Effects of Hypothyroidism on Articular Cartilage in Juvenile Swine

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INTRODUCTION

Articular Cartilage

- Highly specialized connective tissue
- Functions as smooth, wear resistant joint surface
- Composition includes:
  - Chondrocytes
  - Extracellular matrix (ECM)
    - Collagen fibrils
    - Proteoglycans
- Relatively avascular and poor ability to repair

Thyroid Hormone

- Influence articular cartilage growth
- Triiodothyronine (T3) increases in vitro collagen production
- Unknown effects on developing articular cartilage

Theory

- Understanding articular cartilage development may be the link to understanding repair
- Because pediatric donor tissue is difficult to obtain, and miniature swine proximal femoral anatomy resembles human anatomy, an animal model is appropriate

Purpose

- To compare the effects on articular cartilage in hypothyroid animals to control animals

METHODS

- Established hypothyroidism in two (2) juvenile miniature swine by administering 6-Propyl-2-thiouracil (PTU) in drinking water with two (2) additional animals serving as controls
- Serum TSH, T3, and T4 levels monitored weekly
- Sacrificed at 25 weeks of age
- Proximal femurs harvested, fixed, demineralized, and processed for histology and immunohistochemistry (IHC)

Measures & Analysis

- Histomorphometry
  - Mean articular cartilage thickness
  - Mean articular cartilage cell density
- Nested mixed effects ANOVA with $\alpha = 0.05$

RESULTS

- Hypothyroid articular cartilage demonstrates changes in gross tissue morphology and histology staining, compared to controls (See Figures 1 and 2)
  - Increased proteoglycan
  - Decreased type II collagen
- Hypothyroid articular cartilage demonstrates differences in histomorphometry, compared to controls (See Table 1)
  - Increased mean articular cartilage thickness
  - Decreased mean articular cartilage cell density

Figure 1: Toluidine blue stained articular cartilage demonstrating tissue thickness

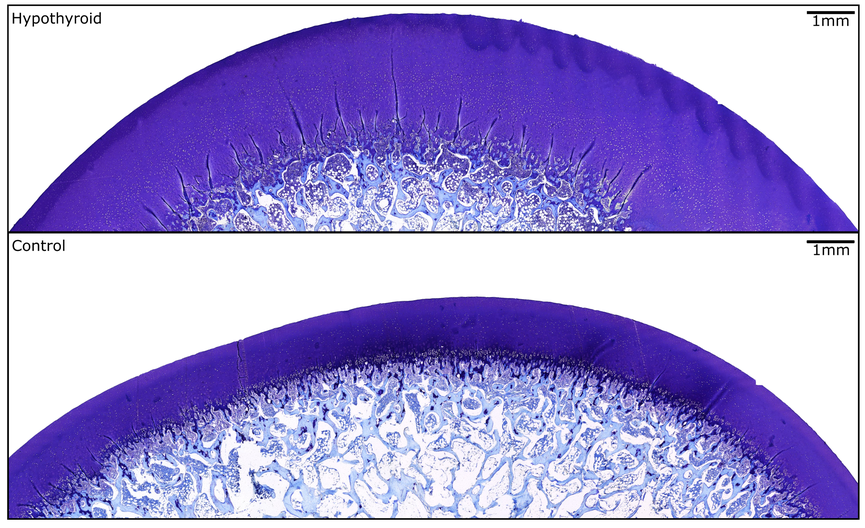
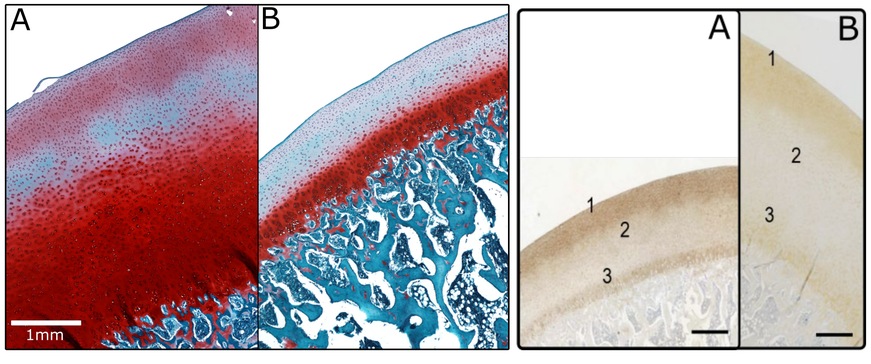


Figure 2: Safranin-O and type II collagen IHC demonstrating proteoglycan and type II collagen protein expression, respectively.



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RESULTS

Table 1: Histomorphometry of articular cartilage

	n	$\bar{x}$	SD	p-value
Thickness (μm)				
Control	2	1076	–	–
Hypothyroid	2	2335	±133	0.021 *
Cell Density (cells/cm^2)				
Control	2	27.6	–	–
Hypothyroid	2	31.0	±1.0	0.016 *

DISCUSSION

- First study to investigate the effects of hypothyroidism on articular cartilage
- Hypothyroid articular cartilage may be biomechanically weaker
  - Increased proteoglycan
  - Decreased type II collagen
- Findings may help understand articular cartilage development and repair mechanisms
- Findings may help explain genesis of femoral head deformity in pediatric hypothyroidism and Legg–Calvé–Perthes disease (LCPD)

Limitations

- Primarily a qualitative study with a small sample size

Conclusion

- Hypothyroid articular cartilage demonstrated:
  - Increased thickness
  - Decreased cell density
  - Increased proteoglycan staining
  - Decreased type II collagen staining
- These data support the idea that thyroid hormones are fundamental to articular cartilage development

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