

An Evaluative Study of Patient-Based Outcomes Due to IntraDiscNutrosis Treatment

FDA Device / Drug Status used for this research: Accu-SPINA ® System

Randomized, independent medical study conducted by research scientist Paul Thomlinson, Ph.D. and Dr. Joe Mannella of The Disc Institute.

INTRODUCTION

The treatment under evaluation in this study is called IntraDiscNutrosis®, a non-surgical therapeutic intervention for patients with bulging, herniated, degenerative discs and other discogenic disorders. These conditions result in substantial back and/or neck pain, radiculopathies and extremity pain and/or numbness, along with associated disabilities and functional limitations. What distinguishes this treatment from other forms of treatment (e.g., physical therapy, surgery, chiropractic, epidural injections, pain management, exercise, stretching, yoga, Pilates, weight loss, etc.) is that (a) it noninvasively and specifically treats the disc directly, and the associated pain indirectly; (b) it treats the problem of why the disc is dying, instead of treating the conditions or symptoms that manifest from a dying disc; (c) it recreates the missing physiology of the disc, so that the established and innate physiological mechanisms are restored and bring back the natural self-repair process to the disc; and (d) it promotes and honors the natural healing process of the disc while all other forms of treatment ignore this in favor of only altering pain perception. Unlike many forms of treatment for these conditions, IntraDiscNutrosis® is not simply a palliative approach to care and has no iatrogenic risks.

BACKGROUND ON PATHOPHYSIOLOGY OF DISC DEGENERATION

Intervertebral disc (IVD) degeneration and associated lesions are strongly associated with back and extremity pain, affect a large proportion of the population and are a burden for the affected patients and because of high

health-care and societal costs (Khan et al., 2017; Wenig, Schmidt, Kohlmann, & Schweikert, 2009). These disorders represent a complex problem with multiple contributing factors, and despite a significant increase in spinal research and number of studies, the pathologic pathway is not fully understood. Although genetic predisposition appears significant (Adams & Dolan, 2012), degenerative pathways are also influenced by factors such as mechanical loading (Fahy, Alini, & Stoddart, 2018; Neidlinger-Wilke et al., 2012) and changes and alterations to the physiochemical environment (Urban & Winlove, 2007) of the disc cells. Of the environmental factors thought to influence degenerative changes in the disc, decreased nutrition is widely thought to be a key contributor (Neidlinger-Wilke & Wilke, 2010).

Normal healthy discs are avascular and nutrient supply and removal of wastes occurs via diffusion through the blood vessels at the cartilaginous end plate. Disc cells require glucose and produce lactic acid at a high rate (Bibby, Jones, Ripley, & Urban, 2005; Maroudas, Stockwell, Nachemson, & Urban, 1975). It is thought that a reduction in supply of required nutrients and water or the failure to remove lactic acid is a major reason for disc degeneration. Disc cells are very sensitive to changes and alterations of nutritional components and accumulation of metabolites.

In vitro experiments have demonstrated that disc cells need to maintain critical concentrations of glucose, a suitable pH and oxygen supply to stay viable and metabolically active (Grunhagen, Wilde, Soukane, Shirazi-Adl, & Urban, 2006; Urban, Smith, & Fairbank, 2004) It has been demonstrated in the literature

that disc cells die if glucose levels fall below around 0.5mM. Also, disc cells are very sensitive to fall in pH arising from accumulation of lactic acid. This accumulation of lactic acid inhibits the production of proteoglycans and increases the activation of matrix-degrading enzymes. All of the above mentioned physiology contributes to degenerative changes to the IVD (Raj, 2008). Some well-designed in vivo studies have examined the effects of controlled dynamic distraction and the effects of mechanical loading on diffusion of solutes in the recent literature. These observations may be related to the IntraDiscNutrosis methodology since this treatment is designed to replicate the normal pump mechanism of the targeted IVD. In the Kroeber study, they were able to induce disc degeneration by axial dynamic loading, presumably due to a complex path mechanism initiated through a change in cell shape, or an adverse biochemical environment produced by water loss. They demonstrated a slowing and declining diffusion of substances through the IVD and a demonstrated a slowing and declining diffusion of substances through the IVD and a deprivation of oxygen that compromised cell viability. As cell density decreased, consequently, synthesis of matrix macromolecules is adversely affected. The accumulated breakdown of matrix materials in turn impairs diffusion. A vicious circle is created, with progressive deterioration in oxygen, nutrient, and waste transport, leading to further cell death and depletion of the matrix (Rinkler et al., 2010).

In the same study the unloaded IVDs demonstrated through histological studies a physiologic organization of the nucleus, annulus and cartilage endplate after distraction. The authors stated that the discs showed signs of tissue regeneration. With increased duration of distraction, the changes became more pronounced with the disappearance clefts or fissures in the annulus fibrosis and less herniation of disc materials or osteophyte formation (Rinkler et al., 2010). The developers of IntraDiscNutrosis®, the treatment under review in this evaluative Study, believe that similar physiological and biochemical mechanisms may be involved in vivo with proper application of approach. This is logical in that one major clinical goal of IntraDiscNutrosis® is the specific targeting of the biomechanical pump mechanism movement restoration of the IVD. The researchers involved in the present study plan to expand research in this area and are clearly encouraged with the clinical results and outcomes detailed later in this report.

