Expansion Thoracoplasty: Is Earlier Better? Evaluation Using a Rabbit Model of Thoracic Insufficiency Syndrome

Olson JC[1,2]; Glotzbecker MP[3]; Takahashi A[2]; Snyder BD[1,3]

[1]Center for Advanced Orthopaedic Studies, Beth Israel Deaconess Medical Center;
[2]Dept. of Bioengineering, Boston University Graduate School of Engineering;
[3]Dept. of Orthopaedic Surgery, Children's Hospital; Harvard Medical School

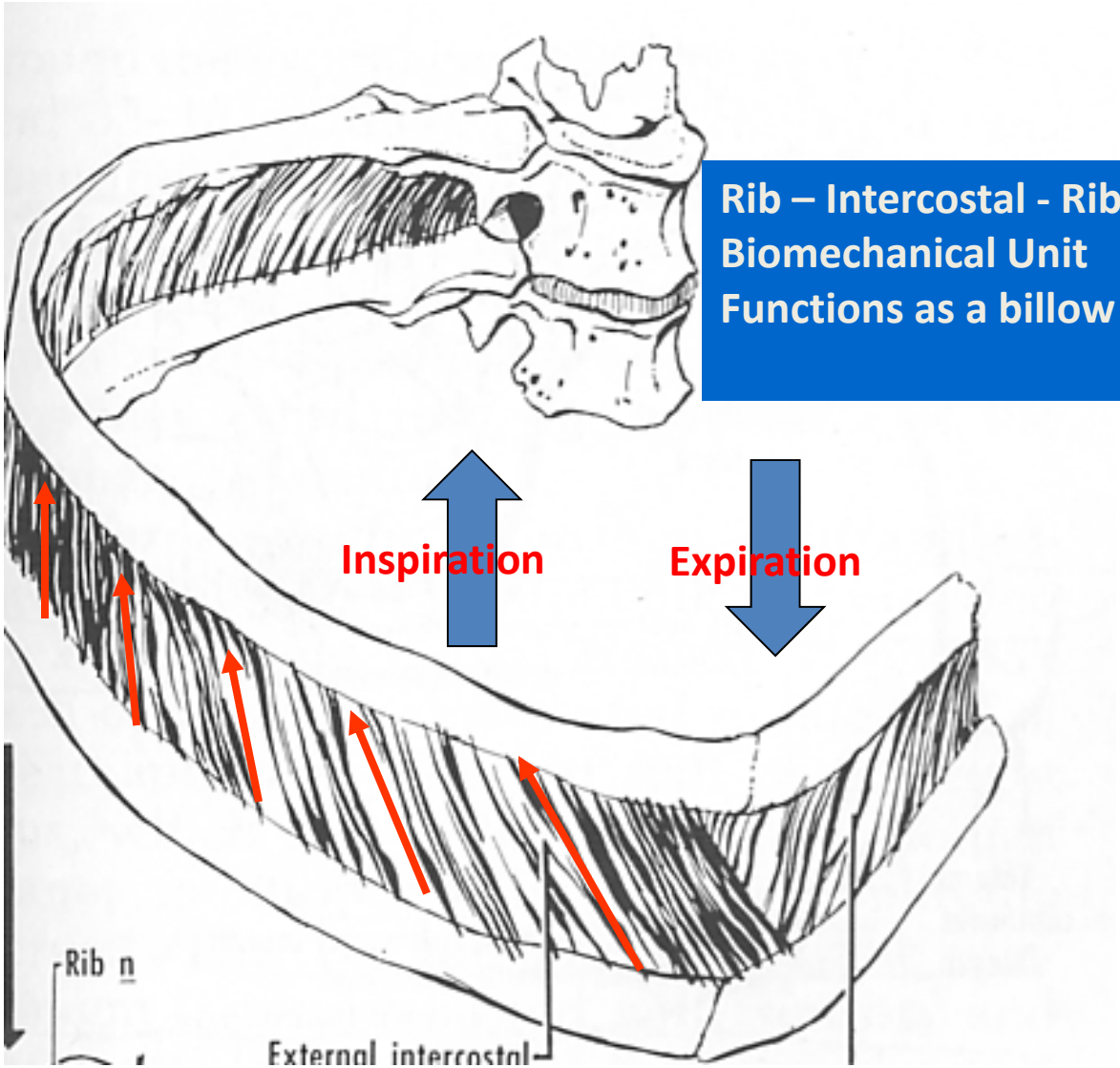
Disclosures

Supported by grants from:

- ✓ Scoliosis Research Society
- ✓ Chest Wall and Spinal Deformity Study Group
- ✓ Synthes Spine, North America
- ✓ NIH R21

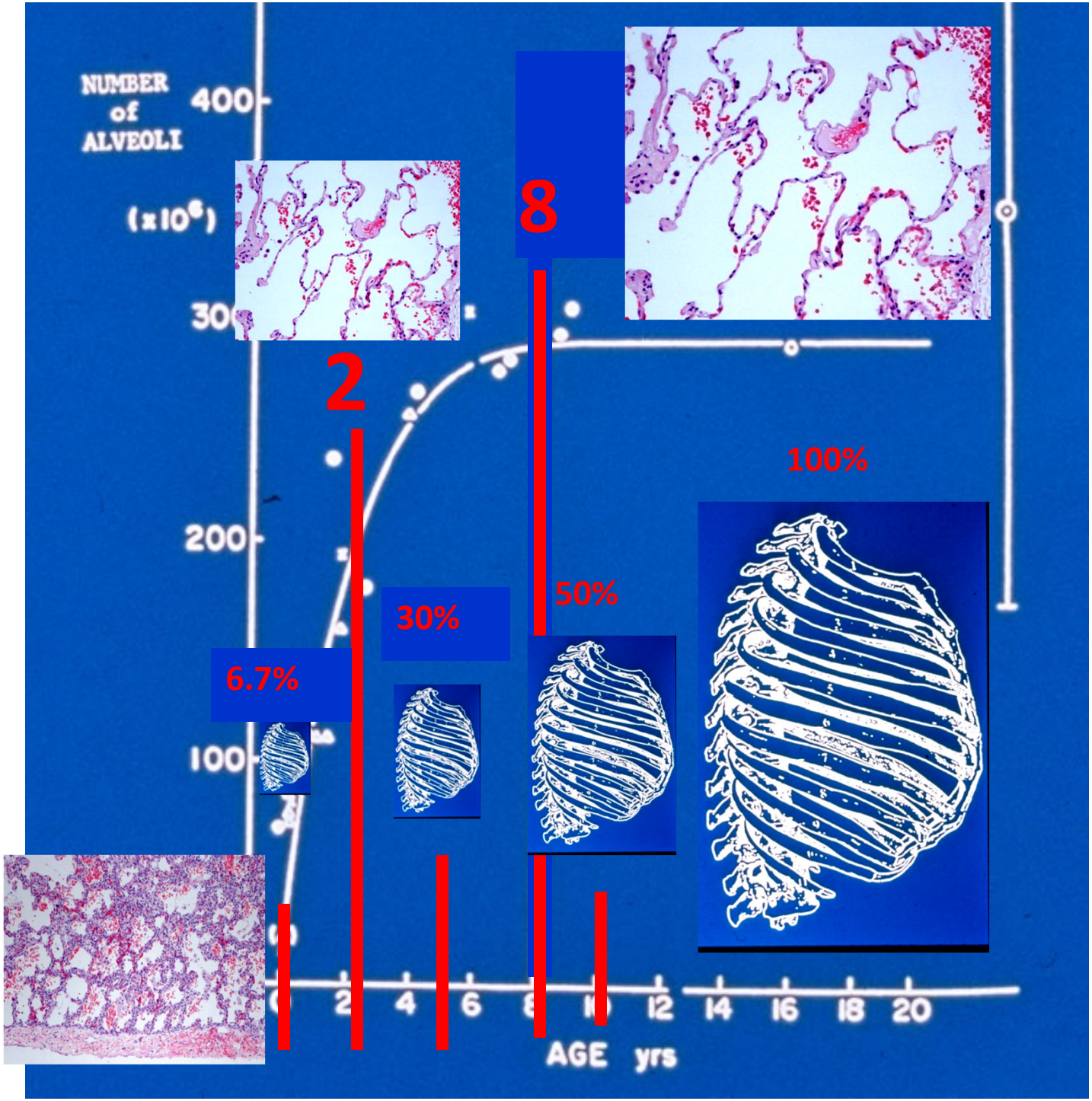
Lungs and thorax directly linked:

- biomechanically in act of respiration
- biologically with respect to lung growth



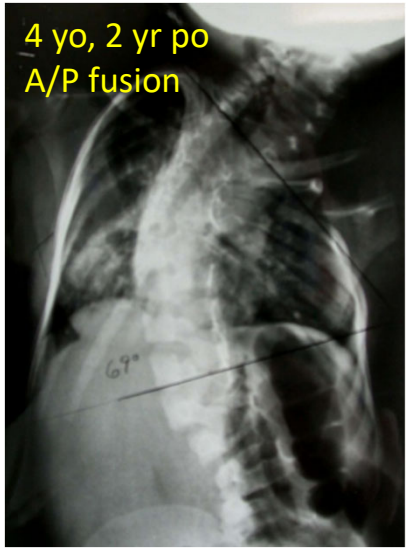
Lung and Thoracic Growth Inter-Dependent

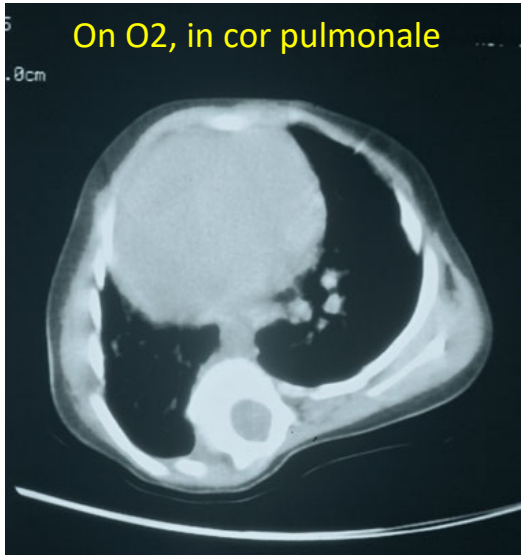
but max number of alveoli attained by age 8

