Gelstik™ implantation: An intradiscal hydrogel for Nucleus Augmentation

Anthony T. Yeung, M.D.
Desert Institute for spine Care
Phoenix, Arizona

Voluntary Professor of Neurosurgery
University of New Mexico School of Medicine
Albuquerque, New Mexico

Ann Prewett, PhD
CEO Replication Medical

Disclosure

- Investor in Replication Medical
- Medical Advisory Board
- Clinical Data provided by Ann Prewett, CEO Replication Medical
- Clinical expertise in discogenic pain as the developer of the YESS endoscopic spine system **focusing on identifying the source of discogenic pain,** but expanding to all painful degenerative conditions of the lumbar spine
- Advisor to Elliquence in developing Disc FX

Back Pain

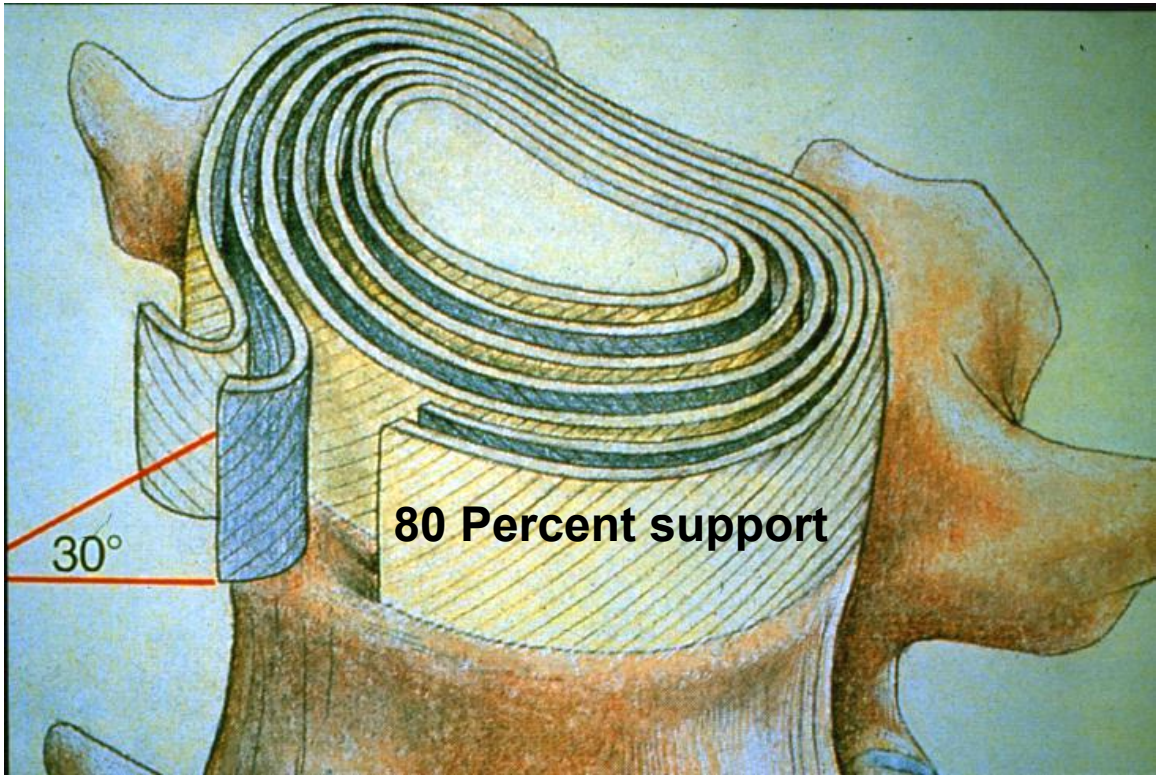
- Chronic back pain afflicts hundreds of millions of people worldwide

- Most common early cause is deterioration of the intervertebral disc from trauma or aging

- Current Therapies exist to treat back pain range from nonsurgical techniques: ie. physical medicine + pain management , followed by various techniques of MIS and traditional disc surgery,but **PREMATURELY** ending in fusion

Intervertebral Disc Anatomy

- **Nucleus pulposus:** a hydrogel like substance
- **Annulus fibroses:** collagen fibers (20 layers)



Disc Degeneration

- **A normal Aging Condition**
- **Accelerated by trauma**
- **Begins with disc degeneration and annular dehiscence, shifting spinal loads from the anterior column (disc) to posterior column (facet Joints)**

Spinal Degeneration of the Lumbar Disc

- **The degenerative process may produce pain that is usually well tolerated, but**
  - **Why some patients have disabling pain and others not is not completely understood**
  - **Endoscopic Visualization of Patho anatomy intradiscally provides evidence that the degenerative process, when accompanied by changes in PH and inflammation caused by annular tears can provide rational early and successful treatment to mitigate pain**
    - **The DRG Responsible for intolerable sciatica tears (site of "toxic" annular tears)**

Chronic Back Pain Is Multifactorial

Traditional Surgical Treatment Guideline

- **Discectomy is standard when spinal nerves are being compressed or irritated and severely painful**
  - **Discectomy is beneficial and cost effective (U.S. multicenter SPORT study)**
    - **Weinstein JN, Tosteson TD, Lurie JD, Tosteson An, Hanscom B, Skinner JS, et al. Surgical vs nonoperative treatment for lumbar disc herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. JAMA. 2006; 296:2441-50.**

Current Salvage Surgical Treatment

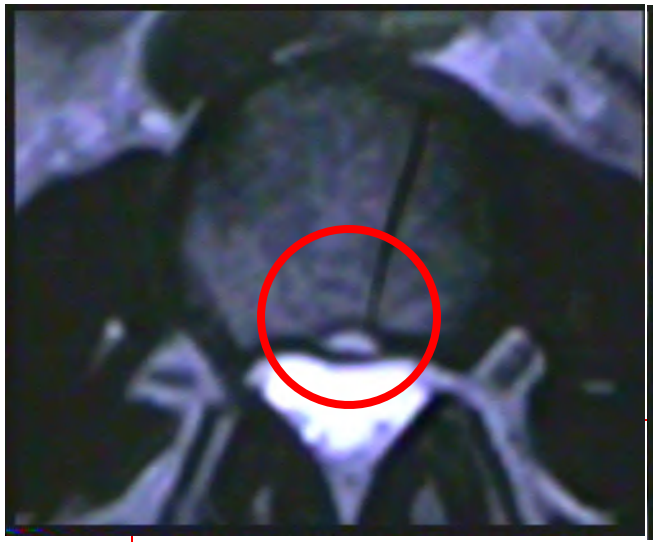
- **FOR Painful Progression to lumbar stenosis and spondylosis is surgically treated by Decompression and ULTIMATELY Fusion..but**
  - **Cost / Benefit of treatment is being questioned**
    - **Expensive Implants and Hardware**
    - **30% Failed Back Surgery Syndrome**

