1. DEGENERATIVE DISC DISEASE

A. Clinical Response: Clinical response demonstrates increasing evidence of effective degenerative disc disease reversal by increasing disc height, increasing disc water content, and improved appropriate gene expression. In addition to physical examinations prior to stem cell procedure and 6 months post-procedure, laboratory test results serve as evidence of repair process. Recognized lab tests for monitoring Degenerative Disc Disease include:

- Imaging Test (X-Ray, CT and MRI Scan)
- Electromyography (EMG, Myogram, or Nerve Conduction Test)
- Discography • Bone Scan • Blood Tests

2. PRELIMINARIES

A. Background: Degenerative disc disease is one of the more common causes of lower back and neck pain, causing radiating pain from damaged discs in the spine. These discs act as shock absorbers, which allow the joints in the spine to move easily. As a person ages, the spinal discs naturally undergo degenerative changes, but not all people will experience symptoms as a result of these changes (asymptomatic). Most commonly, symptoms are seen in 30 to 50 year olds. By the age of 50, 85% of the population will show some evidence of disc degeneration. With more than 65 million Americans suffering from lower back pain each year, changes in the discs have been found in patients who smoke cigarettes and those who do heavy physical work (heavy lifting). Obese patients are also more likely to have symptoms of degenerative disc disease.

B. Types of the Condition: As one ages the spinal discs degenerate. This breakdown can occur throughout anywhere in the spine, but most often occurs in the lumbar (lower back) and cervical (neck) regions.

- Lumbar Degenerative Disc Disease: This type of degenerative disc disease causes a lower back pain. Depending on the severity, lumbar degenerative disc disease may produce leg pain, numbness, and tingling. If there is weakness in the leg muscles (foot drop), this is an indicator for nerve root damage.

- Cervical Degenerative Disc Disease: Cervical Degenerative Disc Disease is a common cause of neck pain. Most often described as a “stiff neck.” Numbness, tingling, or even weakness in the neck, arms, or shoulders is known to be apparent when dealing with this type of condition; which is a result from the nerves in the cervical area becoming irritated or pinched. Cervical degenerative disc disease is much less common than lumbar degenerative disc disease.

C. Causes: Aging itself is known to be a cause of degenerative disc disease in some patients. Additional causes are: loss of fluid in discs (reduces the shock absorbance abilities and flexibility, thins discs narrowing distance between vertebrae) and tiny tears/cracks in outer later of the discs (forces inner material outside though the cracks causing a bulge or rupture). Injuries are also identified in playing a role in degenerative disc disease. Discs do not have a blood supply, therefore if injury occurs, the discs cannot repair themselves and can start a degenerative cascade. Additionally, there has been strong evidence that there is a genetic component to disc degeneration. Patients with an immediate family member with disc-related low back pain have been found to be four times more likely to have low-back pain themselves.

D. Treatment: Treatments for degenerative disc disease include but are not limited to occupational and physical therapies, special exercises, medications, losing weight, and surgery.

Non-Surgical Options:

- Wearing a brace or corset.
- Special exercises to build back muscles.
- Medications: non-steroidal anti-inflammatory drugs (NSAIDs), steroids and sometimes muscle relaxers
- Facet rhizotomy: deadens the nerves around the facet joint, preventing pain signals from reaching the brain. Recommended if patient responds to facet joint injections.
• Intradiscal electrothermal annuloplasty (IDET): discs are heated up using discography CT with a copper coil. At the right temperature the disc hardens, making it better at resisting weight-bearing movements.

**Surgical Options:**

• **Stabilization Surgery:** Spinal Fusion: two vertebrae are fused together to provide stability.

• **Decompression Surgery:** facetectomy (removing the facet joint), foraminotomy (enlarging the opening of the foramen so the nerve is not compressed), laminectomy (removing all or part of the lamina to relieve pressure on the spinal cord), laminotomy (like a laminectomy, but the opening is larger, giving the nerves more room)

### 3. POTENTIAL BENEFITS OF STEM CELL TREATMENT

Mesenchymal Stem Cells (MSCs) display long-term proliferation, efficient self-renewal, and multipotent differentiation [1]. MSCs have the ability to end and reverse degeneration of spinal discs. Studies have shown increased disc height by 23.6%, disc water content, and gene expression after stem cell treatment [2]. One of the main biological functions of MSCs is their ability to reproduce cartilage and bone tissue cells (multipotent differentiation capability). This is important in degenerative disk disease, since a large number of cells from the outer ring (annulus fibrosus) and the inner gelatinous (nucleus pulposus) of the disks are of a cartilaginous nature [3].


