Regenerative Medicine Update
The Disc
TPS 2017
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Precision Spine Care | Baylor Scott and White
Texas Spine and Joint Hospital
Tyler, Texas
Disclosure

Consulting and Research agreements with:

- Medtronic
- Stimwave
- SI Bone
- Stryker

Speaking Only:

- Apex Biologix
Disclosure

Investigator:
• Mesoblast Phase II and III Trial
  • Mesenchymal Precursor Cells (MPC’s)
• Spinal Restoration Phase III Trial
  • Biostat Biologx (Fibrin Sealant)
What are we discussing?

- **Regenerative Medicine** involves delivering specific types of cells or cell products to diseased tissues, with the goal of restoring tissue and organ function.

- **Accomplished via** cell-based therapy or by using cell products, such as growth factors.
- PRP is an autologous blood product that concentrates platelets, which contain over 30 biologically active growth factors stored in alpha granules.
- MSCs can be derived from a variety of sources, though the primary sites of extraction have focused on bone marrow and adipose tissue.
- Level 1 evidence supports the use of PRP in the treatment of osteoarthritis and lateral epicondylopathy (tennis elbow).
- The evidence base for other MSK application is growing including the disc.
Why are we concerned about the disc, and how does this pertain to the painful disc?
The prevalence of Internal Disc Disruption decreases with age.

However, the prevalence of degenerative disc disease clearly increases with age.

FIGURE 4: Predicted probabilities and 95% confidence intervals for internal disc disruption (IDD), facet joint pain (FJP), sacroiliac joint pain (SIJP), and other sources of low back pain (LBP) as a function of age.
Degenerative Disc Disease
Disc Age Related Change

It is ubiquitous, correlates only with age, not pain.
<table>
<thead>
<tr>
<th>TEST</th>
<th>AUTHOR YEAR</th>
<th>PTS (n)</th>
<th>AGE RANGE (mean)</th>
<th>DISC HERNIATION</th>
<th>DISC BULGE</th>
<th>DISC DEGENERATION</th>
<th>CENTRAL CANAL STENOSIS</th>
<th>ANNULAR FISSURE</th>
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<tbody>
<tr>
<td>X-Ray</td>
<td>Hult 1954</td>
<td>1200</td>
<td>40-44 55-59</td>
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<td>143</td>
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<td>300</td>
<td>(51)</td>
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<tr>
<td>CT</td>
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<td>51</td>
<td>(40)</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>MRI</td>
<td>Weinreb 1989</td>
<td>86</td>
<td>(28)</td>
<td>9% 44%</td>
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<td>MRI</td>
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<td>53</td>
<td>&lt; 60 ≥ 60</td>
<td>22% 36%</td>
<td>54% 79%</td>
<td>46% 93%</td>
<td>1% 21%</td>
<td></td>
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<tr>
<td>MRI</td>
<td>Jensen 1990</td>
<td>98</td>
<td>(42)</td>
<td>28% 52%</td>
<td></td>
<td></td>
<td></td>
<td>7%</td>
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<tr>
<td>MRI</td>
<td>Boos 1995</td>
<td>46</td>
<td>(36)</td>
<td>76% 51%</td>
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<td></td>
<td>85%</td>
</tr>
<tr>
<td>MRI</td>
<td>Stadnik 1998</td>
<td>36</td>
<td>(42)</td>
<td>33% 81%</td>
<td></td>
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<td></td>
<td>56%</td>
</tr>
<tr>
<td>MRI</td>
<td>Weishaupt 1998</td>
<td>60</td>
<td>(35)</td>
<td>60% 28%</td>
<td></td>
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<td></td>
<td>20%</td>
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<tr>
<td>MRI</td>
<td>Jarvik 2001</td>
<td>148</td>
<td>(54)</td>
<td>38% 64%</td>
<td></td>
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<td>10% 38%</td>
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</table>
Internal Disc Disruption (IDD)