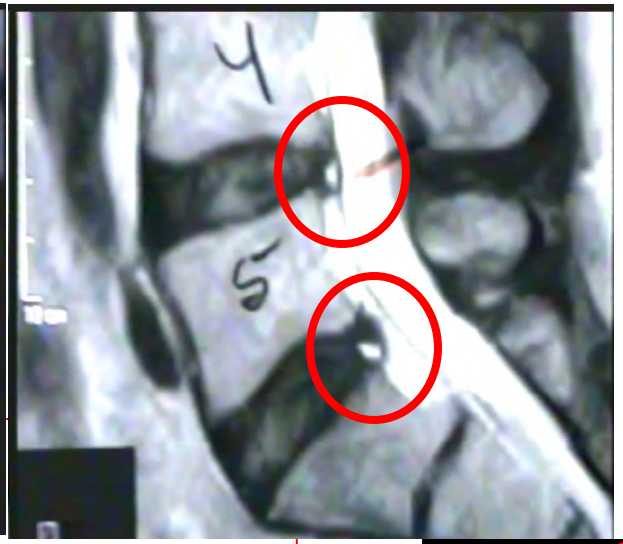
Intradiscal Therapy

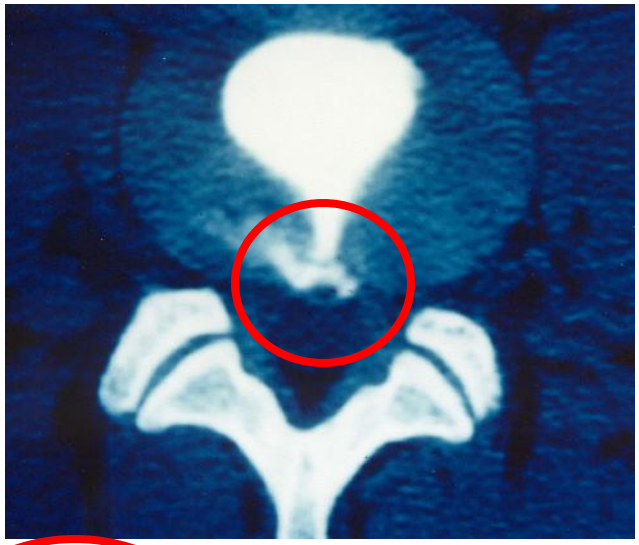
- **Supported by Level I Evidenced Based Treatment**
  - **chymopapain (validated by 2 large double blind, randomized studies and over 32 cohort studies)**
  -
- **Yeung, Tsou "SED and thermal annuloplasty" The Spine Journal 2002**
  - **Stratified the Good/excellent results from endoscopic intradiscal treatment with specific pt selection indication**
  - **SED™ with thermal; modulation (YESS Technique)**
  - **DISC FX (ELLIQUENCE)**
  - **NUCLEUS AUGMENTATION (Gelstik)**
  - **Other (ozone, IDET, coblation, biacuplasty, annular shunt**

Degenerative Cascade Begin with Annular Tears

Ganulation Tissue and Inflammation = Pain Disc protrusion only= numbness

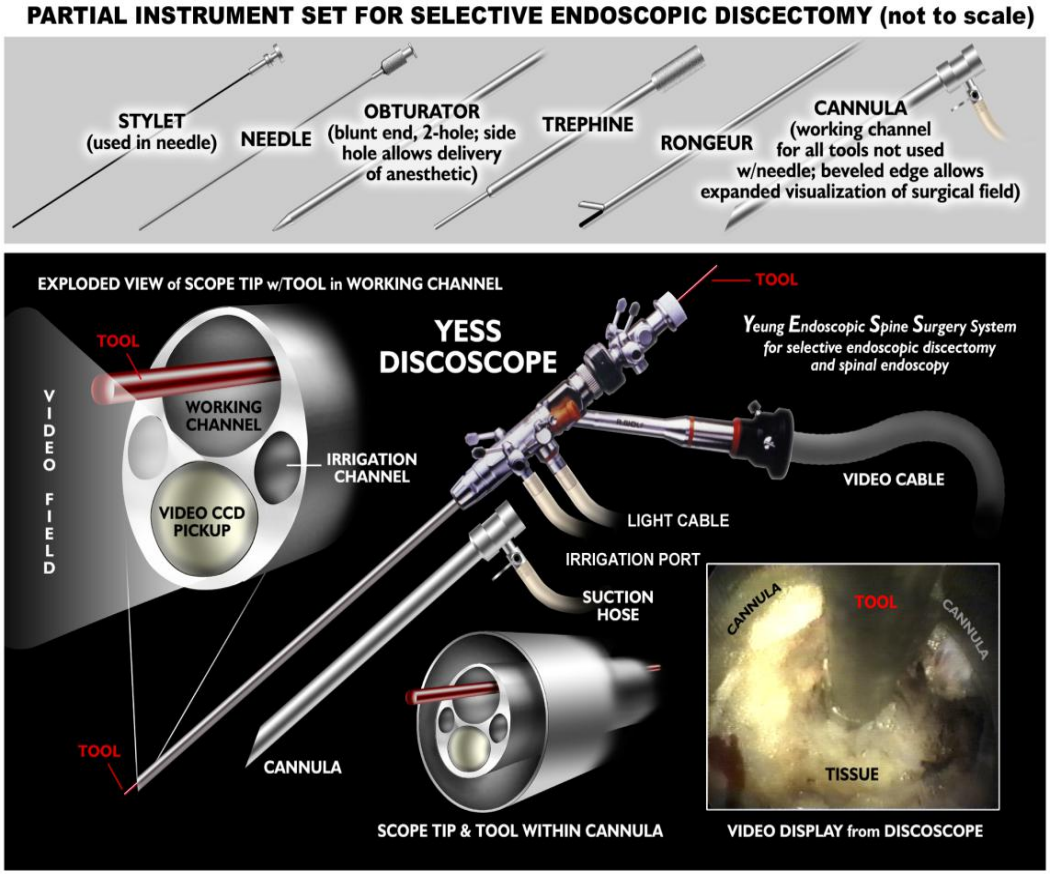






The Yess Endoscope by Wolf

Identifies Painful Patho-anatomy



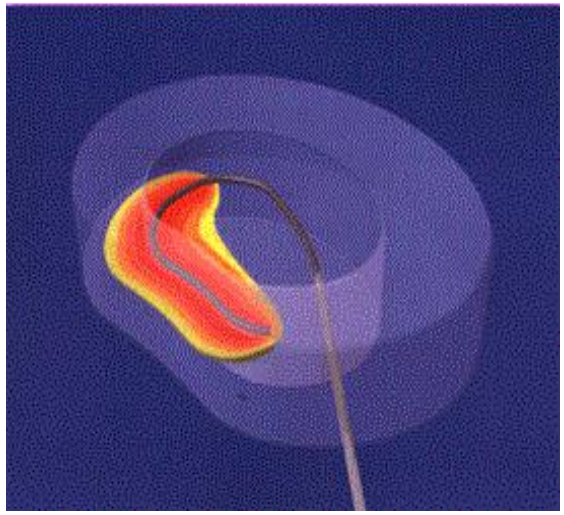
Wolf Y.E.S.S. Multi-Channel Spine Scope

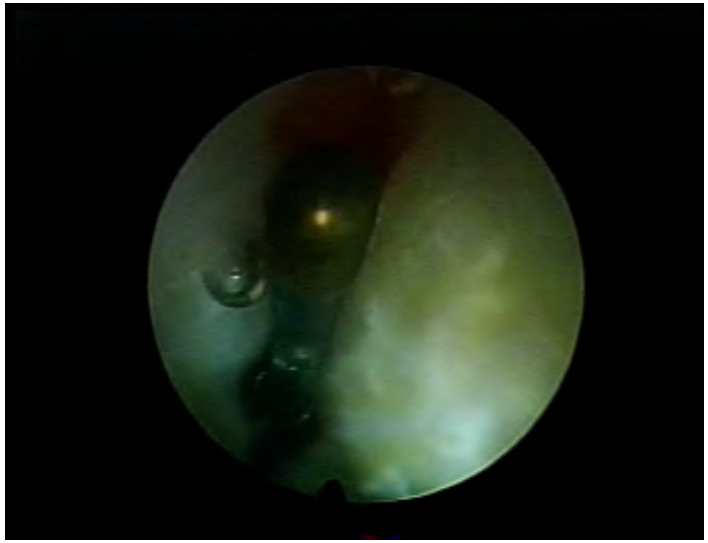
REPLICATION Medical, Inc

Intradiscal Therapies ablate painful annular tears

But… Intradiscal Disc treatments are not all the same!