BACKGROUND ON THE HEALTH ECONOMICS OF DISC DEGENERATION

A growing number of hospitals and health systems around the country are rethinking how they provide spine care; given the mounting research evidence that too many Americans are undergoing unnecessary spinal procedures and experiencing poor outcomes. The steep jump in spine surgeries in the late 1990s and 2010s has prompted many health insurers to tighten coverage policies for particular indications and procedures, particularly spinal fusion for degenerative disc disease in the lower back. With recent studies (e.g., in *The Journal of Bone and Joint Surgery*) suggesting that the total cost of low back pain to the United States totaled \$33 to \$66 billion (\$39 and \$78 billion when expressed in 2014 dollars)(McCarthy, Hostin, O'Brien, Saigal, & Ames, 2013), it is clearly advisable on multiple levels for there to be an honest re-evaluation on policies and standards of care in this particular segment of care. About 87% of spinal procedures in 2013 were fusion-based, according to the research firm Global Data. There were more than 465,000 fusion operations in the U.S. in 2011, compared with 252,400 in 2001, according to the Agency for Healthcare Research and Quality. The estimated cost of spinal fusion procedures was more than \$12.8 billion in 2011, according to AHRQ. Hospital costs alone for this procedure average \$27,568. Total costs can hit well over six figures for major spinal fusion procedures.

CONCLUDING REMARKS

These sobering realities make it all the more crucial that effective treatments be developed and implemented in collaboration with hospitals, health systems and health insurers—that innovators develop statistical models in which further research and analysis can be carried out to demonstrate the potential mitigation of high cost, high risk spinal procedures in favor of lower cost, lower risk non-surgical procedures within a fee-for-service and/or other payment model.

References

1. Adams, M. A., & Dolan, P. (2012). Intervertebral disc degeneration: evidence for two distinct phenotypes. *Journal of anatomy*, 221(6), 497-506.
2. Bibby, S. R., Jones, D. A., Ripley, R. M., & Urban, J. P. (2005). Metabolism of the intervertebral disc: effects of low levels of oxygen, glucose, and pH on rates of energy metabolism of bovine nucleus pulposus cells. *Spine*, 30(5), 487-496.
3. Fahy, N., Alini, M., & Stoddart, M. J. (2018). Mechanical stimulation of mesenchymal stem cells: Implications for cartilage tissue engineering. *Journal of Orthopaedic Research*, 36(1), 52-63.
4. Grunhagen, T., Wilde, G., Soukane, D. M., Shirazi-Adl, S. A., & Urban, J. P. (2006). Nutrient supply and intervertebral disc metabolism. *JBJS*, 88(suppl_2), 30-35.
5. [...]

Legal Notice: Intra Disc Nutrosis® is a registered mark of The Disc Institute for treatment performed at The Disc Institute of Michigan on the Accu-SPINA® IDD Therapy® treatment device, trademark patent-protected technologies developed by North American Medical Corporation.

Notarized statement by Dr. Paul Thomlinson...

Statement on Outcomes Evaluation for THE DISC INSTITUTE®

September 16, 2015

Background: A study has been completed by an external third-party Ph.D. researcher specializing in health care evaluation. This study included sophisticated random selection of a large and statistically valid sample of patients who consented to and completed IntraDiscNutrosis® treatment at THE DISC INSTITUTE®. Results were based on analyses of de-identified data from that representative sample. Measures of treatment success included percentage of improvement in overall functioning, and increases in activities of daily living. The latter, known as ADL, refers to patients' capacity for self-care (e.g., bathing, dressing, grooming, working, homemaking, and leisure)—this measure is used as a very practical indication of ability/disability in many disorders, including back & neck problems.

Results: An analysis of typical patients receiving care at the Institute revealed that 98% reported clinically significant improvement. Among all those patients who showed clinically significant change, the most common range of improvement was between 75% to 90%. Also, among this group, 93% reported significant increases in ADLs resulting from treatment. These statements are accurate, based on a statistical analysis of data collected during the course of standard IntraDiscNutrosis® treatment.


Paul Thomlinson, Ph.D.

STATE OF MISSOURI

COUNTY OF GREENE

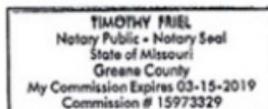
On this 16th day of September in the year 2015, before me, the undersigned notary public, personally appeared Paul Thomlinson, known to me to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged that he/she/they executed the same for the purposes therein contained.

In witness whereof, I hereunto set my hand and official seal.



Notary Public

Print Name: Timothy Friel



My commission expires: 3-15-2019