• In contrast, IDD is a specific entity: isolated, radial fissures
  - Nucleus pulposis  Annulus fibrosis
• This is not age-related change
• IDD correlates with axial pain
Internal Disc Disruption: Etiology

• IDD appears to be associated with endplate fracture

• Endplate fracture causes, over time:
  - Reduction in water, proteoglycans
  - Delamination
  - Reduction in pressure within the nucleus

Cyclic stress applied over time.
Internal Disc Disruption: Etiology

Fatigue failure of the subchondral endplate

Occurs with cyclic loading:

@ 37-50% of Ultimate Tensile Strength (UTS); failure at 2,000 or 1,000 cycles

@ 50-80% UTS; failure at 100 cycles

These are physiologic loads


The biomechanical effect of the endplate disruption can be detected & quantified:

**STRESS PROFILOMETRY**

Distribution

Magnitude

of stresses within and across the disc


Stress Profilometry

A pressure transducer is inserted across a diameter of the disc & slowly withdrawn while intradiscal pressures are measured.
Stress Profilometry

A pressure transducer is inserted across a diameter of the disc & slowly withdrawn while intradiscal pressures are measured.
A pressure transducer is inserted across a diameter of the disc & slowly withdrawn while intradiscal pressures are measured.
Stress Profilometry: Normal Disc

2MPa

posterior

anterior

© N Bogduk 201
Stress Profilometry: Normal Disc

2MPa

STRESS

posterior  anterior

np
Stress Profilometry: Normal Disc

Stress

2MPa

posterior  anterior

© N Bogduk 201
Stress Profilometry: Normal Disc

- **STRESS**: 2MPa
- **posterior** to **anterior**
Stress Profilometry: Normal Disc

Stress

2MPa

posterior anterior

© N Bogduk 2012
Stress Profilometry: Internal Disc Disruption

2MPa

posterior   anterior

np

© N Bogduk 2012
Internal Disc Disruption: Etiology

ENDPLATE FATIGUE FRACTURE

• Precipitates degradation of nuclear matrix
  - Inflammatory response
  - Nutritional / biochemical (pH) insults

• Nuclear dehydration
  - Unable to accept and disburse load
  - Load to transferred to posterior annulus
Internal Disc Disruption: Etiology

• **Evolution of radial fissures**
  - Excessive load on posterior annulus
  - Failure of internal bracing effect of pressurized nucleus
  - Inward buckling, tearing of annular fibers

• **Characteristics of radial fissures**
  - Most common posterolaterally
  - Single or few
  - Unique lesion of IDD
Internal Disc Disruption (IDD)
Internal Disc Disruption (IDD)

RADIAL FISSURE
Internal Disc Disruption (IDD)

CIRCUMFERENTIAL FISSURE
Internal Disc Disruption (IDD)

Grade I

Grade II

Grade III

Grade IV

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Internal Disc Disruption: Etiology

GENERATION OF PAIN

• Pain associated with grade III, IV fissures
  - Allows access of nuclear material to outer third of annulus, nociceptive apparatus
  - Chemical stimulation (Nitric oxide) of nociception

• Excess load on posterior annulus
  - Mechanical stimulation of nociceptors
As important as it is to recognize these macroscopic findings, there are equally important changes occurring within the microenvironment of the disc.
Disc Age Related Change or “Degeneration”
Consequence of Imbalance of Synthesis / Degradation

<table>
<thead>
<tr>
<th></th>
<th>NUCLEAR MATRIX</th>
<th>ANNULUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molecular</strong></td>
<td>Altered PGs</td>
<td>Cross-linking</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
<td></td>
</tr>
<tr>
<td><strong>Microscopic</strong></td>
<td>Cracks</td>
<td>Fibrosis</td>
</tr>
<tr>
<td></td>
<td>Tears</td>
<td></td>
</tr>
<tr>
<td><strong>Macroscopic</strong></td>
<td></td>
<td>Thinning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fragmentation</td>
</tr>
<tr>
<td><strong>Biomechanical</strong></td>
<td></td>
<td>Depressurized</td>
</tr>
<tr>
<td><strong>Imaging</strong></td>
<td></td>
<td>Loss of T2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>signal</td>
</tr>
</tbody>
</table>

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Disc Nucleus

• Nucleus Pulposus is a gel-like matrix containing proteoglycans and type II collagen. The negative charge of the glycosaminoglycans attracts and holds onto water.