(Compare IDET with Selective Endoscopic Discetomy™ and thermal annuloplasty)





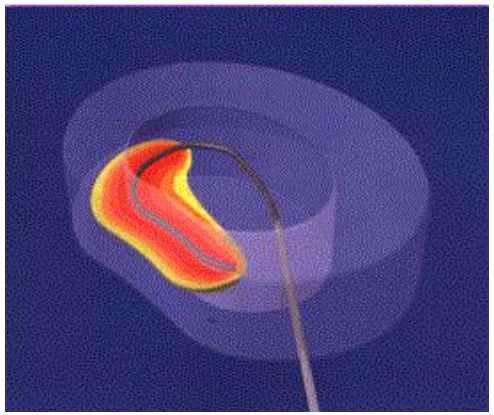
IDET, Coblation, Biacuplasty, PLDD, Ozone, Does not remove interposed disc embedded in the annular tear.

SED™ with Thermal Annuloplasty Successful if embedded nucleus Debrided from annulus, exposing annular tear under visualization

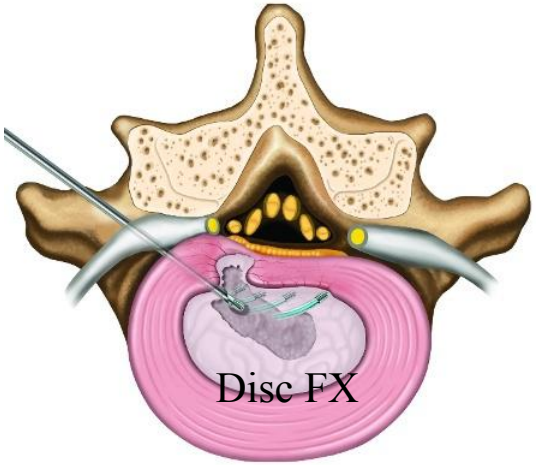
Intradiscal Therapy has had a poor Track Record for Efficacy because the patho-anatomy is not adequately targeted

Flouroscopically guided Intradiscal Disc treatments are not consistently effective (SED™ AND DISC FX comes the closest)

(Compare IDET with Disc FX and S E D™ with thermal annuloplasty)



IDET, Coblation, PLDD, not consistently effective. Pain generators targeted blindly.

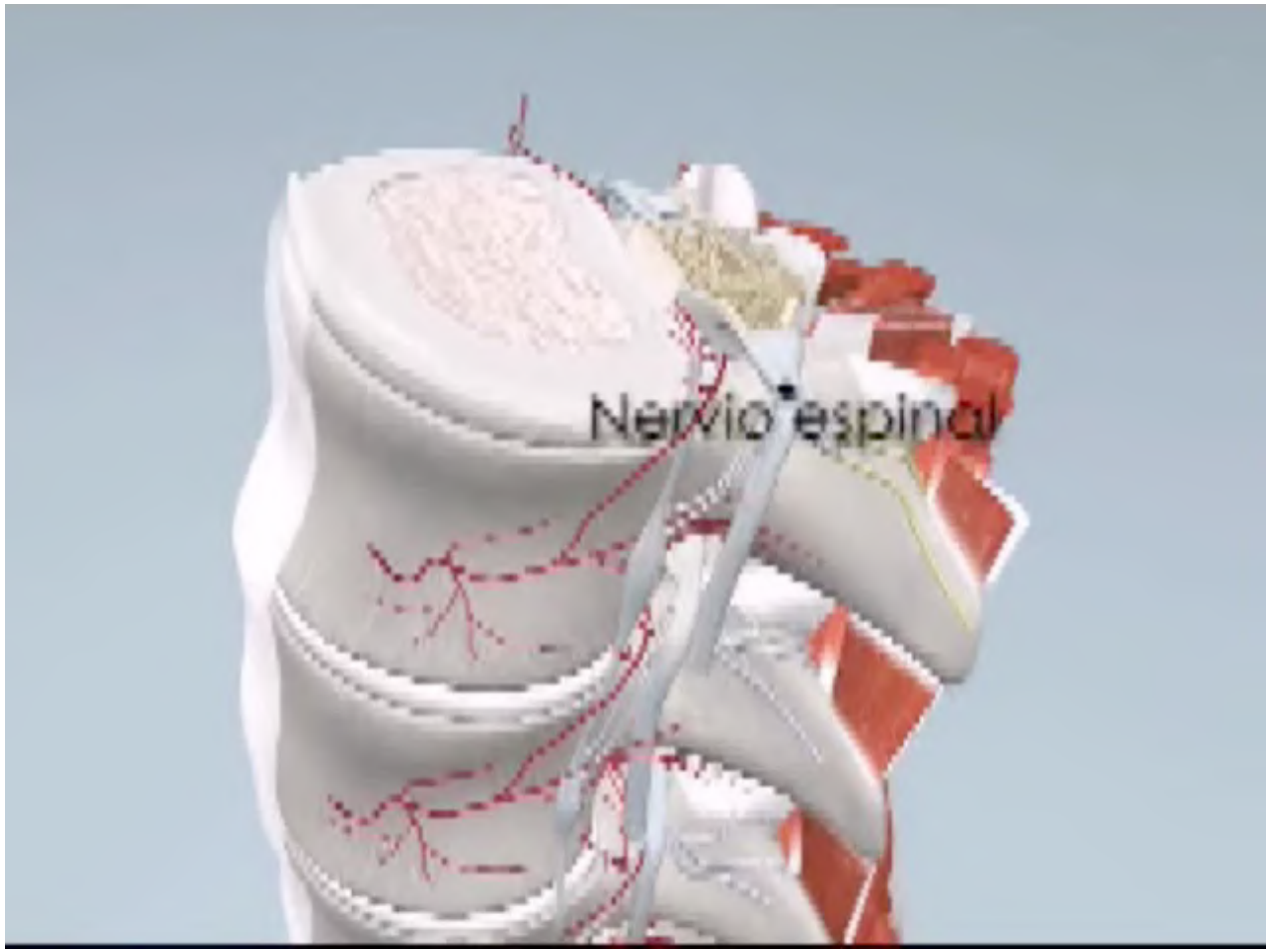


Mimics SED™

SED™ with Elliquence annuloplasty.