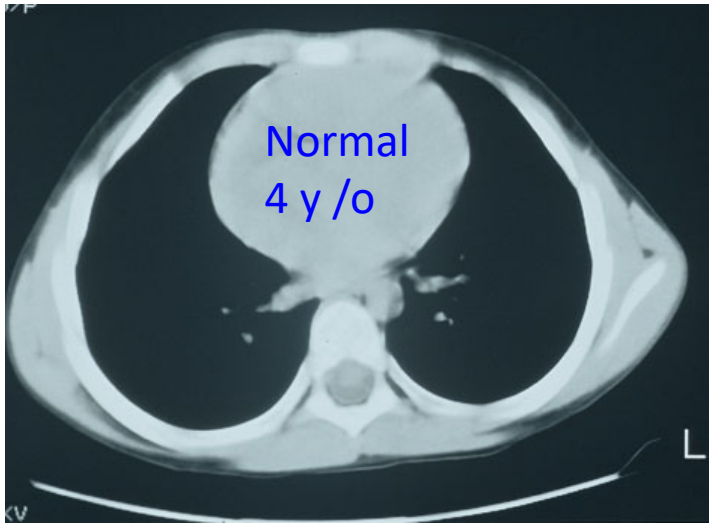


The Growing Thorax

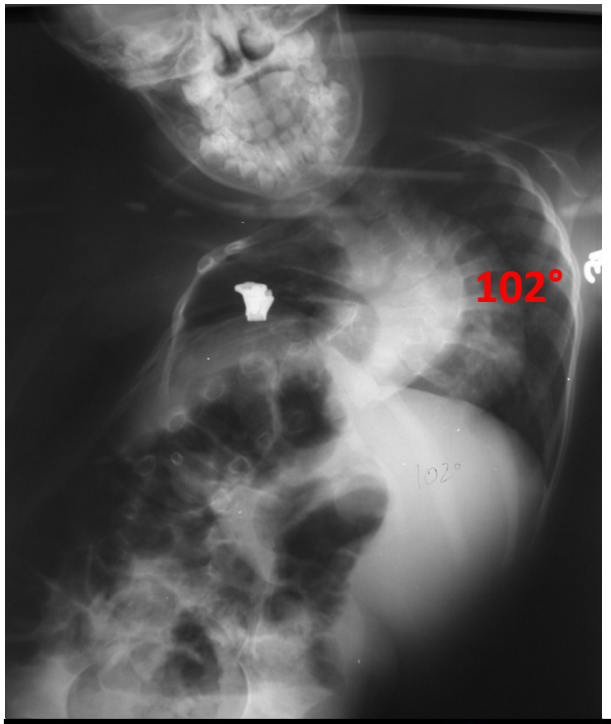
- Must enlarge for lung growth
  - Rib cage provides width and depth
  - Thoracic spine provides height
- Failure of thorax to grow causes extrinsic, restrictive lung disease

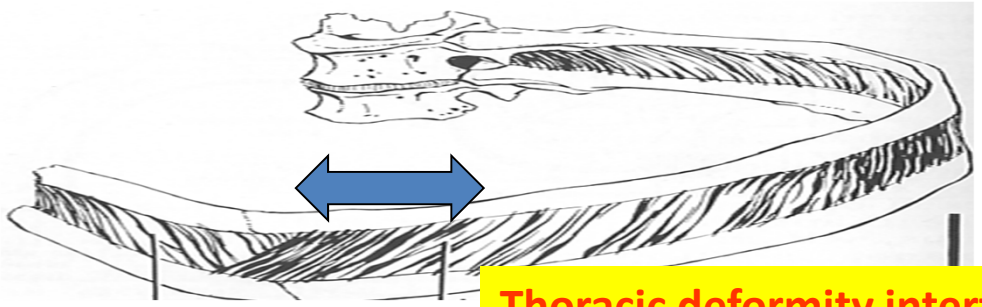






Congenital Scoliosis and Fused Ribs = Failure of Rib Cage to Contribute to Respiratory Function

