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Vertebral growth plate histomorphometry in severe idiopathic scoliosis:

Are hypertrophic zone and cell heights greater than controls?

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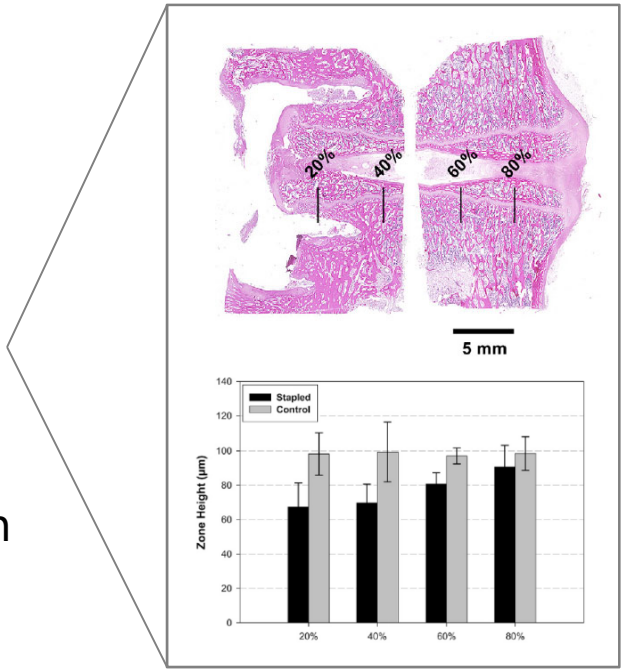
Growth plate structure important to etiology and treatments

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

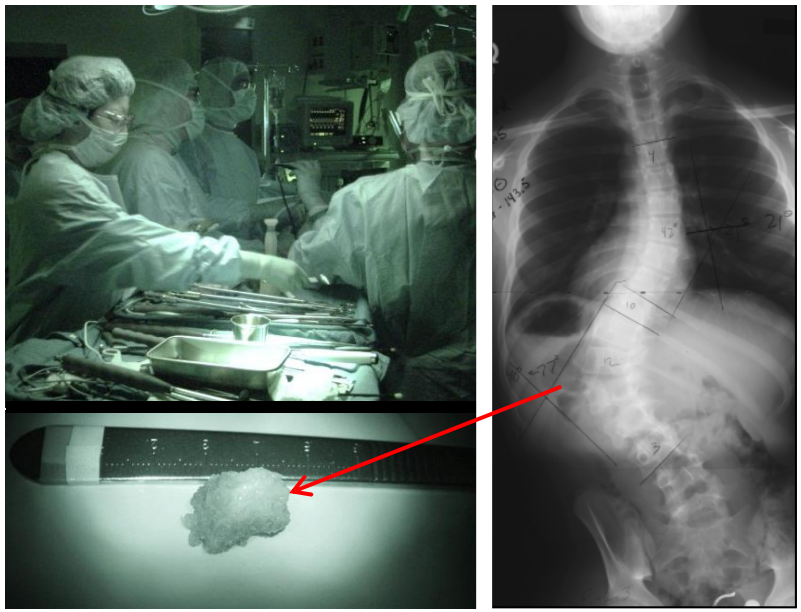
1. Determine whether vertebral body growth plate hypertrophic zone height (H_z), cell height (h_c) and cell width (w_c) of specimens from curve apex of patients with juvenile or adolescent idiopathic scoliosis (IS) differ from controls