Innervation of the lumbar segment

is Complex (connections between dorsal and ventral ramus) source unknown from S Hellinger



Introducing a Novel Intradiscal implant For the treatment of painful discs

GelStix™ Nucleus Augmentation

REPLICATION Medical, Inc

Pathophysiology of Disc Degeneration and Back Pain

- Back pain is strongly associated with degeneration and injury of the intervertebral disc*
- Disc degeneration alters disc height and the mechanics of the spinal column adversely affecting other structures and leading to spondylosis, facet arthrosis, stenosis, causing pain and disability
- As the population ages, and with repetitive disc injury, disc degeneration increases dramatically
- **Reversing or slowing disc degeneration should lead to a reduction in back pain and improvement in quality of life**
- *Luoma K et al Spine 2000 25:487-492

End result of disc degeneration

- Reduced disc height
- Bulge or Prolapse
- Loss of disc support, and Disc instability
  - Reduced hydraulic support, resulting it annular tears
- Thickening of the ligamentum flavum
- Osteoarthritic changes

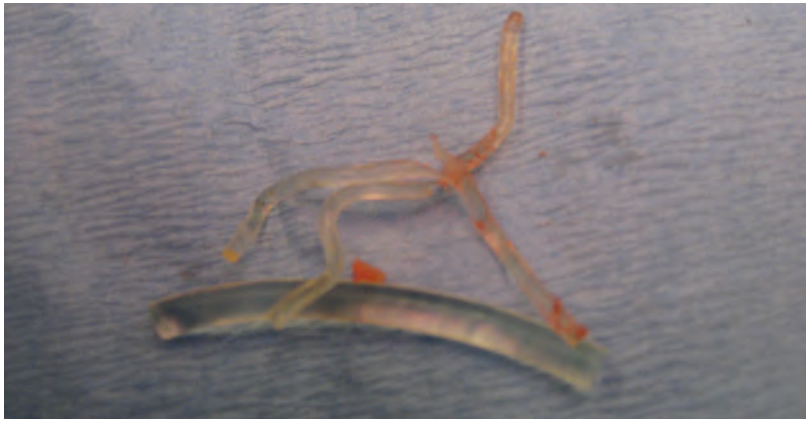
Development of Back Pain AND SCIATICA

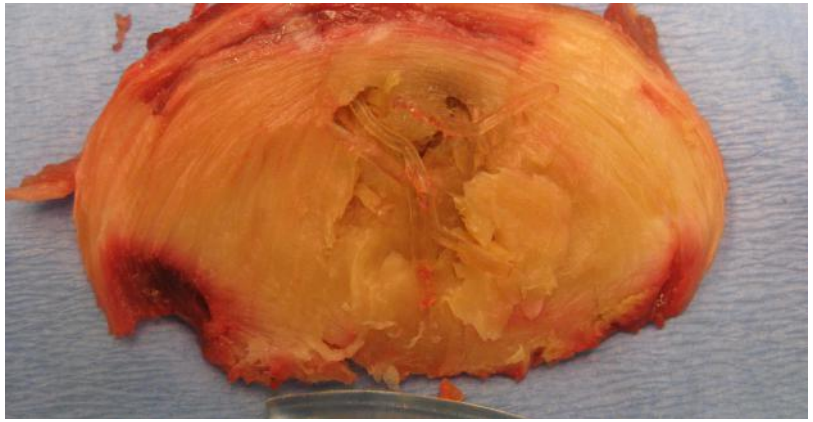
Biomimetic Hypothesis

…can we retard, reverse or otherwise control the progression of disc degeneration by recapitulation of the chemical milieu or environmental state of the healthy disc…?

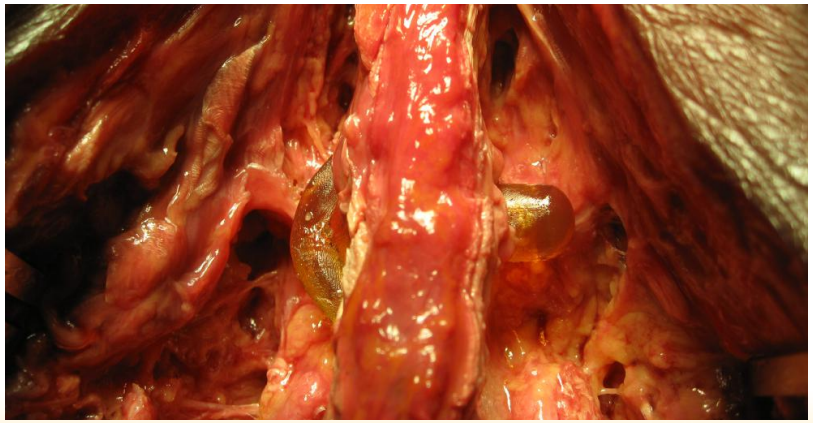
Cadaver studies suggest anatomic feasibility of hydrogel support

Gel Stik™





Gel fix™



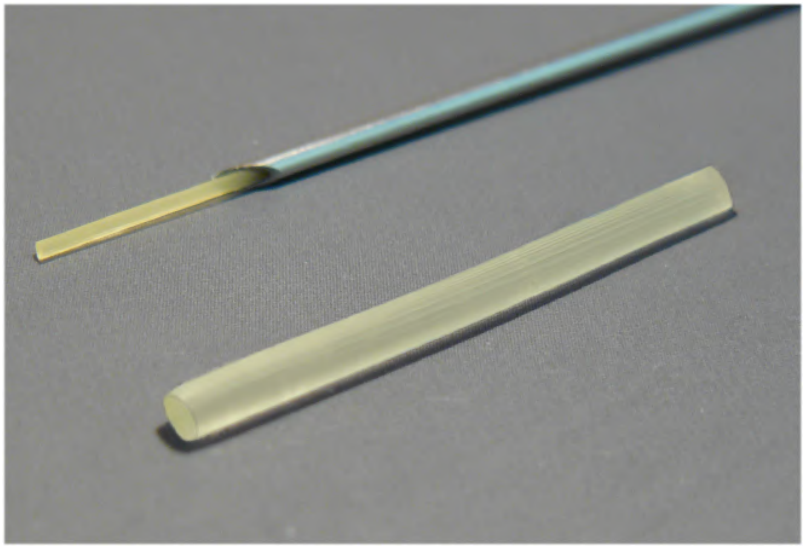
Preliminary Gel Stik™ Clinical Evidence

- **Pilot Study for painful degenerative discs Identified with discography, produced positive effects**
- Barcelona Outcomes Study
  - Rudi Morganstern
- Spinal foundation Study
  - Martin Knight (may be useful in conjunction with foraminoplasty)
- European Studies
  - Robert Plfugmacher
  - Stephan Becker

Rationale for Nucleus Augmentation

- **Restore Hydraulic support for the descicating disc**
- **Hydrogel implant impervious to chemical degradation**
- **Implant Responds to Load**
  - **Able to rapidly bind and express fluid**
- **Neutralize acidic conditions by absorbing plasma**
  - **Hydrogel has buffering capacity, negatively charged**
- **Modulus Elasticity of hypan® similar to nucleus**

GelStix™ product overview



CE Mark

(3) Independent clinical outcomes study underway

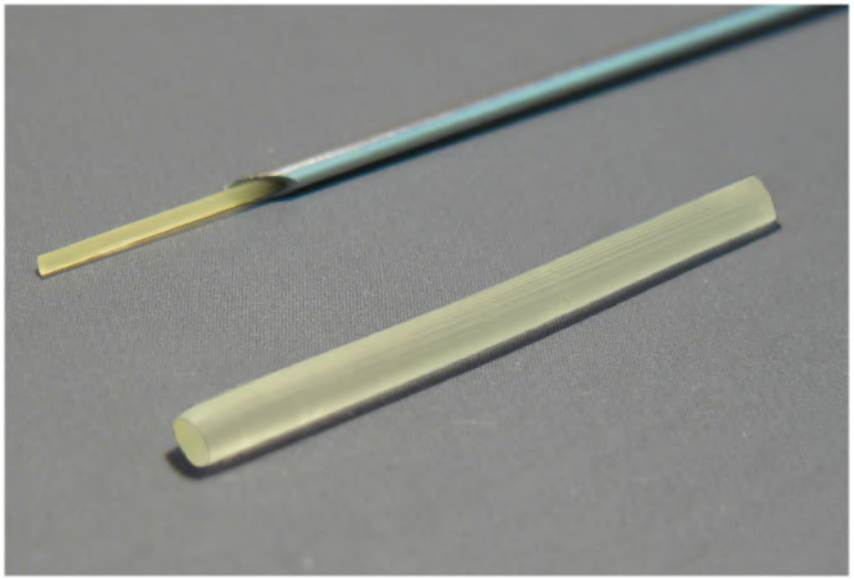
Over 150O Gelstik implants sold to date

Reduction in LBP at all follow-up intervals for patients treated in clinical outcomes study on patients with various degrees of degeneration