• Hydration helps with maintenance of disc height and load-bearing capacity of the disc.

• Chondrocytes within the NP synthesize and maintain matrix.

• Degenerative Disc Disease is related to loss of proteoglycan and water content leading to inability of the disc to resist compressive loading.
The Lumbar Discovertebral Complex

- **Homeostasis**: Chondrocytes control synthesis and degradation of the nuclear matrix:
  - Proteoglycans, collagen, $H_2O$

- **Hostile biochemical environment**
  - No direct blood supply
  - Low $O_2$ tension
  - Anabolic metabolism pH (6.9-7.1)

- A variety of insults may upset this homeostatic balance
  - Metabolic disease (DM)
  - Genetic factors
  - Traumatic endplate injury
  - Nutritional (smoking, vascular disease)
  - Infectious
HOMEOSTASIS
The Balance of Synthesis and Degradation
Growth Factors

• Up-regulate ECM proteins:
  - Transforming growth factor (TGF-beta)
  - Insulin-like growth factor 1 (IGF-1)
  - Epidermal growth factor (EGF)
  - Platelet-derived growth factor
  - Bone morphogenetic proteins (BMP)
  - BMP-7 (OP-1), BMP-2, GDF-5

• Increase Anabolic Activity

• Down-regulate inflammatory cytokines:
  - Interleukin (IL-1, IL-6)
  - Tumor necrosis factor-alpha (TNF)
  - Matrix metalloproteinases (MMPs)
  - Nitric oxide (NO)
  - Prostaglandin E2 (PGE2)

• Decrease Catabolic Activity
It’s Been Said….
The Disc
is where good therapies
go to
DIE
Disc Biologics

- Disc restorative solution
- Ozone
- Methylene blue
- Fibrin sealant
- IDET
- Biaculoplasty
- Nucleoplasty
- Isolated Growth Factors
- Disc Chondrocytes
- Mesenchymal Stem Cells
- Platelet Rich Plasma
Behavior of Mesenchymal Stem Cells in the Chemical Microenvironment of the Intervertebral Disc

Karin Wuertz, PhD*, Karolyn Godburn, BS*, Cornelia Neidlinger-Wilke, PhD†, Jocelyn Urban, PhD‡, and James C. Iatridis, PhD*

*Spine Bioengineering Lab, School of Engineering, University of Vermont, VT †Institute of Orthopaedic Research and Biomechanics, University of Ulm, Germany ‡Physiology Laboratory, University of Oxford, England

Study to determine the microenvironmental conditions that are necessary for MSC-based tissue repair
MSCs isolated from mature and young rats.
Cultured in monolayer suspension similar to IVD.
The response examined measuring gene expression, proliferation and viability

- IVD-like low glucose enhanced matrix biosynthesis and maintained cell proliferation

- IVD-like high osmolarity and low pH conditions were critical factors that reduced biosynthesis and proliferation of young and mature MSCs.

- Combining all conditions resulted in decreased cell proliferation and decreased expression of normal matrix
Cell Viability

Cell Proliferation

Standard conditions

IVD conditions

Figure 3. Cell proliferation under different medium conditions, compared with standard medium. Data are presented as mean ± SEM with P < 0.05 for n = 5 (mature rats) and n = 6 (young rats). Asterisks above bars mark a significant change in cell number relative to standard conditions.