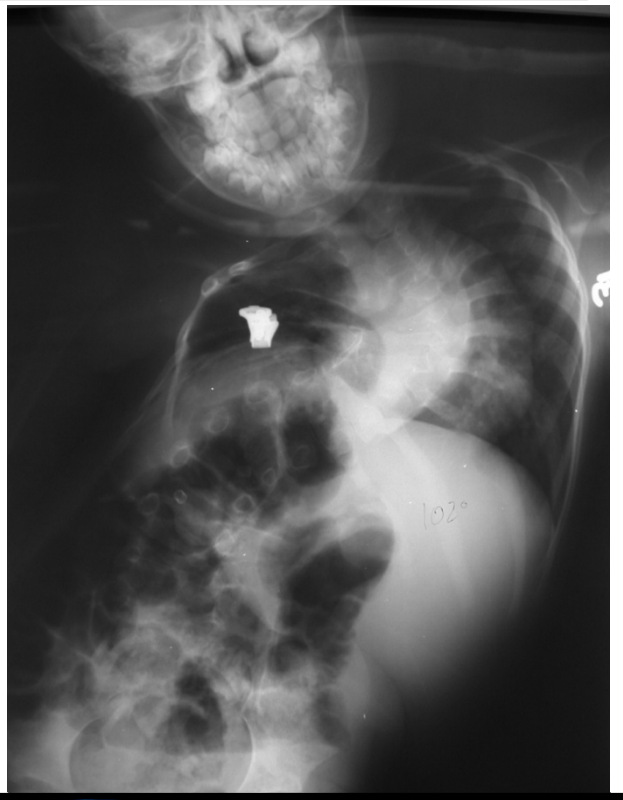




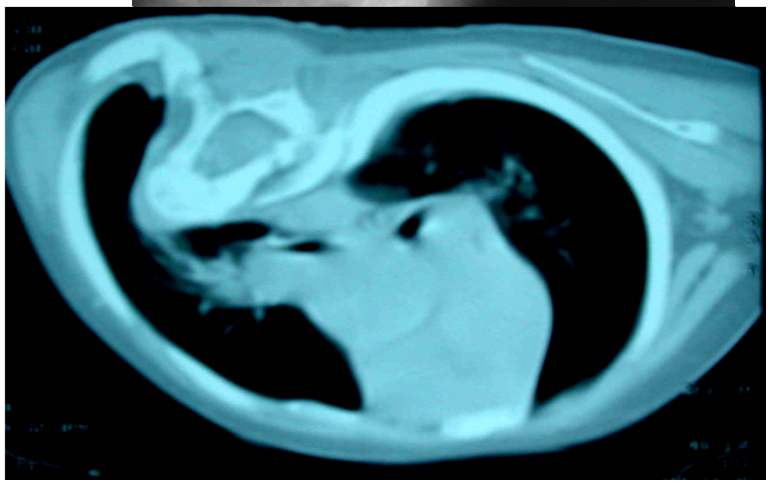
Thoracic deformity interferes with billow action

Thoracic Insufficiency Syndrome

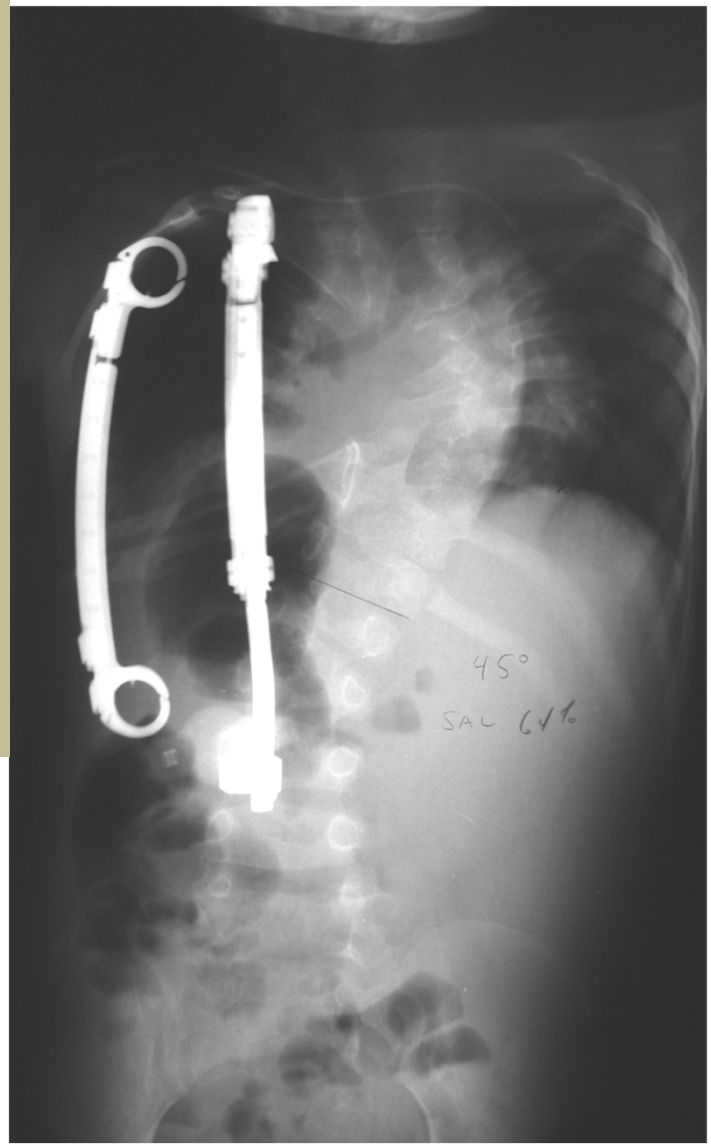
- Inability of thorax to support normal respiration or lung growth
- Results in post-natal pulmonary hypoplasia



Thoracic Insufficiency is *Extrinsic*, restrictive lung disease



Optimizing treatment depends on understanding relationship between growth of thorax and growth/development of the lung



Previously established rabbit model of human TIS-

- Representative of TIS, but did not reproduce severity of the disease observed EOS pts
- IMPROVED MODEL PRESENTED AT LAST YEAR'S ICEOS

SPINE Volume 31, Number 23, pp 2654–2664
©2006, Lippincott Williams & Wilkins, Inc.