Few known complications or adverse events with proper insertion protocol*

***Three known extrusions from new (contralateral) or recurrent HNP following implantation successfully resolved with endoscopic decompression**

GelStix™ Nucleus Augmentation



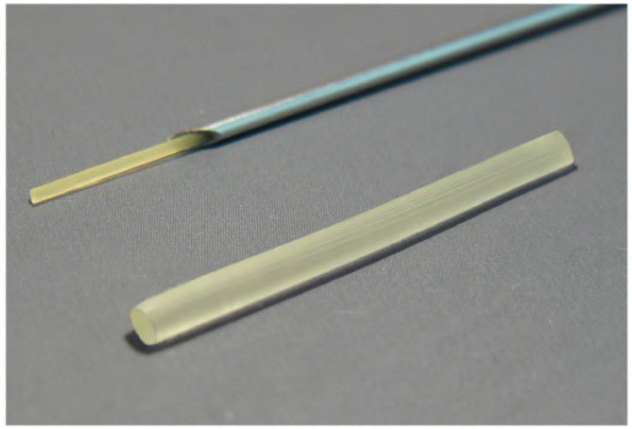
Features:

- Self expanding – biocompatible
- Reverses Low pH associated with disc degeneration, inflammation
- Administered using 18 gauge needle
- Fluid uptake into uptake into nucleus

Advantages:

- Ease of use
- Relieves pain but preserves future treatment options
- Low risk for complications
- Impressive reduction in LBP at 1 wk, 3 wks and 3 and 6 and 12 month post-operative

GelStix™ Nucleus Augmentation



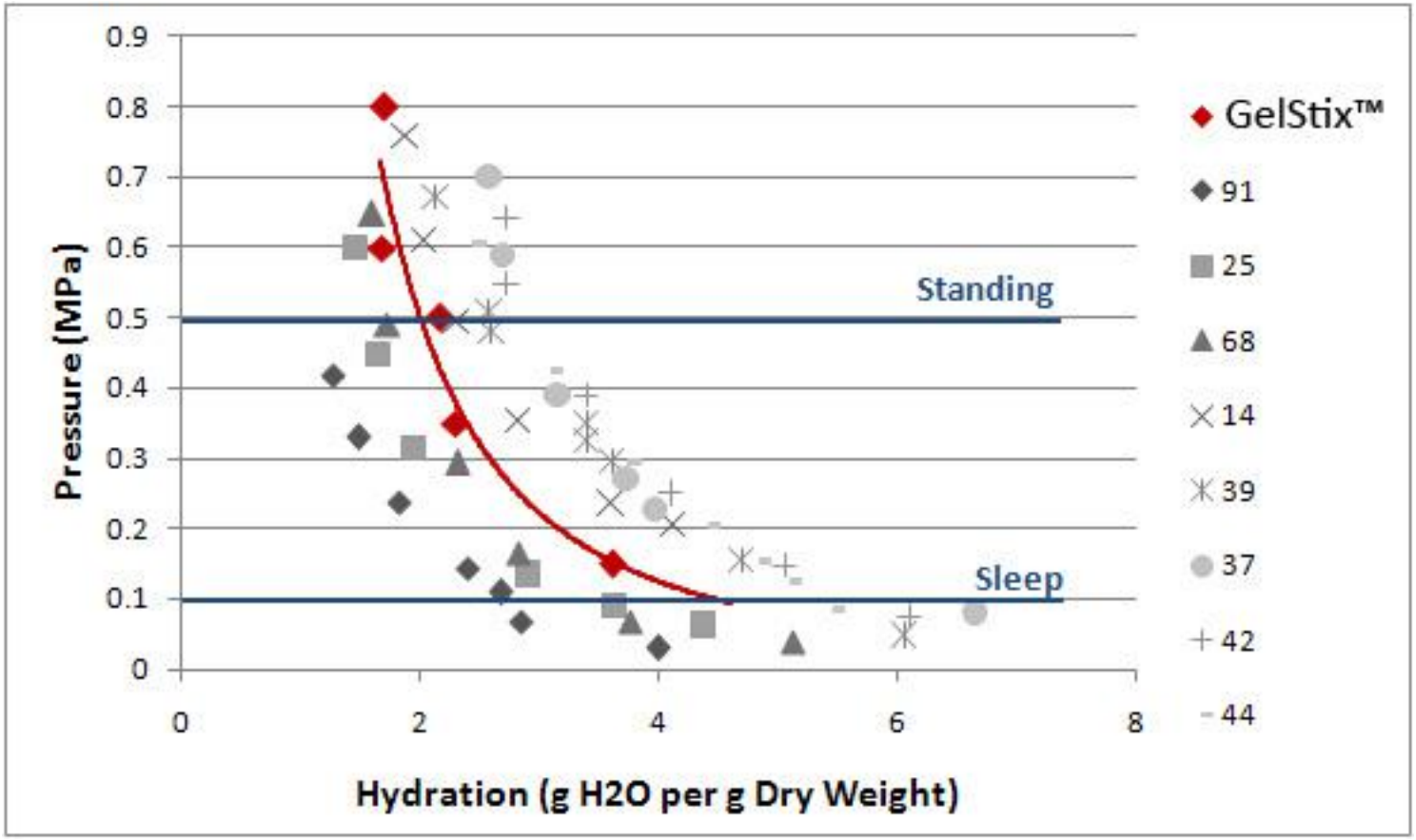
Indication:

- **GelStix™: New means of restoring the diseased disc nucleus to a more physiologically healthy state**
- **Indicated for back pain associated with degenerative disc disease in the presence of little or no leg pain and the absence of instability**