Figure 4. Cell viability under different medium conditions, compared with standard medium; representative pictures of one donor (mature rat) are shown.
RESULTS
The initial search identified 1393 articles, of which 6 studies were eligible for this review. All studies were published from 2006 to 2015 and 74 patients were included.

SAFETY
There were no related adverse events reported in all of the included studies. There was no tumor formation observed in any clinical cases in stem cell transplantation during fellow up period.
Decreased pain score (NRS & VAS, 0-100) after treatment: The pooled mean difference in pain score from baseline to follow-up points was 44.2 points decreased (95%CI: -61.8 to -26.5, p<0.001, $I^2=99.4\%$)
Oswestry Disability index decrease after treatment

<table>
<thead>
<tr>
<th>Study name</th>
<th>Difference in means</th>
<th>Standard error</th>
<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Domagoj Coric 2013</td>
<td>-27.649</td>
<td>0.555</td>
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<td>-28.737</td>
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<td>Hans Joerg Meisel 2006</td>
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<td>2.665</td>
<td>7.104</td>
<td>-47.307</td>
<td>-36.859</td>
<td>-15.789</td>
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<td>Kenneth Pettine 2015</td>
<td>-36.768</td>
<td>0.389</td>
<td>0.136</td>
<td>-37.491</td>
<td>-36.044</td>
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<td>Luis Orozco 2011</td>
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<td>2.205</td>
<td>4.861</td>
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<td>-36.123</td>
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<td>-32.249</td>
<td>4.770</td>
<td>22.751</td>
<td>-41.597</td>
<td>-22.900</td>
<td>-6.761</td>
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Heterogeneity

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<tr>
<th>Q-value</th>
<th>df(Q)</th>
<th>P-value</th>
<th>I-squared</th>
<th>Tau squared</th>
<th>Tau</th>
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<td>887.1</td>
<td>4</td>
<td>0.000</td>
<td>99.5</td>
<td>111.2</td>
<td>10.5</td>
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</table>

Decreased Oswestry Disability Index (ODI, 0-100) after treatment: The pooled mean difference in ODI from baseline to follow-up points was 32.2 points decreased (95%CI: -41.6 to -22.9, p<0.001, I²=99.5%).
Key Points

• Cell-Based Transplantation Therapy
  - (Mesenchymal stem cells or chondrocytes) for patients who have discogenic low back pain is associated with improved pain relief and Oswestry disability index.

• The optimal cell therapy protocol for discogenic low back pain remains unclear.

• Clinical benefits of cell therapy for patients with discogenic low back pain need further investigation and reevaluation to test the clinical efficacy.
# Ongoing Trials

<table>
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<tr>
<th>Sponsor</th>
<th>N</th>
<th>Phase</th>
<th>Design</th>
<th>Cell type</th>
<th>Dosage</th>
<th>Outcomes</th>
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<tbody>
<tr>
<td>Red de Terapia Celular</td>
<td>24</td>
<td>I-II</td>
<td>RCT, 2 arms</td>
<td>Allogeneic BMSC, cultured</td>
<td>25M</td>
<td>VAS, ODI, SF-12, MRI, AEs</td>
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<td>Mesoblast</td>
<td>330</td>
<td>III</td>
<td>RCT, 3 arms</td>
<td>Allogeneic MPC</td>
<td>6M</td>
<td>VAS, ODI</td>
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<td>Bioheart</td>
<td>100</td>
<td>II</td>
<td>Open label, single arm</td>
<td>Autologous AMSC + PRP</td>
<td>Will vary</td>
<td>VAS, ODI</td>
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<td>Biostar</td>
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<td>I-II</td>
<td>Open label, single arm</td>
<td>Autologous AMSC</td>
<td>40M</td>
<td>VAS, MRI, AEs</td>
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<td>Inbo Han, CHA University</td>
<td>10</td>
<td>I</td>
<td>Open label, single arm</td>
<td>Autologous AMSC</td>
<td>20-40M + HA</td>
<td>VAS, ODI, SF-36, MRI, DHI, AEs</td>
</tr>
</tbody>
</table>