### 4. TREATMENT & DELIVERY METHOD REQUIRED

A. **Typical Recommended Treatment:** Adipose Derived Stem Cells suspended in Platelet Rich Plasma.

B. **Typical Delivery Method Required:** Autologous Ad-SVF containing adult stem cells are infused in about 1.5mL of Platelet Rich Plasma and injected via a C-ARM intradiscally.

C. **Recommended dosing:** Recommended repeat dosing MSC’s every 3-4 months and based on patient’s symptoms.

### 5. POTENTIAL RISKS OF STEM CELL INJECTION(S)

There are possibilities for unwanted effects related to the local anesthesia, harvesting procedure, and injection of stem cells. Even with the most established protocol, adequate technique, and careful administration; a medical team may encounter uncontrollable events. Although there is no guarantee of any results, excellent results can be attained. The medical professional provides services in the most responsible, professional and diligent manner, always considering that surgeries imply risks. The risks of complications of adipose tissue harvesting and stem cell infusion are very low. Possible risks include but are not limited to:

- Pain at site of injections
- Bleeding at injection site
- Malaise
- Low-grade fever
- Hot flashes
- Itching at injection site
- Vascular spasm or obstruction
- Bruising
- Nerve or muscle injury
- Allergic reaction
- Dizziness
- Nausea
- Vomiting

Minor complications may include temporary arm or leg weakness, soreness at the injection site, the temporary increase in symptoms and spinal headache. Extremely rare complications can occur including infection, prolonged bleeding, and paralysis.

### 6. FREQUENTLY ASKED QUESTIONS

1. **What are adults stem cells and how do they work?**
   They are undifferentiated cells found in tissues in the body, responsible for maintaining and repairing surrounding cells. They have the ability to differentiate into various cell types, which is what makes them a potential treatment to alleviate and improve degenerative conditions.

2. **What is Adipose-derived stem cells and what makes it unique?**
   Adipose-derived stem cells are stem cells found in the adipose tissue of the patient. The adipose tissue is an abundant source of mesenchymal stem cells which have shown the most healing potential. Adipose Stem cells are autologous (patients stem cells); therefore having low risk of immune rejection once the therapy has been completed.
3. How can stem cell therapy help treat Degenerative Disc Disease?

Stem cell therapy has been seen to help reverse degenerative disc disease by increasing disc height, increasing disc water content, and improving appropriate gene expression. Surrounding ligaments and soft tissue that has been damaged around the area have the ability to heal as well.

4. How will the stem cells be delivered to the patient?

Autologous Ad-SVF containing adult stem cells are infused in about 1.5mL of Platelet Rich Plasma and injected via a C-ARM intradiscally. The surrounding ligaments and soft tissue can be addressed also.

5. How long do you think it would be before I see some improvement?

The response to the treatment varies from patient to patient. Some patients see a response within the first three months, while many studies have shown patients can improve 6-12 months after a stem cell injection. This is an ongoing research topic and results are not guaranteed.

6. How long does the procedure take?

The procedure will take approximately 3-4 hours. If you are traveling out of town, you will need to stay in the local area the night of the procedure.

7. SUPPORTING ARTICLES


Effects of the intradiscal implantation of stromal vascular fraction plus platelet rich plasma in patients with degenerative disc disease.

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Erratum in

• Erratum to: Effects of the intradiscal implantation of stromal vascular fraction plus platelet rich plasma in patients with degenerative disc disease. [J Transl Med. 2017]

Abstract

BACKGROUND:

Stromal vascular fraction (SVF) can easily be obtained from a mini-lipoaspirate procedure of fat tissue and platelet rich plasma (PRP) can be obtained from peripheral blood. The SVF contains a mixture of cells including ADSCs and growth factors and has been depleted of the adipocyte (fat cell) population. We evaluated the safety and efficacy of administering SVF and PRP intra-discally into patients with degenerative disc disease.

METHODS:

A total of 15 patients underwent a local tumescent liposuction procedure to remove approximately 60 ml of fat tissue. The fat was separated to isolate the SVF and the cells were delivered into the disc nucleus of patients with degenerative disc disease. The subjects were then monitored for adverse events, range of motion, visual analog scale (VAS), present pain intensity (PPI), Oswestry Disability Index (ODI), Beck Depression Inventory (BDI), Dallas Pain Questionnaire and Short Form (SF)-12 scores over a period of 6 months. Safety events were followed for 12 months.

RESULTS:

No severe adverse events (SAEs) were reported during a 12 month follow up period with no incidences of infection. Patients demonstrated statistically significant improvements in several parameters including flexion, pain ratings, VAS, PPI, and short form questionnaires. In addition, both ODI and BDI data was trending positive and a majority of patients reported improvements in their Dallas Pain Questionnaire scores.