Mode of Action

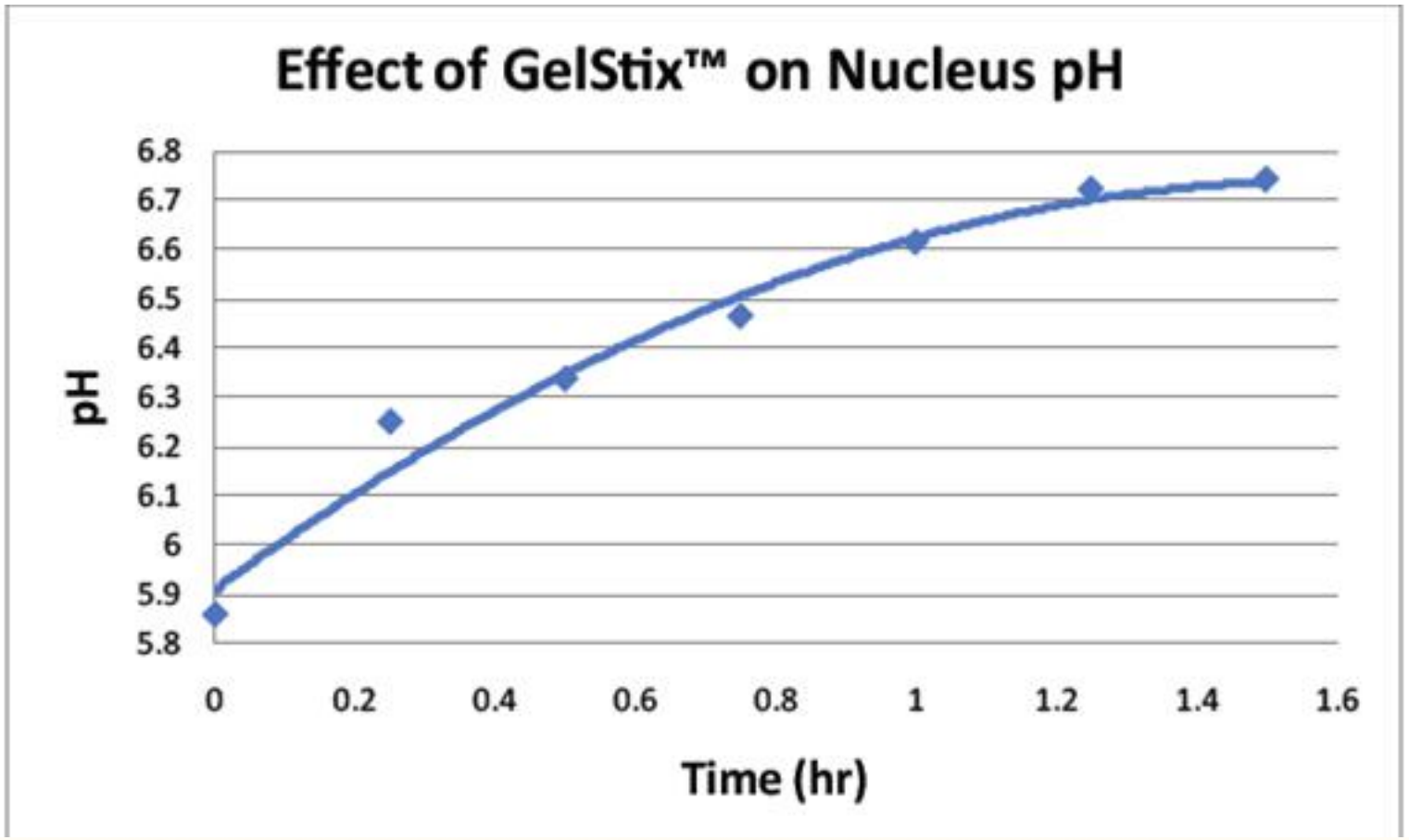
- **Increases pH – low pH is associated with degeneration and inflammation**
- **Increased pH leads to increased hydration and swelling of native nucleus (negative charge facilitates water uptake)**
- **Increases osmotic pressure in disc by adding fluid and volume**
- **Restore hydraulic support of nucleus**

Hydrostatic Response to load (like native nucleus)

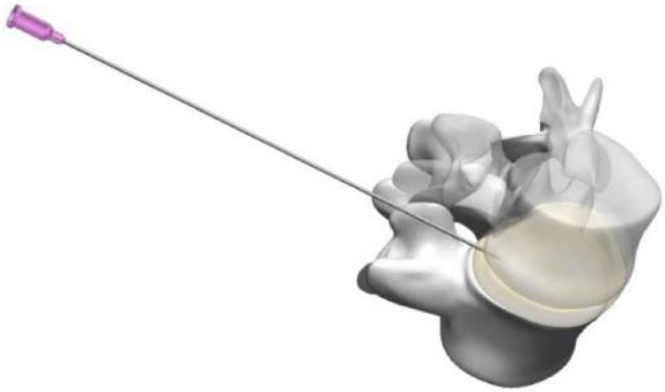


GelStix™ hydration response to pressure mimics cadaveric nucleus.

Restores PH to neutral, mitigates inflammation



Delivery Technique follows Discogram Needle



1. Position Needle. Perform Discography (If Desired)

2. Attach Preloaded GelStix™ Cartridge

3. Push Implant into Needle

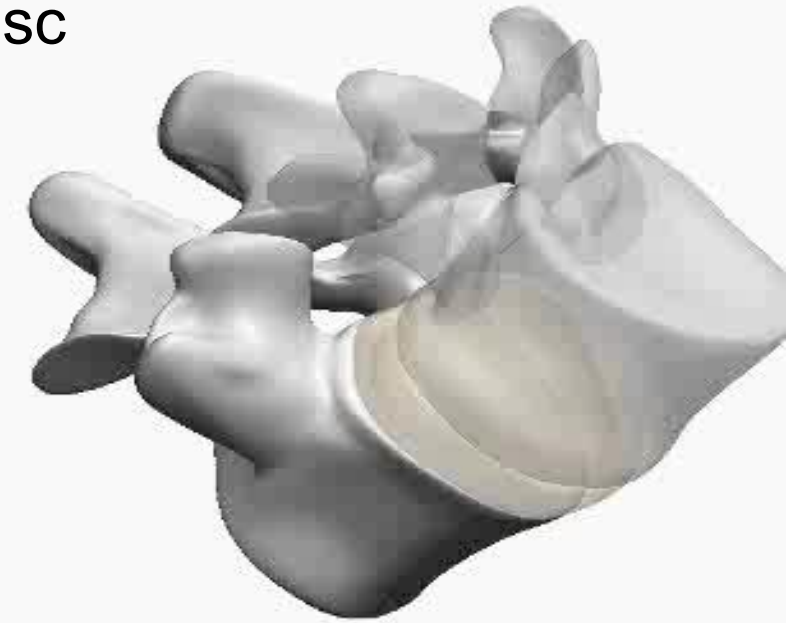
Key Features

Meticulous implant positioning protocol

Meticulous insertion protocol: 2 step process:
Insertion into needle, delivery into disc

Timing protocol : 15 seconds

Delivery of number of implants according to evocative discography volume



1st GelStix™ Pilot for a broad spectrum of Discogenic Pain

- Wide variety of patients with low back pain including
  - **Patients with previous discectomies (endoscopic and microdiscectomy_**
  - **Patients in various stages of degeneration**
  - **Patients with significant leg, buttock and groin pain**
  - **Patients with mild spondylolisthesis**
  - **Patients with multi-level disease**