**Legend:**
- **N**: Number of participants
- **Phase**: Clinical trial phase
- **Design**: Study design
- **Cell type**: Source of stem cells
- **Dosage**: Treatment dosage
- **Outcomes**: Clinical outcomes measured
Ongoing trials at Precision Spine Care

“A Multi-Center, Randomized, Controlled, Double-blind Study Evaluating Safety and Efficacy of Hemocyte Autograft for Treatment of Single-Level and Multi-Level Lumbar, Thoracic and Cervical Discogenic Pain”

Study Overview
• Treatment of discogenic pain in the cervical, thoracic or lumbar spine
• No exclusion for extravasion
• Utilize a high-yield PRP low in monocytes and neutrophils, and utilizing a concentration of the PPP creating a concentration and scaffold of proteins including A2M and fibrinogen
• Double blinded and randomized
• Functional endpoint for the neck – Average patient specific functional scale (PSFS) – Numeric Parin rating scale – Oswestry disability (ODI)
Ongoing Studies at Precision Spine Care

Platelet Rich Plasma vs. Bone Marrow Aspirate for Lumbar Intradiscal Injections

• A Multicenter Prospective Randomized Controlled Trial in Patients with Internal Disc Disruption
• 4 centers in United States, Funded
• Total of 60 patients randomized into control, PRP and BMA group
• Follow up until 1 year
• Primary outcome: Safety and efficacy
• Secondary outcome: Patient satisfaction, Changes in disc morphology, Change in medication use, spine surgery
Allogeneic MSC’s
Mesoblast
Safety and Preliminary Efficacy Study for Disc Repair (Mesoblast)

- MPC’s for Lumbar Disc Disease in Adults
- Primary Objective: Safety @ 6 months
- Secondary Objective: Efficacy
- 100 Patients Worldwide
- Randomized to:
  - Normal Saline
  - Hyaluronic Acid (HA)
  - Low Dose (6 Million) MPC’s in HA
  - High Dose (18 Million) MPC’s in HA

1. Safety and Preliminary Efficacy Study of Mesenchymal Precursor Cells (MPCs) in Subjects With Lumbar Back Pain
MPC groups have a greater proportion of patients with at least a 50% improvement in back pain or minimal/no residual back pain at 12 months relative to controls.

Proportion of patients with 50% back pain reduction at 12 months:
- Pooled Controls: 33.3%
- 6M MPCs: 69.2%
- 18M MPCs: 61.5%

Proportion of patients with no back pain reduction at 12 months:
- Pooled Controls: 50%
- 6M MPCs: 18.1%
- 18M MPCs: 42.3%

* from post-hoc analysis
Take away points from MESOBLAST STUDY

• MPC’s for Lumbar Disc Disease in Adults
• Primary Objective: Safety at 6 months
• Secondary Objective: Efficacy
• 100 Patients Worldwide

• Randomized to:
  - Normal Saline
  - Hyaluronic Acid (HA)
  - Low Dose (6 Million) MPC’s in HA
  - High Dose (18 Million) MPC’s in HA
Autologous MSC’s
BMC
Interventional Disc Repair by Autologous Mesenchymal Bone Marrow Cells: A Pilot Study

• 10 patients, LBP > 6 months, mean age 35, mean number of cells injected 23 x 10^6
• Improved disability in 7/10 and pain in 9/10 patients.
• Improved T2 signal on MRI, but not disc height.

## Two-Year Results of the Use of Autologous Point-of-Care Bone Marrow Concentrate for the Treatment of Discogenic Low Back Pain

International Orthopaedics | 2015 | Kenneth Pettine, M.D.

