Cationic Nucleus Therapy: A Novel Treatment Option for Addressing Disc Herniation

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Technology Summary

Cationic nucleus therapy is a tissue modifying technology that offers a simple, nonsurgical treatment for the symptomatic relief of pain, weakness and sciatica associated with herniated discs. The product delivers, through a percutaneous injection into the disc nucleus, a small volume of a cationic polymer solution capable of interfering with and collapsing the proteoglycan component of the extracellular matrix. The net result is a rapid volumetric change in the disc nucleus and reduction of the herniation.

Spinal Disc Biochemistry

The extracellular matrix of the nucleus is composed of large aggregating proteoglycan molecules called aggrecan that interact with long, linear strands of hyaluronan. The molecules become entangled in a fibrillar network composed mainly of type II collagen. Additionally, the fibrous annulus in conjunction with the endplates serve to constrain the nucleus. The swelling, fluid and ion-transport properties, as well as the intrinsic mechanical properties of the collagen-aggrecan matrix, govern its deformational behavior. The primary proteoglycan constituent, aggrecan, comprises a protein core and one or more covalently attached glycosaminoglycan chains. (See Exhibit 1.)

Exhibit 1: Illustration of Aggrecan.

The abundance of negatively charged glycosaminoglycans maintain fluid pressure by attracting water molecules, while the collagen network gives the tissue tensile strength and hinders excessive expansion of the proteoglycan molecules. This macromolecular and tissue organization endows the disc with compressive stiffness and the ability for reversible deformation.

Enzymatic Treatment for Herniated Discs

Approximately 30 years ago, chemonucleolysis enjoyed significant popularity as a treatment for disc herniation. The procedure utilized a broad spectrum protease named chymopapain which indiscriminately and irreversibly digested protein structures. When delivered to the disc nucleus, the net result was a rapid reduction in the volume of the nucleus and relief of symptoms associated with herniation. However, due to complications resulting from the non-specific nature of the enzyme, the delivery system and allergies to the source of the enzyme, the product was discontinued. Recently, advances in delivery and imaging technologies have led to the resurgence of interest in chemonucleolysis. In addition, researchers have proposed using a class of enzymes with greater specificity as an alternative to chymopapain. These enzymes, called glycosidases, are able to catalyze the hydrolysis of the glycosidic linkage between sugar residues of specific proteoglycan molecules without affecting other structures. While the use of glycosidases is still an enzymatic approach, it is believed that using one or more of these specific enzymes may present a more favorable safety profile and limit complications. To date, no products containing a glycosidase have progressed out of preclinical development for the treatment of herniated discs. The mechanism behind both enzymatic treatments for disc herniation is similar: disturb the arrangement and interaction of macromolecular components within the disc nucleus, allowing it to occupy less space and thereby relieve symptoms.
We have proposed a non-enzymatic treatment that specifically targets proteoglycan function to achieve a similar result: reduction of disc nucleus volume without destruction of matrix structures.

Cationic Nucleus Therapy

By their nature, enzymatic treatments irreversibly destroy protein structures. As an alternative treatment option, we have proposed a non-enzymatic treatment that specifically targets proteoglycan function to achieve a similar result: reduction of disc nucleus volume without destruction of matrix structures. Cationic nucleus therapy uses a polymeric cationic solution to compete with and negate the negative charges on proteoglycans. After treatment, the proteoglycans no longer effectively attract and hold water at the same capacity, resulting in a rapid volumetric reduction of the nucleus. Because it lacks any enzymatic activity, cationic treatment reduces disc nucleus volume without destroying or removing any of the structural, molecular or cellular components. Cationic nucleus therapy, similar to chemonucleolysis, uses a minimally invasive percutaneous approach in which a needle is used to deliver treatment directly to the disc nucleus; no “open” surgical site is required. Delivering therapeutic treatments via a percutaneous approach aligns with a strategy to address early stage disease or trauma with non-fusion, minimally invasive, structure-and motion-sparing technologies. In initial preclinical animal studies, a 20 percent reduction in disc height index was maintained for six weeks after injection. In these experiments, not only was the treatment effective at overcoming the inherent intradiscal pressure of a healthy disc, but it was able to reduce the effective height of the disc by an additional 20 percent. While not measured past the six week time point in these initial studies, it is likely that the effects of this treatment are maintained much longer.

Cationic nucleus therapy allows for the immediate treatment of symptomatic pain soon after a herniation occurs without needing to determine which may respond to conservative treatments and which patients may require more invasive procedures. The treatment quickly reduces the herniation, associated pain and sciatica, allowing the patient to better tolerate and respond to additional conservative treatment options. The treatment is tissue sparing and designed to delay or prevent the need for more invasive procedures, resulting in an immediate and dramatic improvement in a patient’s quality of life by relieving debilitating pain. The treatment does not prevent the ability to perform subsequent procedures. The ideal patients for this treatment are those presenting symptomatic pain, weakness or sciatica from a contained herniated disc. The procedure can be performed by surgical and non-surgical specialists who treat patients with spinal disorders, and is similar to the current diagnostic discography procedure (CPT code 72295; See Exhibit 2.) which has a reimbursement rate of approximately $1,500.

Exhibit 2: Percutaneous injection during a discography procedure. Photographs depict a patient receiving an injection into the spinal disc nucleus and the corresponding anteroposterior and lateral radiographic projections.

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Articular Engineering is a privately-owned regenerative medicine company based in Northbrook, Illinois that is focused on the development of innovative cell-based and tissue-modifying therapies designed to repair and regenerate articular cartilage and the spinal disc.

REFERENCES
