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Mechanical testing and development of novel hydrogel system for intervertebral disc augmentation

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Introduction

Nucleus augmentation is a potential treatment for disc degeneration where a biomaterial is injected into the disc. *In vitro* testing can bring potential biomaterials closer to clinical such by assessing biomaterial mechanical performance and addressing clinical concerns. This study utilizes the University of Leeds self-assembling peptide glycosaminoglycan (GAG) hybrid hydrogel [1]The aim of this study was to:

1) Assess high cycle disc behavior *in vitro* and apply predictive analysis to assess use of shorter tests

2) Assess mechanical damage from needle puncture comparing a specialist designed needle to standard hypodermics

Methods

Linear prediction study

48 bovine bone-disc-bone units **mechanically tested sequentially** [2], as shown in Figure 1:

1. Native only state (n=8)
2. Degenerate only state (n=8)
3. 0.3 ml treated state peptide:GAG (PEP:GAG) (n=6)
4. 1 ml treated state PEP:GAG (n=6)
5. 'sham' degenerate procedure (n=6)
6. 1 ml saline:GAG (SAL:GAG) treatment group (n=6)
7. 1 ml saline:saline (SAL:SAL) treatment group (n=6)

Change of sample stiffness in different states was recorded (paired t-tests with post hoc Bonferroni correction, α=0.05).
Prediction of the 20,000 cycle stiffness for the treated specimens from the 1,000 cycle native and degenerate data (linear regression with 95% confidence intervals).

Needle puncture study

26 bovine bone-disc-bone units also had needle punctures only (120° apart) as shown in Figure 2:

1. No puncture controls (n=8)
2. 12G puncture group (n=6)
3. 21G puncture group (n=6)
4. Specialist needle puncture group (n=6)

Change of sample stiffness between native and punctured states was recorded (paired t-tests with post hoc Bonferroni correction, α=0.05).

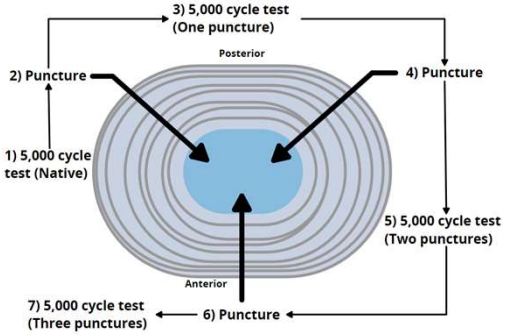

Figure 2. Needle puncture test method.

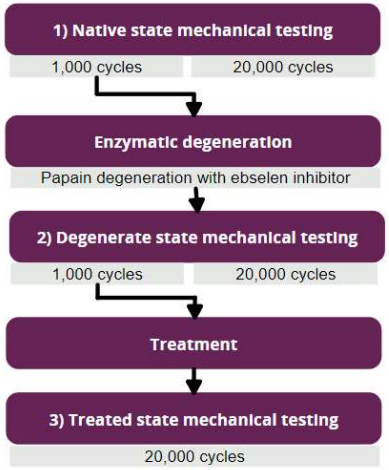

Figure 1. 20,000 cycle test method.

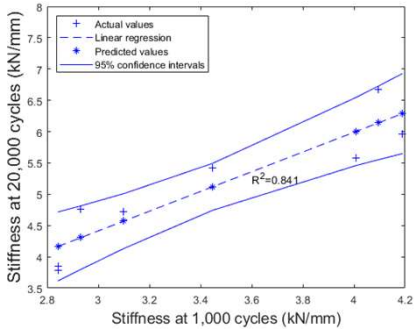

Figure 3. Native linear regression predictions.

Results

Linear prediction study

It was found that:

- Enzymes instigate mechanical degeneration (statistical difference at 1,000 cycles)
- 1 ml injections restore disc stiffness (Statistical difference at 1,000 cycles) (Table 1).
- Linear regression (Figure 3) is sufficient to derive predictions of stiffness at 20,000 cycles (example in Figure 4):
  - 0.3 ml PEP:GAG group did not restore stiffness,
  - 1 ml PEP:GAG group successfully restored stiffness
  - 1 ml SAL:GAG group consistently caused damage
  - 1 ml SAL:SAL group did not demonstrate any predominate behavior

Needle puncture study

- Repeat tests with or w/o puncture generated stiffness difference
- Magnitude of the difference was small and of similar order in the no puncture group, puncture with 21G and specialist needle groups
- 12G group showed larger differences than the no puncture controls across all three punctures.

Table 1. 1,000 cycles statistical testing results (p-values, significance in color).

Group	States Compared	
	Native to Treated	Degenerate to Treated
0.3 ml PEP:GAG	2.80E-03	0.64
1 ml PEP:GAG	0.27	0.01
1 ml SAL:GAG	0.16	0.02
1 ml SAL:SAL	0.02	0.02

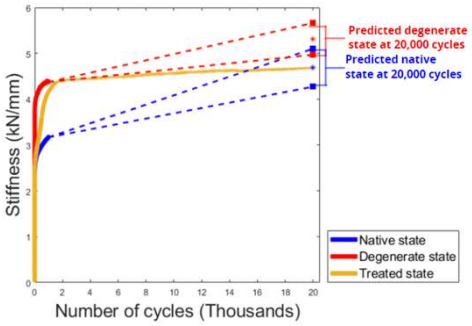

Figure 4. Example predictive analysis showing restored stiffness specimen from the 1ml PEP:GAG group

Conclusions

- Specialist needle system developed with minimal effect on the bulk mechanical properties of the disc
- The peptide hydrogel was able to restore the biomechanics of the intervertebral disc
- Mechanical restoration was dependent on the volume injected
- The treatment controls showed some restorative effects at 1,000 cycles, which were not maintained to 20,000 cycles

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References:

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2. Dixon et al, ORS Abstracts, 2021, 1648-LB, PS-52

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