

## Slowly Progressive Disc Degeneration in a Goat Model

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**INTRODUCTION** Factors compromising interspecies comparison of intervertebral disc (IVD) degeneration in currently used *in vivo* models include relatively small disc size, different notochordal cell status and/or the fast progression of induced degeneration<sup>1</sup>.

The goat IVD has similar geometrical and mechanical properties compared to human IVDs.<sup>2</sup> Also, notochordal cells are absent in mature goats.<sup>3</sup> Therefore, the goat is a suitable animal for disc degeneration models and we investigated two methods to *slowly* induce disc degeneration: injection of 0.25% Chondroitinase ABC (CABC) and vertebral endplate perforation with a 3.5 mm drill (EP).

**METHODS** In each of 17 skeletally mature Dutch milk goats, at random, two lumbar IVDs were induced with EP, two with CABC, two with PBS and two sham-treated (Control) IVDs. Follow-up periods were 4, 8, 12, 18 and 26 weeks (n≥3). Both before surgery and before sacrifice, X-rays were taken. Subsequently, the spinal column was harvested and directly scanned with MRI. Next, individual levels were cut into 3 mm sagittal slices and digitally photographed for macroscopic analysis

**IVD height:** For each goat, IVD space (IVDsp) and cranial vertebral body height (CVBh) were measured at three points and averaged, both in the pre-operative and the pre-autopsy X-ray. Subsequently, the disc height index (DHI; the IVDsp/CVBh ratio) was calculated for each time point, and used to determine the loss of disc height (expressed as % decrease).

**MRI:** All levels were scored using a modified Thompson classification for degeneration.<sup>4</sup>

**Macroscopy:** The digital photographs were scored using the Thompson grading system.<sup>5</sup>

**RESULTS IVD height:** No differences were found between control and PBS groups. The DHI was significantly decreased in EP treated levels at 18 weeks (p<0.01) and in CABC treated levels after 12 and 18 weeks (p<0.05) compared to PBS injected levels (Fig.1A.)

**MRI:** MRI data showed a trend towards degeneration over time but, due to low sample size, never reached significant levels over reference values (NL goats) (Fig. 1B).

**Macroscopy:** Control and PBS levels were not different. EP levels had significantly higher Thompson grades at 4 (p<0.001) and 18 (p<0.001) weeks and CABC treated levels at 8 (p<0.05) and 18 weeks (p<0.001) compared to PBS injected levels. Also, scores increased significantly over time in CABC levels.

**DISCUSSION** Despite the limited number of animals, the data presented show a progressive trend of degenerative symptoms in time for both EP and CABC. At 26 weeks, these symptoms decrease slightly. Whether this is due to recovery or an artefact is now being addressed in a follow-up study. The non-significant increase of DHI, seen in figure 1A for the PBS/control levels, might be explained by different angles of the radiographs.

EP levels demonstrated gross morphologic destruction caused by the drill at all time-points, and EP was therefore considered to be less suitable for de- and regeneration research.

CABC levels demonstrated degeneration in approximately 2/3 of the treated levels. Because besides interspecies comparability, reliability and reproducibility of the degeneration are essential for a good degeneration model, this is also addressed in the follow-up study.

In conclusion: The goat disc degeneration model presented here is very promising, shows slowly progressive degeneration and mimics the human situation better than the currently used models.

**REFERENCES** <sup>1</sup> J.C. Lotz. (2004) *Spine* **29**: 2742-2750. <sup>2</sup> T.H.Smit. (2002) *Eur Spine J* **11**: 137-144. <sup>3</sup> R.J.W.Hoogendoorn et al. (2005) *Abstract*. <sup>4</sup> K. Masuda et al. (2004) *Spine* **30**: 5-14. <sup>5</sup> J.P.Thompson (1990) *Spine* **15**:411-415

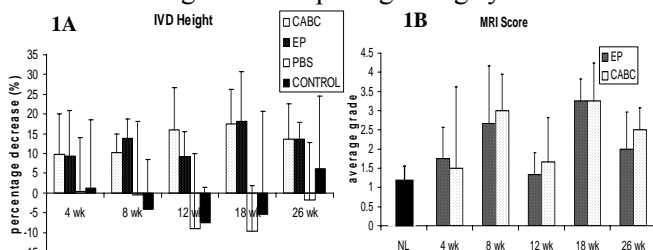


Figure 1A. Percentile decrease in disc height.  
Figure 1B. MRI grades scored according to the modified Thompson protocol. NL = reference goats.