2. Compare concave versus convex sides in IS

Methods: Materials

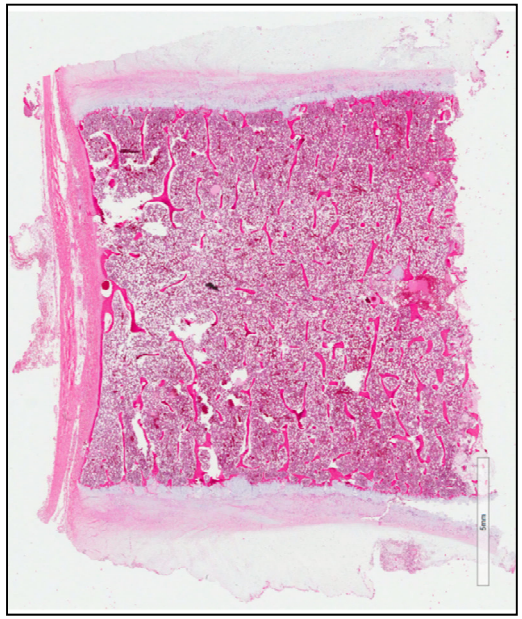
Scoliosis specimens

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



Control specimens

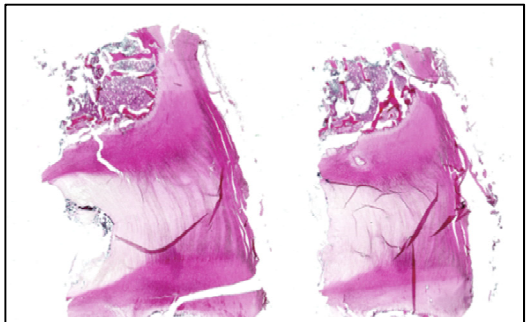
- Pathology slide files
- Age-matched
- No spinal deformity
- Chronic condition



