investigation for intradiscal augmentation in cases of symptomatic lumbar DDD.[16] In contrast to NP allograft, intradiscal hydrogel augmentation with HydraFil (PVA/PEG/PVP/barium Sulfate, ReGelTec), for example, may increase the risk of thermally mediated tissue damage and large bore access trauma.[6] Preclinical data confirm collagen denaturation and probable cell death at temperatures >60°C, thresholds transiently exceeded during hydrogel curing.[6] Early feasibility results documented implant displacement or extrusion in 15% of treated discs and an SAE incidence of 25% by 6 months postprocedure.[17] Additionally, case-level evidence has described neurocompressive herniation of extruded hydrogel requiring emergent decompressive laminectomy, reinforcing concerns that 17-gauge access and viscoelastic hydrogel expansion may be associated with annular strain disruption and secondary degeneration.[18]

It should be emphasized that to achieve the procedural safety margins reported herein for intradiscally delivered NP allograft, strict adherence to target disc morphological characteristics should be maintained. Intradiscal delivery of NP allograft should only be undertaken in an intact disc without substantial internal disruption of the annulus.[19] Cases of disc herniation with radiculopathy are not candidates for this procedure, as increased pressure within the NP could exacerbate radial annular fissures extending to and compromising the outer annular wall.

While the current analysis represents level 4 evidence due to its retrospective and pooled design, it is important to consider the broader context of clinical applicability. According to evidence-based frameworks such as GRADE, the strength of a clinical recommendation may exceed the nominal level of evidence when an intervention demonstrates high safety, low cost, technical simplicity, and addresses a meaningful therapeutic gap.[20,21] The NP allograft procedure exemplifies this paradigm: it is microinvasive, motion-preserving, and supplements the native disc without the need for synthetic or permanent structural implants. It has demonstrated an exceedingly low incidence of AEs in both clinical and commercial settings. Given the lack of durable, nonsurgical options for symptomatic discogenic pain, the favorable risk-benefit profile supports a stronger recommendation than the evidence grade alone might suggest. Notably, the NP allograft is classified by the US Food and Drug Administration as a human cell and tissue product regulated under Section 361 of the Public Health Service Act, reinforcing its use as a biological supplement rather than a structural implant.

The primary limitation of this analysis of AEs and clinical complaints involves the inclusion of heterogeneous real-world cohorts from a registry population, which may not capture all relevant complications associated with intradiscal delivery of NP allograft.

CONCLUSIONS

Collectively, the current pooled analysis yielded a SAE rate ≤1%, a product-related AE burden <3%, and a <1% field complaint frequency, all of which outperform published findings for other intradiscal investigational products. These findings validate the NP allograft procedure as a microinvasive, motion-preserving intervention that bridges the therapeutic gap between conservative care and invasive spine surgery while maintaining an exemplary safety profile.

These findings are further supported by a recent Delphi consensus algorithm, developed by a multidisciplinary panel of experts, which recommends NP allograft as a guideline-concordant, first-line intradiscal therapy for discogenic pain patients with modified Pfirrmann grade 3 to 7 degeneration.[19] This external validation reinforces the clinical rationale and safety profile demonstrated in our pooled analysis.

ACKNOWLEDGMENTS

The authors appreciate the thorough review provided by Jon E. Block, PhD, and manuscript preparation by Malahki Thorn.

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Funding: Financial support for the research, authorship, and publication of this article was supported by Vivex Biologics, Inc. (Miami, FL, USA).

Disclosures and Conflicts: Amol Soin reports patents planned, issued, or pending with Soin Neuroscience, Soin Bioscience, Neuronoff, Avanos, and Synaptrix; participation on a data safety monitoring board or advisory board for Vivex; leadership role for ASIPP and OHSIPP; stock/stock options for Neuronoff and Neuros Medical; receipt of equipment, materials, drugs, medical writing, gifts, or other services from Avanos; and other interests with Alt5Sigma, Neuronoff, Neuros, and Synaptrix. Siddardth Umapathy reports consulting fees from Vivex Biologics. The remaining authors have nothing to disclose.

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