<table>
<thead>
<tr>
<th></th>
<th>One-Level</th>
<th>Two-Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>13</td>
<td>13</td>
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<tr>
<td>Median Age</td>
<td>40 (Range 25-51)</td>
<td>37 (Range 18-61)</td>
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<tr>
<td>Average BMI</td>
<td>27.1</td>
<td>26.1</td>
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<td>Cause of Injury</td>
<td>Trauma</td>
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<tr>
<td></td>
<td>Unknown</td>
<td>6</td>
</tr>
<tr>
<td>Discs of Modified Pfirrmann Grade:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>V</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>VI</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>VII</td>
<td>3</td>
<td>8</td>
</tr>
</tbody>
</table>

Stem Cells, 2015 (1-yr results)

### Clinical Study

- Failed conventional therapy >3 mo.
- Eligible for surgical relief
- IRB cleared protocol

- Failed conventional therapy >3 mo.
- Eligible for surgical relief
- IRB cleared protocol

Stem Cells, 2015 (1-yr results)

- Failed conventional therapy >3 mo.
- Eligible for surgical relief
- IRB cleared protocol
Disc Injection Therapy

60cc BMA drawn from the posterior iliac crest

BMA centrifuged for 12 min. 6cc bone marrow concentrate (BMC) drawn

Total procedure time: 30-45 min.
Autologous bone marrow concentrate intradiscal injection for the treatment of degenerative disc disease with three-year follow-up

Kenneth A. Pettine¹ · Richard K. Suzuki² · Theodore T. Sand² · Matthew B. Murphy²,³

ODI Scores for 3 Year Survivors

VAS Scores for 3 Year Survivors by # of Discs Injected

Disc Injection Therapy
3-year Survivor Cohort (n = 20)
Progenitor Cells & Disc Injections

% Improvement from Baseline 3 years post-BMC Injection (20 surviving of 26)

<table>
<thead>
<tr>
<th></th>
<th>All Patients</th>
<th>CFU-F &lt;2000</th>
<th>CFU-F &gt;2000</th>
<th>CD34+ &lt;1 mil</th>
<th>CD34+ &gt;2 mil</th>
<th>One Level</th>
<th>Two Levels</th>
<th>Age &lt;30</th>
<th>Age 30-45</th>
<th>Age &gt;45</th>
</tr>
</thead>
<tbody>
<tr>
<td>% ODI Improvement</td>
<td>67%</td>
<td>41%</td>
<td>86%</td>
<td>38%</td>
<td>79%</td>
<td>71%</td>
<td>64%</td>
<td>64%</td>
<td>72%</td>
<td>56%</td>
</tr>
<tr>
<td>% VAS Improvement</td>
<td>73%</td>
<td>48%</td>
<td>90%</td>
<td>42%</td>
<td>83%</td>
<td>77%</td>
<td>70%</td>
<td>74%</td>
<td>75%</td>
<td>66%</td>
</tr>
</tbody>
</table>

8 of 20 patients w/ 1-yr MRI improved a Pfirrmann grade; 6/8 had >2000 MSCs/cc
Disc Injection Therapy

Patient Outcomes (September 2015)

- 8 patients showed a single grade level improvement in their Pfirrmann score at 1-yr (40% of enrolled patients)
- 3 1-level and 3 2-level patients progressed to surgical repair by 3-yr (77% avoided surgery through three years)
- 2 Patients received a 2nd injection two years ago; no additional 2nd injections have occurred
- 73% average reduction in pain and 67% average improvement in ODI at 3-yr for the surviving 20 patients
- >2000 CFU-F patients: 86% improvement in ODI/90% reduction in VAS; <2000 CFU-F: 41% ODI/48% VAS
How does this compare to surgery?

- The overall improvement with an artificial disc was a 57% improvement in ODI and 63% improvement in VAS.
- The overall improvement with a lumbar fusion was 43.3% improvement in ODI and 52.7% improvement in VAS.
- This compares with a 71% improvement in ODI and 70% improvement in VAS in this BMC injection group.
- The difference in hospital stay (2.2 to 5 days) in the surgery groups versus one hour in the BMC group is significant. Also very significant is the difference in cost between surgery and the BMC procedure.