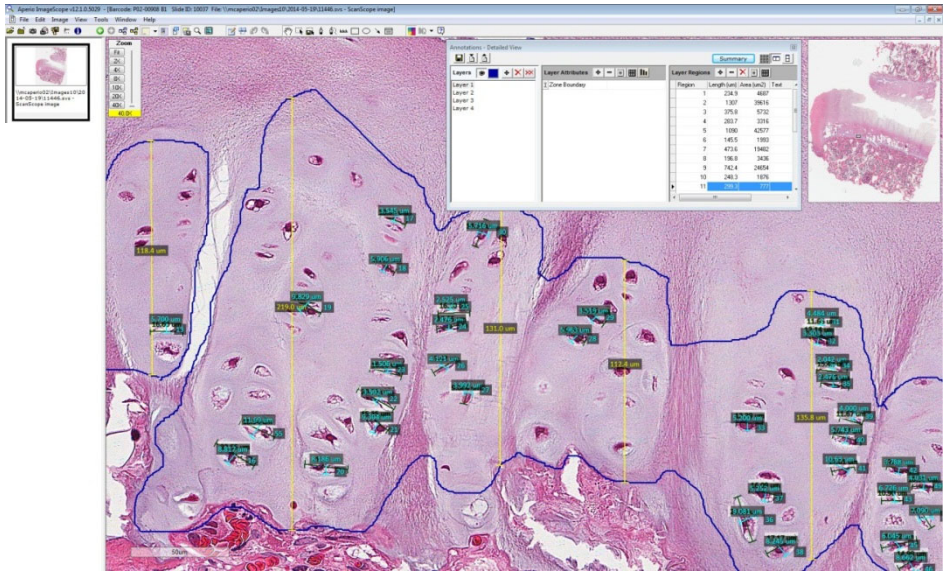
Histology processing & analysis

Surgical specimen histology

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



Surgical specimen



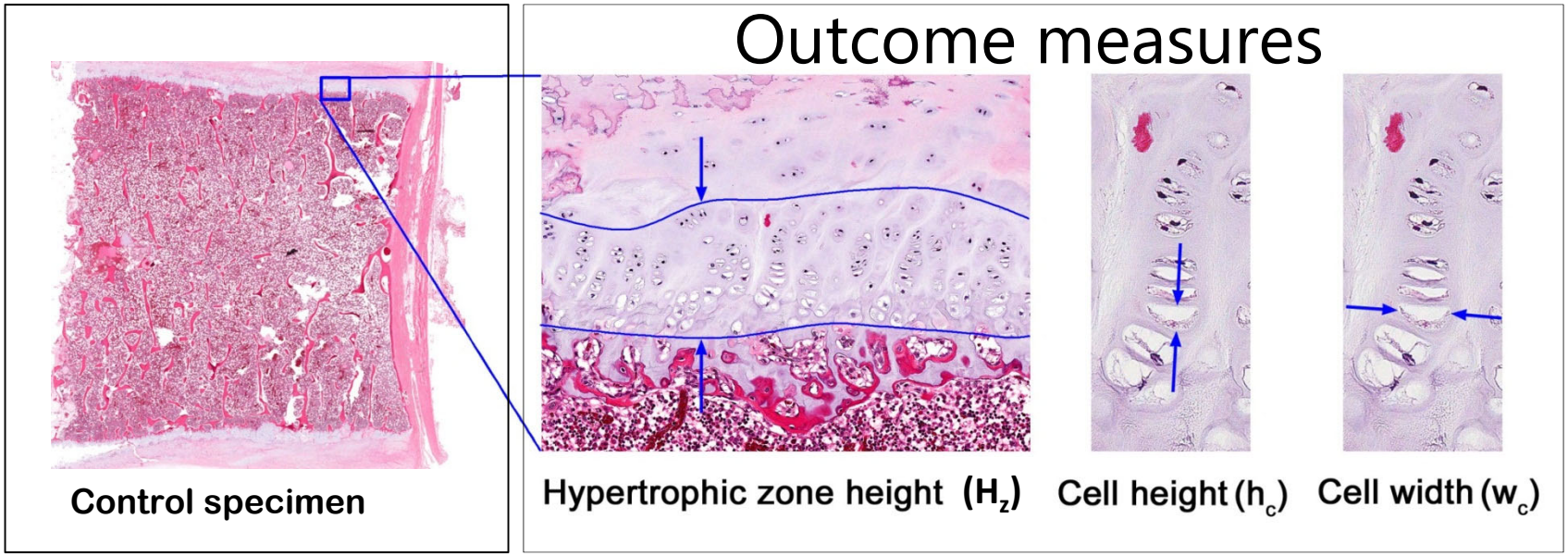
All slides digitized & analyzed

- 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



Statistics: IS *vs* control

- t-tests, two-tailed
- Bonferroni, 2 primary comparisons
  - Zone height, cell height
    - $\alpha = 0.05/2 = 0.025$

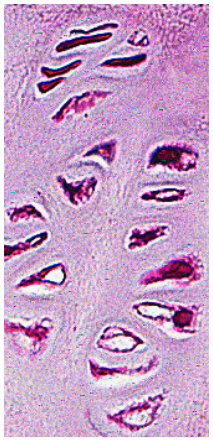
Results: Demographics

Control

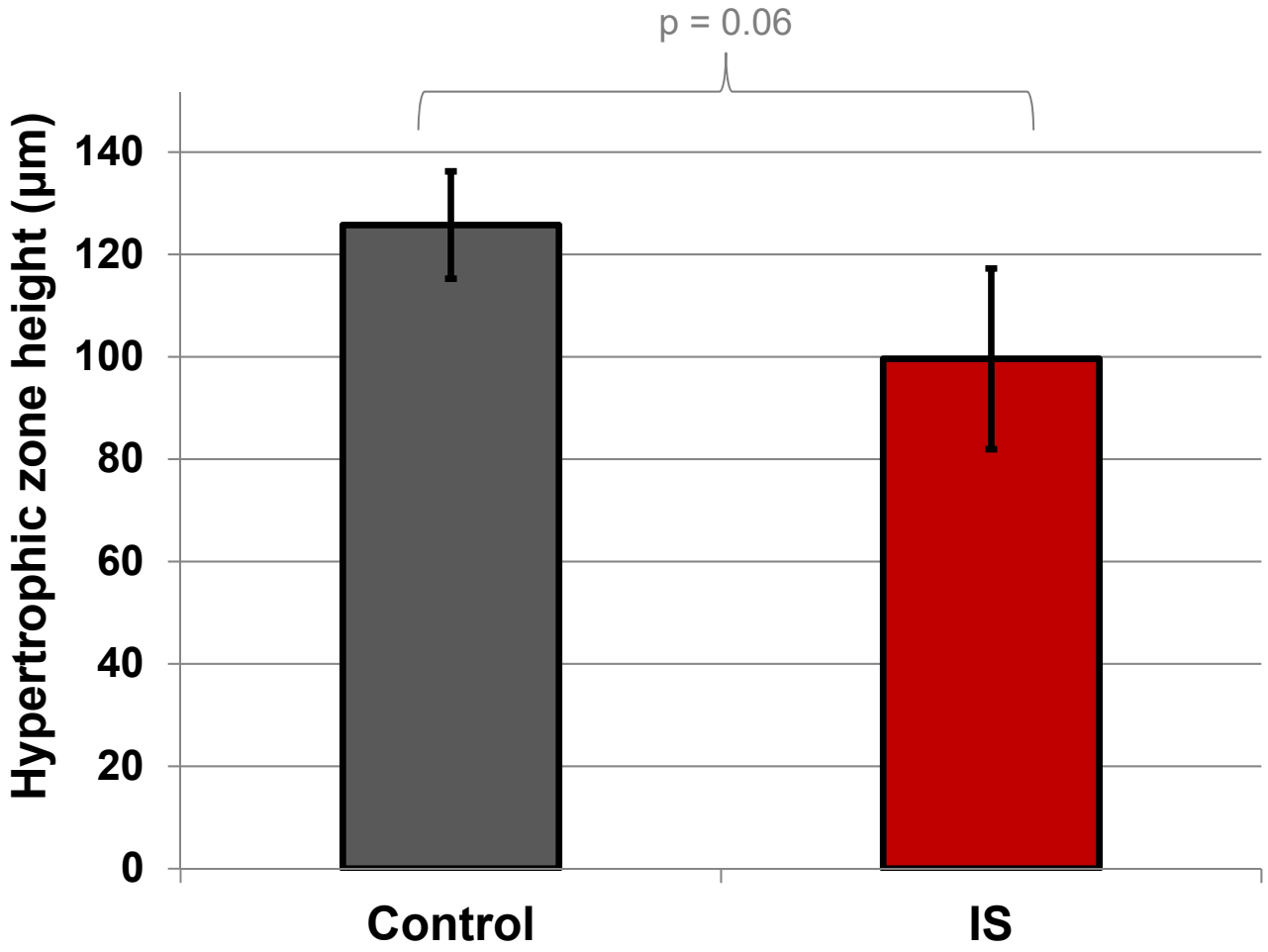
- n = 3, 2 female, 1 male
  - Age range 13 – 16 years of age
  - Diagnoses: Aneurysm, diabetes, meningitis

