Effectiveness of an Anular Closure Device in Patients that Meet RCT Screening Criteria vs. a "Real-world" Population: Retrospective Analysis of a Prospective Registry

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Disclosures

- Both the authors (AK and SAR) have previously received research support fees from Intrinsic Therapeutics, Inc. for being site investigators in an industry (Intrinsic)-sponsored clinical trial.
- AK has received consulting fees from Intrinsic Therapeutics, Inc. (unrelated to this study).

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Background: Randomized Controlled Trials

- Most randomized controlled trials (RCTs) implement highly specific inclusion and exclusion criteria (Kuršumović et al, Med Devices (Auckl), 2018)

- Consequently, study populations represent only a subset of patients that will ultimately be treated with an experimental device (Kennedy-Martin et al, Trials, 2015; Lisspers et al, NPJ Prim Care Respir Med, 2016; Ruokoniemi et al, BMJ Open, 2014; Ziemssen et al, BMC Ophthalmol, 2017)

RCT population

"Real world"

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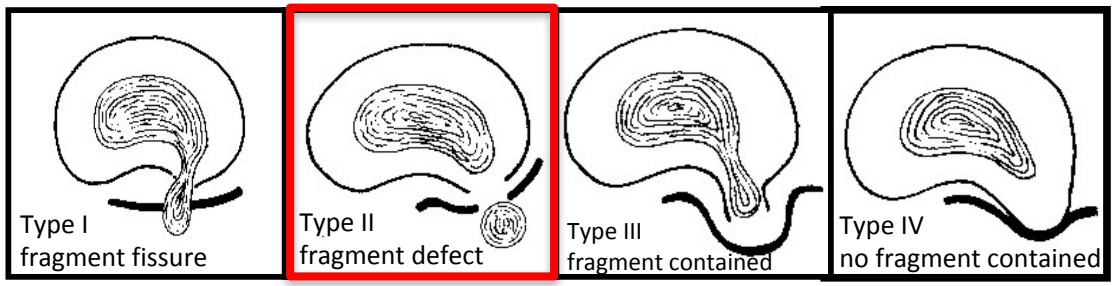
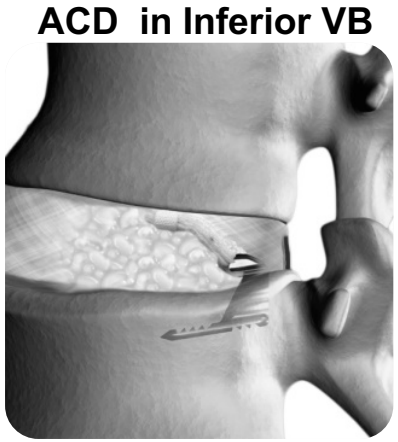
Background: Anular Closure Device

- Large anular defects after lumbar discectomy are a known risk factor for reherniation and reoperation
  (Miller et al, Spine. 2018)



- Anular closure devices (ACD) are used to occlude or seal the defect in the anular ring through the use of suture techniques or mesh inserts
  (Bailey et al, Spine (Phila 1976); Qi et al, Medicine (Baltimore), 2016; Thomé et al, Spine J, 2018)



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Study Aim

- Assess the performance of an ACD in a consecutive series of 'real-world' patients retrospectively stratified according to the screening criteria of an RCT

RCT-eligible population

Vs.

All others eligible for treatment

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Methods: Patient sample

- Patients who received an ACD were screened against the inclusion criteria for an RCT (Clinicaltrials.gov: NCT01283438)
  - Patients included in this study were never enrolled in the RCT
- Inclusion criteria (for 'Trial' group)
  - Failed at least 6 wks conservative therapy
  - ODI ≥ 40/100 and VAS leg pain ≥ 40/100
  - Age 21-75 y
  - No prior herniation at the index level
  - Minimum posterior disc height of 5 mm
  - Min/max annular defect height of 4/6 mm
  - Min/max annular defect width of 6/12* mm
- 'Non-Trial' patients did not meet the inclusion criteria

*Patients with defects wider than 10 mm were assigned to the non-Trial group.
ODI=Oswestry Disability Index; VAS=visual analog scale

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Methods: Outcomes

- Patient reported outcomes (PROs) included ODI scores and VAS for leg and back pain scores.
  - Clinical success was defined as ≥15-point improvement in ODI score and ≥20-point improvement in VAS scores
- Adverse events were collected from baseline to last follow-up
- Latest follow-up
  - Mean: Trial = 15.6 months; Non-Trial = 14.6 months

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Results – Stratification and Baseline PROs

- A total of 164 patients were included
  - 44 Trial patients
  - 120 Non-Trial patients
  - Reasons for exclusion from Trial group:
    - < 6 weeks conservative treatment (51%)
    - Preoperative ODI scores < 40 (26%)
    - Revision discectomy (14%)
- Baseline demographics were not significantly different between groups, but worse ODI and VAS scores due to inclusion criteria for Trial group

Table 1. Baseline PROs

Outcome metric	Trial group (n=44)	Non-Trial group (n=120)	p-value
Baseline (preoperative)			
ODI	59.5±13.8	50.5±22.5	0.03*
VAS leg	87.7±12.6	76.1±25.5	0.02*
VAS back	67.0±28.2	55.7±31.7	0.04*

Data entered as mean±SD
* Indicates p<0.05

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Results – Follow-up PROs

- No significant difference between Trial and Non-Trial groups for:
  - ODI or VAS scores (Table 2)
  - Clinical success rates (Table 3)

Table 2. Follow-up PROs

Outcome metric	Trial group (n=44)	Non-Trial group (n=120)	p-value
ODI	24.2±20.8	18.7±17.4	**0.15**
VAS leg	28.2±29.9	27.6±27.6	**0.97**
VAS back	38.4±32.7	30.5±24.8	**0.28**

Table 3. Clinical success rate*

Outcome metric	Trial group (n=44)	Non-Trial group (n=120)	p-value
ODI	84% (37/44)	71% (85/120)	**0.11**
VAS leg	84% (37/44)	79% (94/119)	**0.52**
VAS back	68% (30/44)	62% (74/119)	**0.58**

* ≥15-point improvement in ODI score and ≥20-point improvement in VAS

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Results – Reherniation, reoperation, complications

- Three Trial (6.8%) and three Non-Trial (2.5%) patients experienced symptomatic reherniation (p=0.34)
- Rates of reoperation, ACD mesh dislocation/separation, and other radiographic findings were also similar between groups (p=1.00)

Table 4. Rates of subsequent surgical interventions

Intervention	Trial group (n=44)	Non-Trial group (n=120)
Re-discectomy	**2.3% (1/44)**	**1.7% (2/120)**
Fusion	**4.5% (2/44)**	**2.5% (3/120)**
Wound	0%	3.3% (4/120)
Decompression	0%	2.5% (3/120)

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Conclusions

- There was a low incidence of adverse events, including reherniations, reported in both groups
- Similar clinical outcomes between the Trial and Non-Trial groups suggest a robust safety and efficacy profile in patients with large anular defects
- Real-world evidence is important to supplement RCT data to confirm similar outcomes in specific populations outside of the RCT inclusion criteria

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