CONCLUSIONS:

Overall, patients were pleased with the treatment results. More importantly, the procedure demonstrated a strong safety profile with no severe adverse events or complications linked to the therapy. Trial registration NCT02097862. Name of registry: www.clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/NCT02097862?term=bioheart&rank=6. Date of registration: March 25, 2014; Date of enrollment: March 2014
Adipose-derived stem cells improve the viability of nucleus pulposus cells in degenerated intervertebral discs.
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Abstract
Patients with degenerative disc disease (DDD) experience serious clinical symptoms, including chronic low back pain. A series of therapies have been developed to treat DDD, including physical therapy and surgical treatment. However, the therapeutic effect of such treatments has remained insufficient. Recently, stem cell-based therapy, in which stem cells are injected into the nucleus pulposus in degenerated intervertebral disc tissue, has appeared to be effective in the treatment of DDD. In the present study, the effect of adipose-derived stem cells on degenerated nucleus pulposus cells was investigated using a co-culture system to evaluate the biological activity of degenerated nucleus pulposus cells. Human degenerated nucleus pulposus tissue was obtained from surgical specimens and the adipose-derived stem cells were derived from adipose tissue. The degenerated nucleus pulposus cells were cultured in a mono-culture or in a co-culture with adipose-derived stem cells using 0.4-μm Transwell inserts. The results indicated that adipose-derived stem cells were able to stimulate matrix synthesis and the cell proliferation of degenerated nucleus pulposus cells, promoting the restoration of nucleus pulposus cells in the degenerated intervertebral disc.

PMID: 26059030 DOI: 10.3892/mmr.2015.3895

3. Stem cells in preclinical spine studies

Abstract
Review Article
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BACKGROUND CONTEXT: The recent identification and characterization of mesenchymal stem cells have introduced a shift in the research focus for future technologies in spinal surgery to achieve spinal fusion and treat degenerative disc disease. Current and past techniques use allo- graft to replace diseased tissue or rely on host responses to recruit necessary cellular progenitors. Adult stem cells display long-term proliferation, efficient self-renewal, and multipotent differentiation.

PURPOSE: This review will focus on two important applications of stem cells in spinal surgery: spine fusion and the management of degenerative disc disease.

STUDY DESIGN: Review of the literature.

METHODS: Relevant preclinical literature regarding stem cell sources, growth factors, scaffolds, and animal models for both osteogenesis and chondrogenesis will be reviewed, with an emphasis on those studies that focus on spine applications of these technologies.

RESULTS: In both osteogenesis and chondrogenesis, adult stem cells derived from bone marrow or adipose show promise in preclinical studies. Various growth factors and scaffolds have also been shown to enhance the properties and eventual clinical potential of these cells. Although its utility in clinical applications has yet to be proven, gene therapy has also been shown to hold promise in pre-clinical studies.

CONCLUSIONS: The future of spine surgery is constantly evolving, and the recent advancements in stem cell–based technologies for both spine fusion and the treatment of degenerative disc disease is promising and indicative that stem cells will undoubtedly play a major role clinically. It is likely that these stem cells, growth factors, and scaffolds will play a critical role in the future for replacing diseased tissue in disease processes such as degenerative disc disease and in enhancing host tissue to achieve more reliable spine fusion.

PMID: 26059030 DOI: 10.3892/mmr.2015.3895

3. Promising stem cell treatment of degenerative disc disease


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ROCHESTER, Minn., March 8, 2014 -- Stem cell transplantation proved viable and effective in halting or reversing degenerative disc disease of the spine: a meta-analysis of animal studies showed, in a development expected to open up research in humans. Recent developments in stem cell research have made it possible to assess its effect on intervertebral disc (IVD) height, Mayo Clinic researchers reported in a scientific poster today at the annual meeting of the American Academy of Pain Medicine. In preclinical animal studies stem cell therapy for disc degenerative disease was shown to be a potentially effective treatment for the very common condition that affects people's quality of life and productivity.

4. Cell Therapy for Age Related Intervertebral Disc Pathologies

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Abstract — Any spinal pathology is accompanied by a significant loss in the quality of life and a high disability rate. The rate of occurrence of spinal impairments increases with advancing age. Spinal impairments may be etiologically different and characterized by a wide range of significant and very diverse clinical symptoms. At the same time, the "lower back pain" (as well as the back pain) syndrome is the most common complaint. The main cause for the development of the syndrome is degenerative disc disease (DDD) of a nonspecific nature that leads to irreversible structural damage to intervertebral discs. Surgical DDD treatment methods, including those based on bone tissue autografting, are not radical; this compels researchers to search for alternative approaches. This review analyzes the principles of regenerative cellular and cell replacement therapies that are based on the use of a variety of cell types, in the treatment of intervertebral pathologies and compares various cell substrates for these therapies.

Keywords: spine, intervertebral joints, age-related degeneration, cell therapy, stem cells DOI: 10.1134/S2079057012040029

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