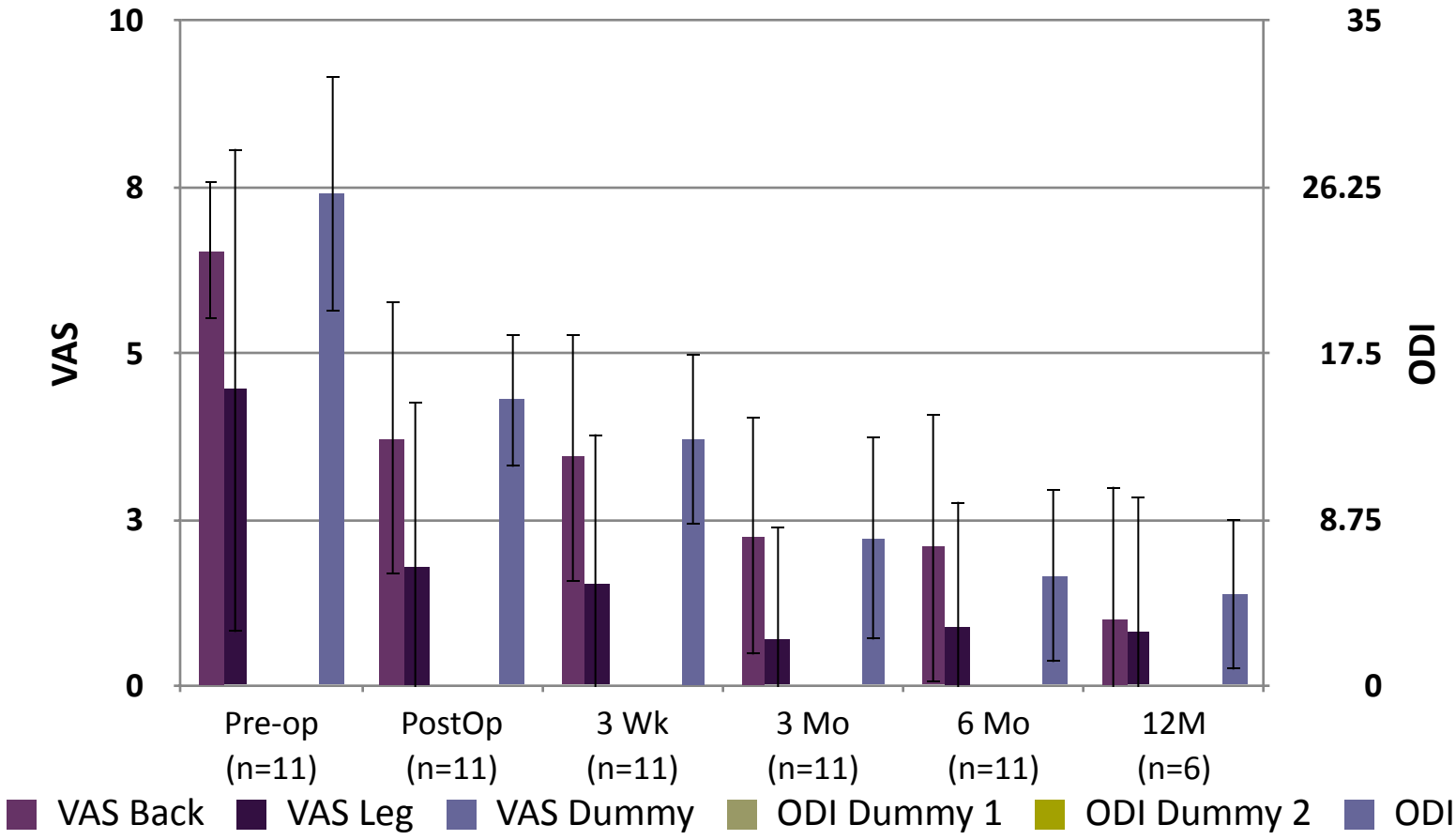
1st GelStix Study
Patient Population

	Level	Sex	Age	Previous Surgery	Imaging	Back Pain	Leg Pain
661	L5/S1	M	65	Left endoscopic discectomy L5-S1 in Jan 2005	DDD at L5-S1	For 2 Mo	None
669	L4/5, L5/S1	F	48	-	DDD at L4-L5 and L5-S1	For 1 Yr	None
685	L5/S1	F	45	L5-S1 microdiscectomy in 2001	DDD at L5-S1	For 1 Yr	Right Radiating
686	L4/5	M	48	-	L4-L5 Spondy Grade I	For 2 Yr	Right Radiating
691	L4/5	F	57	-	DDD at L4-L5	For 2 Yr	Left Radiating
697	L5/S1	M	38	-	DDD at L5/S1	For 3 Yr	Right Radiating
707	L5/S1	M	66	-	DDD at L5/S1	Yes	None
708	L4/L5	F	51	-	DDD at L4/L5	Yes	None
713	L4/5, L5/S1	F	50	-	DDD at L4/5 and L5/S1, Minor Scoliosis	Yes	Left Radiating
720	L5/S1	M	25	-	Annular rupture at L5/S1	Yes	Left Radiating
722	L3/4, L4/5	M	55	-	DDD w/ HIZ at L3/4 and L4/5	Bilateral	Left Buttock
724	L2/3, L3/4	F	51	L4/5 and L5/S1 Fusion in 2005	DDD at L2/3 and L3/4	Bilateral	Left Buttock

Results of First Study (Morganstern, Barcelona)

- All patients improved to some extent with the exception of the patient with unstable **spondylolisthesis (relative contraindication)**
- Dramatic improvement in leg, buttock and groin pain were observed in most patients
- **No device related complications or adverse events**

Barcelona Outcomes Study



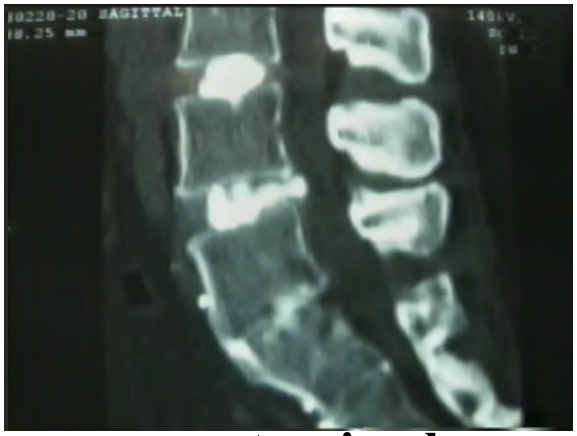
Ideal Patient

- LBP without nerve root compression – “axial back pain”
- Dark disc on MRI
- Painful level confirmed by imaging and **discography**
- Intact annulus (no full thickness grade V tears)
- Minimal to moderate modic changes
- Minor loss in disc height
- **HIZ may be present or absent**

Example: Ideal Diagnostic Study

Dark disc on T2

Bulging disc on MRI



Discogram protrusion larger than MRI

Gr IV Tear

Positive evocative discography

Inclusion Criteria

- **Predominant low back pain**
- **Failure of Non surgical care**
- **Presence of degenerative disc disease on magnetic resonance imaging**
- **Annulus should be competent as determined by intra-operative lumbar discography or CT-MRI.**

Relative Exclusion Criteria

- **Radiculopathy caused by nerve root compression.**
- **Frank herniations, extruded or sequestered fragments, bulge/ protrusions >3mm.**
- **Severe symptomatic central, foraminal or lateral recess stenosis, spondylolysis, spondylolisthesis, acute fractures, severely degenerated facet joints, or ankylosing spondylitis.**
- **Surgical access issues (L5-S1)**
- **Active infection**
- **Neurogenic claudication due to spinal stenosis.**

Spinal foundation Study

MARTIN KNIGHT

- Combine Gelstik implant in advanced disc degeneration causing foraminal stenosis with foraminoplasty
  - BACK PAIN RELIEF AS WELL AS RADICULAR SYMPTOM RELIEF

Combination Foraminoplasty

- Interventions over 3 Years: 188 Patients

Dispersal of Major Procedure Levels					
Level 1	Level 2	Level 3	Level 4	Level 5	
Foraminoplasty	Foraminoplasty				72
Foraminoplasty	Foraminoplasty	Laser Discectomy			16
Foraminoplasty	Foraminoplasty	Gelstix			5
Foraminoplasty	Foraminoplasty	Laser Discectomy	Gelstix		6
Foraminoplasty	Foraminotomy	Laser Discectomy			53
Foraminoplasty	Foraminotomy	Gelstix			8
Foraminoplasty		Laser Discectomy	Gelstix		18
Foraminoplasty	Foraminoplasty	Gelstix	Gelstix		5
Foraminoplasty	Foraminotomy	Gelstix	Gelstix		4
Foraminoplasty	Foraminoplasty	Gelstix	Gelstix	Gelstix	1
					188