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

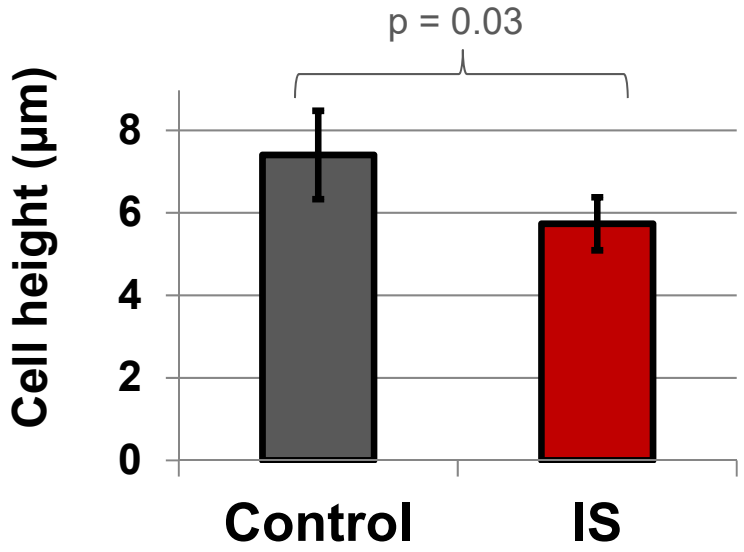


Zone height

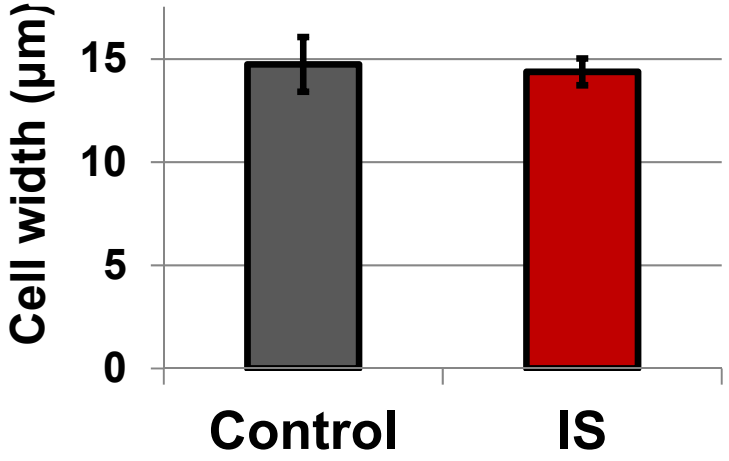

p = 0.06
Hypertrophic zone height (µm)
140
120
100
80
60
40
20
0
Control
IS

Cell size

Hypertrophic cell height (µm)