Platelet Rich Plasma

PRP
LR-PRP Disc Double-Blind RCT

• 47 patients:
  - 29 Contrast Dye+LR-PRP
  - 18 Contrast Dye only
• NRS, SF-36, NASS scores improved.
• Statistically significant improvement in best NRS scores at 8 weeks.

MRI Pre- and Post L5-S1 PRP

Progress through 24mo. Post-PRP

NRS Pain

Pain Right Now: -6 points
Pain at Best: -4 points
Pain at Worst: -6 points

24 month Δ
LR-PRP Disc Double-Blind RCT

VAS > 50%, ODI > 30 achieved in:
• 14% (3/22) patients at 1 month
• 32% (7/22) patients at 2 months
• 47% (9/19) patients at 6 months

Alpha-2-Macroglobulin (A2M) for Disc

• A2M is derived from PPP
• Trial of 24 patients, assessed for Fibronectin-Aggregate Complex (FAC) via disc lavage.
• 12 out of 24 patients (50%) were FAC (+).
Intradiscal Alpha-2-Macroglobulin

3 and 6 months ODI and VAS for FAC (-) and FAC (+) patients.

Black = FAC (-) | Red = FAC (+)
LP-PRP: Intradiscal, Intra-articular facet, Epidural Space

- 86 patients, LBP>3M, prospective trial. PRP activated with CaCl.
- VAS Scores
  - Pre-Injection 8/10
  - 1 month 4/10
  - 2 months 2/10
  - 6 months 1/10

Biologics and Spine Pain

• Can biologics slow or even reverse the cascade of DDD or OA?

• Will transplantation of cells into the disc improve the production of proteoglycan rich extracellular matrix and lead to better hydration and biomechanical properties?
Biologics and Spine Pain

• The Degenerative disc and OA joint contains:
  - Elevated levels of matrix metalloproteinases
  - Elevated levels of IL-1

• Bone marrow and PRP contains:
  - alpha-2-Macroglobulin (inhibitor of MMP’s)
  - IL-1RAP (Interleukin-1 receptor accessory protein- reduces the pain associated with IL-1)
Regenerative Injection Therapy

BMC is a multi-modal therapeutic agent
It contains:
  - Biochemical Modifiers
  - MSC’s, EPC’s, HSC’s and other progenitor cells
• Takes control of the “pro-inflammatory” environment in the disc or joint.
Mesenchymal stem cells in regenerative medicine: Focus on articular cartilage and intervertebral disc regeneration

Stephen M. Richardson a,1, Gauthaman Kalamegam b,1, Peter N. Pushparaj b, Csaba Matta c, Adnan Memic d, Ali Khademhosseini e,f,g,h, Reza Mobasher i, Fabian L. Poletti i, Judith A. Hoyland a,k, Ali Mobasher i,c,j,b, *

- Review article focusing on stem-cell based therapies for cartilage and IVD repair
The degenerative microenvironment is characterized by high levels of catabolic mediators and inflammatory cytokines.

The addition of MSC leads to the increased expression of growth, anti-inflammatory, and anti-catabolic factors.

These lead to the restoration of a healthy anabolic cell phenotype and tissue regeneration.

- AC/NP markers: SOX-9, Type II Collagen, Aggrecan, Versican.
- NP markers: KRT18/19, CA12, Brachyury, CD24.

Tissue regeneration

MMPs, ADAMTSs, Cytokines
RM

- Regenerative Medicine (RM) is an emerging area of medical practice.
- Its use in the treatment of common musculoskeletal diseases is supported by Level 1 evidence.
- Further research is necessary to elucidate the parameters that optimize outcomes
  - patient selection
  - pre- and post-injection protocols
  - choice of RM injectate.
The End
Thank you for your time.

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