IN VIVO EVALUATION OF A NOVEL PROTEIN POLYMER HYDROGEL FOR NUCLEUS PULPOSUS REPLACEMENT

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INTRODUCTION

Nucleus pulposus replacement has emerged as a minimally invasive surgical alternative for treating the early stages of degenerative disc disease (DDD) as well as an adjunct to microdiscectomy. Nucleus replacement offers the potential to retain the motion and restore the biomechanics of the spinal segment while being less invasive than other procedures. The restoration of biomechanics may reduce degeneration at the affected and adjacent levels. Hydrogels stand out as a possible synthetic nucleus replacement due to their mechanical properties, hydrophilicity and relative inertness in the body. While some hydrogels have been tested in vitro little has been done to test the reaction of the body to these materials in the environment of the intervertebral disc (Bertagnoli, Sabatino et al. 2005; Di Martino, Vaccaro et al. 2005; Joshi, Fussell et al. 2006).

This study evaluated the biocompatibility of a novel protein hydrogel (NuCore™ Injectable Nucleus, Spine Wave, CT) as a nucleus replacement in a sheep intervertebral disc model at 4, 26, and 52 weeks. The material used was an injectable sequential block copolymer of silk and elastin, crosslinked in situ using diisocyanate to form a hydrogel.

METHODS

Twenty five adult sheep (18 months old) were used following ethical approval. The vertebral column was exposed through a ventrolateral approach. Levels L1-L2, L2-L3, and L3-L4 were randomly assigned a sham, discectomy, or discectomy and hydrogel treatment. The sham treatment consisted of exposing the level without disrupting the annulus. The discectomy was performed with a 1 mm k-wire placed in the lateral annulus followed by a 2.9mm shaver (Smith & Nephew Endoscopy, Andover, MA) with suction to remove the nucleus. No incision of the annulus was made. Care was taken not to damage the endplate during insertion of the shaver into the disc or during use. A portion of the tissue removed from the shaver was processed for histology. The treated level was exposed and the nucleus removed followed by injection of the hydrogel. The polymer and crosslinker were mixed in a custom device and injected into the nucleus space. The soft tissues were reflected back and the skin closed. Animals received post operative analgesia for 3 days following surgery.

Animals were euthanized at 4 (n=5), 26 (n=10), and 52 weeks (n=10) following surgery. The lumbar spines were harvested and CT scanned as well as processed for paraffin histology. Axial slices (0.5 mm) were taken using a Toshiba CT scanner (Toshiba, Japan). The DICOM data sets were used to produce 3D models using MIMICS (Materialise, Belgium) to investigate changes in the morphology of the vertebral bodies at each level. A standard threshold value was used to create all models. The spinal segments were fixed in phosphate buffered formalin, decalcified in formic acid – formalin and paraffin embedded. Decalcified segments were grossly sectioned perpendicular to the entry into the disc prior to placement into cassettes for paraffin embedding. Sections using a Lecia microtome (Leica, Germany) were stained with H&E and evaluated using an Olympus BH2 Microscope. Histology was evaluated for evidence of degeneration as well as biocompatibility with the injected hydrogel.

RESULTS

Animals recovered uneventfully following this 3 level model and reached their allocated time points. Histology of the samples of material harvested at the time of surgery during the discectomy confirmed the removed tissue to be nucleus pulposus. No bone tissue was detected. Figure 1 presents an example of a 3D model at 26 weeks. The treated sites performed similar to the sham in terms of bony response at all time points. The defect sites showed increased osteophyte formation by 52 weeks compared to sham and treated sites.

Decalcified paraffin histology confirmed the gross findings obtained from the CT data. Sham sites presented normal disc morphology with an intact nucleus pulposus and no evidence of degeneration. The discectomy sites confirmed the removal of the nucleus without evidence of disc degeneration at 4 and 26 weeks. Hydrogel material was present in the disc where the nucleus had been removed. The material was integrated well into the defect site filling the void as well as interdigitating into the remaining tissues. No cellular reaction to the hydrogel was observed. The interface did not present any signs of a chronic inflammatory reaction or foreign body response. Figure 2 presents typical histology findings associated with the hydrogel at 26 weeks.

Figure 1: Typical 3D model built from DICOM data revealed no evidence of endplate reaction at 26 weeks in the Defect, NuCore™ and sham sites.

Figure 2: Histology of the NuCore™ hydrogel in the disc at 26 weeks did not reveal any evidence of inflammatory response.

DISCUSSION

A sheep model was developed to evaluate the in vivo response to a novel hydrogel following discectomy at 4, 26 and 52 weeks post surgery. The technique using a shaver to remove the nucleus provided a reproducible and minimally invasive method to achieve the discectomy. Three dimensional models revealed a similar response between the sham and those treated with the hydrogel, while the defect sites demonstrated increased osteophytes. Histology confirmed a quiet interface in the presence of NuCore™ hydrogel with no evidence of any inflammatory cells or adverse reactions.

This study is limited in that we did not examine the biomechanical properties of the motion segments. The data supports the biocompatibility of this novel material when placed into the environment of the intervertebral disc. The sheep model represents a useful large animal model to evaluate nucleus replacement materials.

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REFERENCES


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