Presentation #16

Total Disc Replacement using Tissue-Engineered Intervertebral Discs: In Vivo Outcome in a Canine Model

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Introduction: Despite the efficacy of the most commonly performed treatments for degenerative disc disease, anterior cervical decompression and fusion and prosthetic total disc replacement devices (TDR), they still pose risks of pseudoarthrosis, implant dislodgement, and adjacent segment disease. Tissue engineered intervertebral disc (TE-IVD), an alternative treatment option, has been previously developed by our group as a biological TDR device and tested in a rat tail model. In order to bring closer to clinical application, we developed a TDR model using our TE-IVD in the canine cervical spine. In the presented study, we evaluate implant stability at different levels and its ability to maintain disc height, size and hydration, and tissue viability.

Materials/Methods: Canine-sized TE-IVDs were constructed as previously described [Bowles 2011]. Cervical IVDs from skeletally mature beagles were separated into AF and NP tissues by macroscopic appearance; component cells were isolated and cultured in vitro. The cultured NP cells were seeded with alginate, injected into a predesigned mold, and encircled with two layers of an AF cell-laden collagen gel. The combined construct was kept in media for 2 weeks as surrounding annulus fibrous aligned and contracted until required diameter of TE-IVD was reached. 13 skeletally mature beagles underwent discectomy with whole IVD resection at different levels and were divided into two groups: solely discectomized control and TE-IVD implanted group. Adjacent proximal segments served as internal healthy control. Dogs were imaged post-operatively at 4, 8, and 16 weeks. Quantitative analysis using T2 intensity measured NP size and hydration of implanted TE-IVD, while X-rays measured disc height indices of treated segments. Qualitative histological analysis evaluated implant engraftment and ingrowth over time plus secondary degeneration post discectomy.
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**Results:** Discectomy and TE-IVD implantation were performed anteriorly under segmental distraction sans major complications. Upon distraction release, 30% in volume of 5 TE-IVDs were anteriorly displaced from the surgical site (unstable group), whereas the remaining 6 implants had no displacement (stable group). There was a correlation between surgical level and implant stability, with implants at C3/4 having greatest stability. The stable group outperformed unstable group in the following postoperative assessment (Figure 1, 2). Quantitative analysis showed stable group had significant retention of disc height at 4 weeks compared to discectomy group. There was a trend of higher NP size in the stable group compared to that of discectomy group. Conversely, unstable group showed a downward trend over time. 4-week histology reveals chondrocytic cells surrounded by proteoglycan-rich matrices in NP portion and by fibrocartilaginous matrices in AF. These NP-like and AF-like tissues were sustained at 16 weeks. Integration of TE-IVDs to the host tissues was observed both at 4 and 16 weeks.

**Conclusions:** Biological total disc replacement demonstrated level-dependent implant stability in a canine model. Despite significant biomechanical demands of the beagle cervical milieu, securely implanted TE-IVDs, remained in the disc segment and yielded disc-like tissues over 16 weeks. Discs displayed dynamic adaptation to the host environment, with extracellular matrix production and cell proliferation. Further long-term experiments will elucidate the clinical applicability and efficacy of the presented innovation.

![Image](image-url)

Figure 1. Postoperative outcome examples at 4 and 16 weeks. Adjacent segment served as healthy control. Discectomy group demonstrated collapsed, black disc. In the TE-IVD implanted group, location of the implant was confirmed by sagittal and axial MRIs (yellow arrows). Stable group outperformed unstable one, maintaining disc height on X-rays as well as signal intensity on T2 MRI mapping, which was corroborated by abundant proteoglycan rich matrices on histology.

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Figure 2. Quantitative assessment demonstrated the stable TE-IVD group had significant retention of disc height at 4 weeks compared to discectomy group.