Combination Outcomes

- General Outcomes – multifactorial causation
  - Catchment group - 40% Failed Back Surgery
  - Age 46 – 89 Years
  - Complications
    - No DVT, Embolism, Coronary Thrombosis, CVA, UTI, Wound or Disc Infections
- Audit

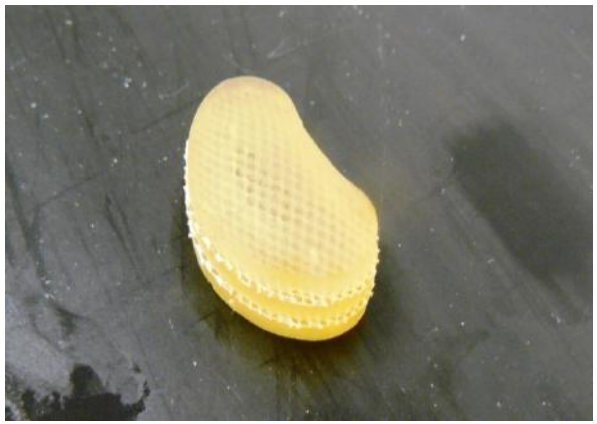
Outcome		%
Excellent	79	42%
Good	70	37%
Satisfactory	36	19%
Poor	3	2%
Worse	0	0%
	188	

- Use Only Supplied Needle
- Avoid bending the needle or deforming needle tip on bone during needle insertion
- **If contrast medium is used, plunge remaining fluid from needle**
  - May use sterile saline to flush needle if lidocaine or other fluids are used
  - Plunge residual fluids from needle using stylet before inserting GelStix cartridge
- **GelStix swells quickly and must be deployed within 15 seconds after loading**
- **Gelstix Supplied Needle has beveled stylet – rotate stylet if resistance is felt**
- **Use special blunt, flat 18 gage stylet to advance GelStix if it becomes difficult to advance down needle**

DISCUSSION Expanded indications?

- 1. AUGMENT DISC FX?
- 2. AUGMENT SED™ , ANNULOPLASTY?
  - YESS TECHNIQUE
- **STAGED TREATMENT DEPENDING ON CLINICAL RESPONSE TO 1 OR 2?**
  - **Insert imlant on contralateral side?**
- AUGMENT OTHER FDA APPROVED INTRADISCAL THERAPIES?
- OTHER HYDROGEL IMPLANTS…INTERSPINOUS IMPLANT
  - GEL FIX™, GEL PERC™ FOR DORSAL COLUMN SUPPORT

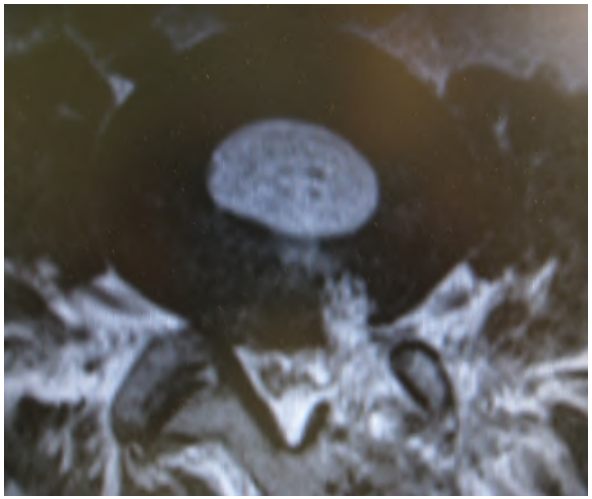
The Future of Intradiscal Therapy: Nucleus Replacement



Neudisc ,

Gel stik

- **Replacement of nucleus with hydrating nucleus implant to replace void after discectomy**
- **Annular Reinforcement of annulus to prevent extrusion**



Ouroboros

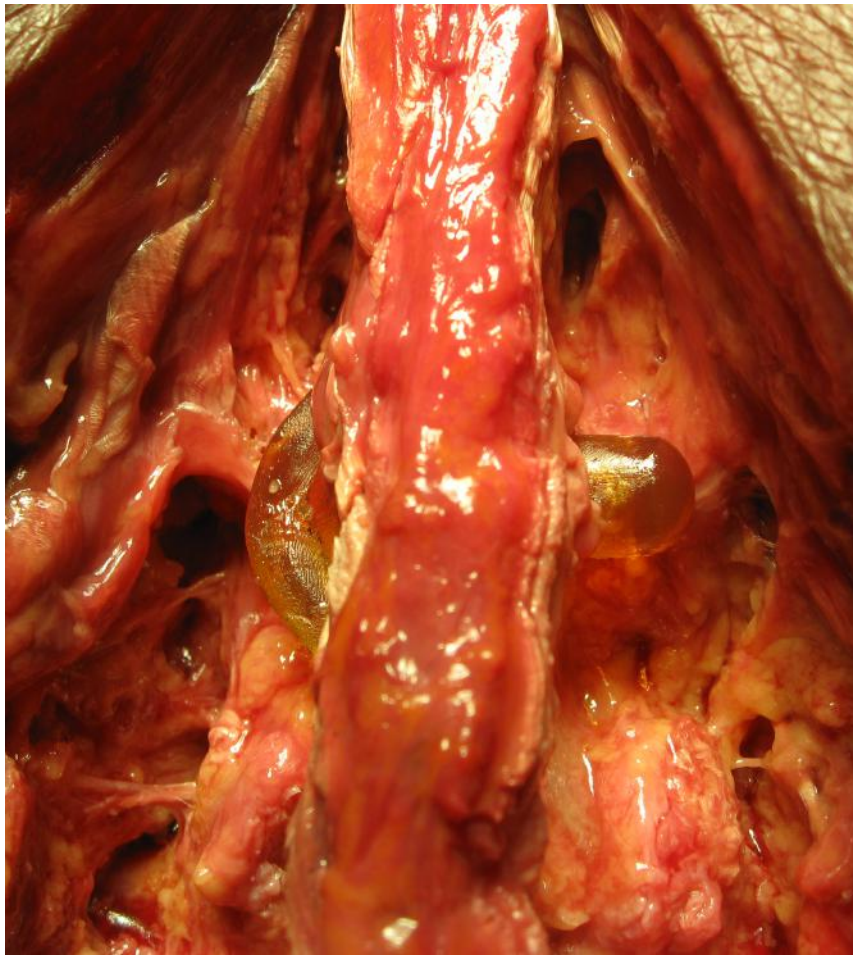
China Pilot Study 2+ years follow-up

REPLICATION Medical, Inc

Conclusion

- Nucleus Gelstix™ augmentation a potential viable and effective intradiscal implant for early treatment of discogenic pain
- Extremely low complication rate
- High level of efficacy in relieving discogenic pain
- Does not “burn bridges” for more invasive traditional treatment
- Indication to augment other accepted therapies by providing intradiscal support
- Combining axial support to the dorsal column may add to the clinical efficacy of chronic back pain syndrome
  - Gel fix, Gel perc

Gelfix interspinous implant to support dorsal column



Thank You