Vertebral growth plate histomorphometry in severe idiopathic scoliosis:
Are hypertrophic zone and cell heights greater than controls?

Bylski-Austrow DI, Okonny M, Glos DL, Wall EJ, Crawford AH
Growth plate structure important to etiology and treatments

Heights of hypertrophic zone and cells

• Correlate directly with biological and mechanical factors
  — Bone growth rate
    • Farnum et al Cells Tissues Organs 2000
  — Magnitude of compression
    • Stokes et al J Bone Joint Surg Am 2002
  — Experimental growth modulation
    • Bylski-Austrow et al J Bone Joint Surg Am 2009

• Inform etiologic theories
  — Relative anterior column overgrowth
    • Zhu et al 2006
Purpose

1. Determine whether vertebral body growth plate hypertrophic zone height ($H_z$), cell height ($h_c$) and cell width ($w_c$) of specimens from curve apex of patients with juvenile or adolescent idiopathic scoliosis (IS) differ from controls

2. Compare concave versus convex sides in IS
Methods: Materials

Scoliosis specimens
- Surgical removal of disc
- At or near apex
- Severe spine deformity
  - IRB approved

Control specimens
- Pathology slide files
- Age-matched
- No spinal deformity
- Chronic condition
Histology processing & analysis

Surgical specimen histology

- Routine protocol for autopsy
  - Paraffin embedded, 4 µm sections, H&E
    - CCHMC Pathology

All slides digitized & analyzed

- Scanner and software
  - Aperio Technologies, Spectrum 11.1

Sampling protocol

- Hypertrophic zone height intervals
  - 250 µm for controls
  - 150 µm for surgical specimens

- Hypertrophic cells counted
  - All cells with clear boundaries
  - ~ 75% of all cells measured
Quantitative analysis

Outcome measures

Control specimen

Hypertrophic zone height \( (H_z) \)
Cell height \( (h_c) \)
Cell width \( (w_c) \)

Statistics: IS vs control

- t-tests, two-tailed
- Bonferroni, 2 primary comparisons
  - Zone height, cell height
    - \( \alpha = 0.05/2 = 0.025 \)
Results: Demographics

Control
• n = 3, 2 female, 1 male
  – Age range 13 – 16 years of age
  – Diagnoses: Aneurysm, diabetes, meningitis

IS
• 5 patients, 4 AIS, 1 JIS (f); 4 F, 1 M
• Age 12.8 years, range 10 - 14
• Main curvature 62° (± 13°)
• 2 cases with both convex and concave sides
  – AIS, 1 M, 1 F, age 13 years
Zone height

Hypertrophic zone height (μm)

Control

IS

p = 0.06
Cell size

- Mean IS cell height less than control
- Aspect ratios: Cell heights ~50% widths
- IS cell width not different than control (p=0.6)
IS: Concave vs convex

Zone height

- Concave: 80 μm
- Convex: 120 μm

Cell height

- Concave: 5 μm
- Convex: 6 μm

Cell width

- Concave: 14 μm
- Convex: 15 μm

(n = 2)
Conclusions

• Structure of vertebral body growth plate hypertrophic zones taken from curve apex in IS were not statistically significantly different than controls

• However, IS hypertrophic zone heights and cell heights were not greater than control
  - On average, for all outcome measures
    • IS < Control
    • Concave < Convex

• Comparisons: Results do not support greater anterior growth, and/or lower compression of anterior column, in IS

• Limitations: Small numbers, and large 3D late-stage deformities

• Significance: Results are clinically relevant to growth modification methods & mechanobiological etiology theories
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