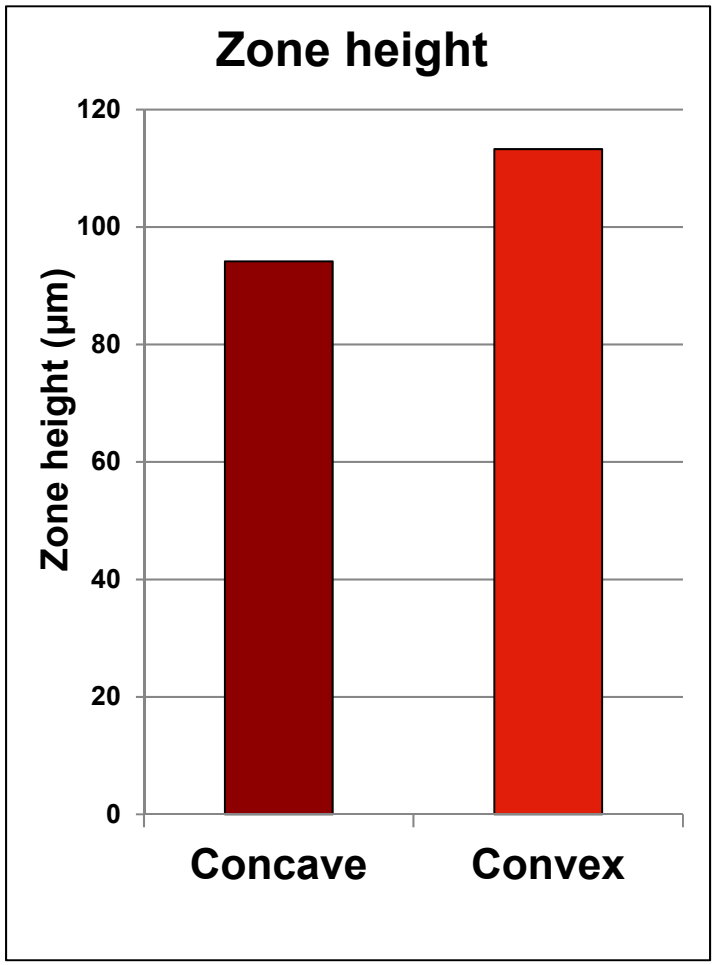


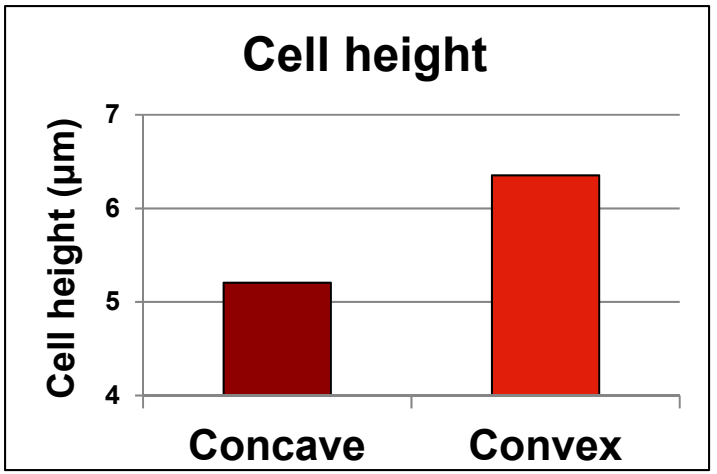
Hypertrophic cell width (µm)

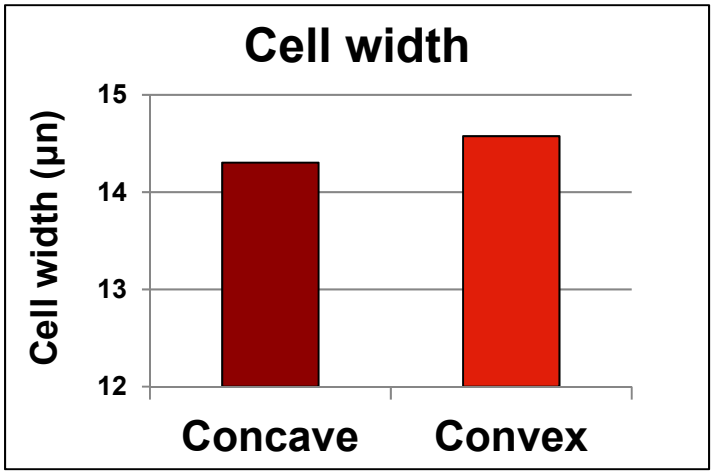


- Mean IS cell height less than control
- Aspect ratios: Cell heights ~50% widths
- IS cell width not different than control (p=0.6)

IS: Concave vs convex







(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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