The Reciprocal Relationship Between Thoracic and Spinal Deformity and Its Effect on Pulmonary Function in a Rabbit Model

A Pilot Study

Hemal P. Mehta, MS,*† Brian D. Snyder, MD, PhD,*‡ Natasha N. Callender, BS,†
Carissa L. Bellardine, MS,† and Andrew C. Jackson, PhD†

SPINE Volume 35, Number 2, pp 153–161
©2010, Lippincott Williams & Wilkins

Expansion Thoracoplasty Improves Respiratory Function in a Rabbit Model of Postnatal Pulmonary Hypoplasia

A Pilot Study

Hemal P. Mehta, MS,*† Brian D. Snyder, MD, PhD,*‡ Stephen R. Baldassarri, BA,*
Melissa J. Hayward, MD,§ Michael J. Giuffrida, MD,§ Vahid Entezari, MD,*
and Andrew C. Jackson, PhD†

Clin Orthop Relat Res (2011) 469:1375–1382
DOI 10.1007/s11999-011-1807-0

SYMPOSIUM: EARLY ONSET SCOLIOSIS

Expansion Thoracoplasty Affects Lung Growth and Morphology in a Rabbit Model

A Pilot Study

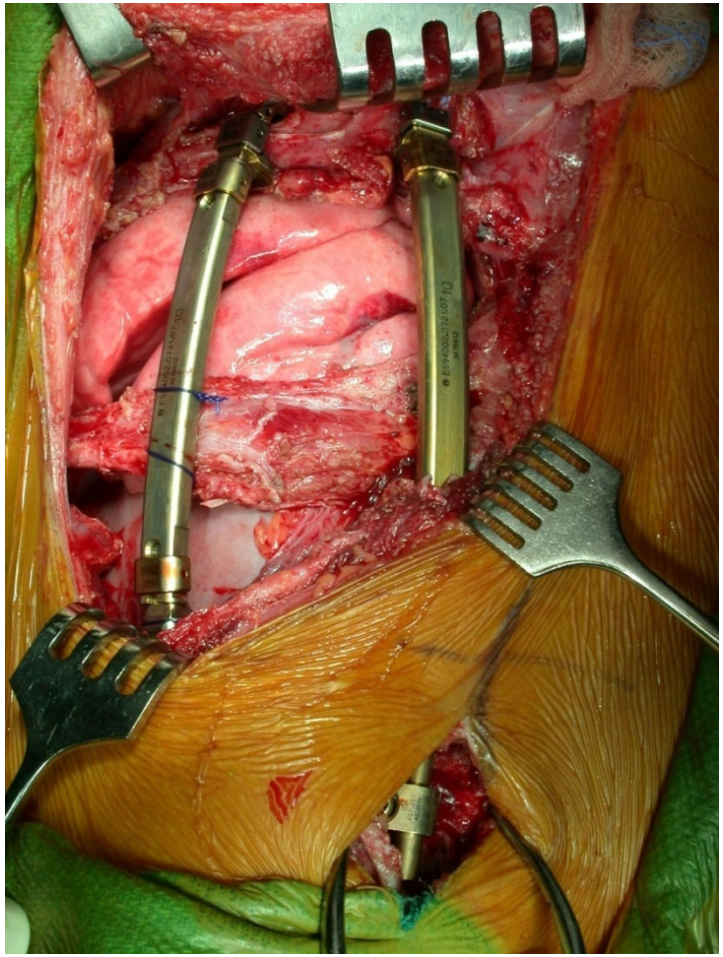
**J. Casey Olson MS, Kyle C. Kurek MD,
Hemal P. Mehta MS, Matt L. Warman MD,
Brian D. Snyder MD, PhD**

Study Aim

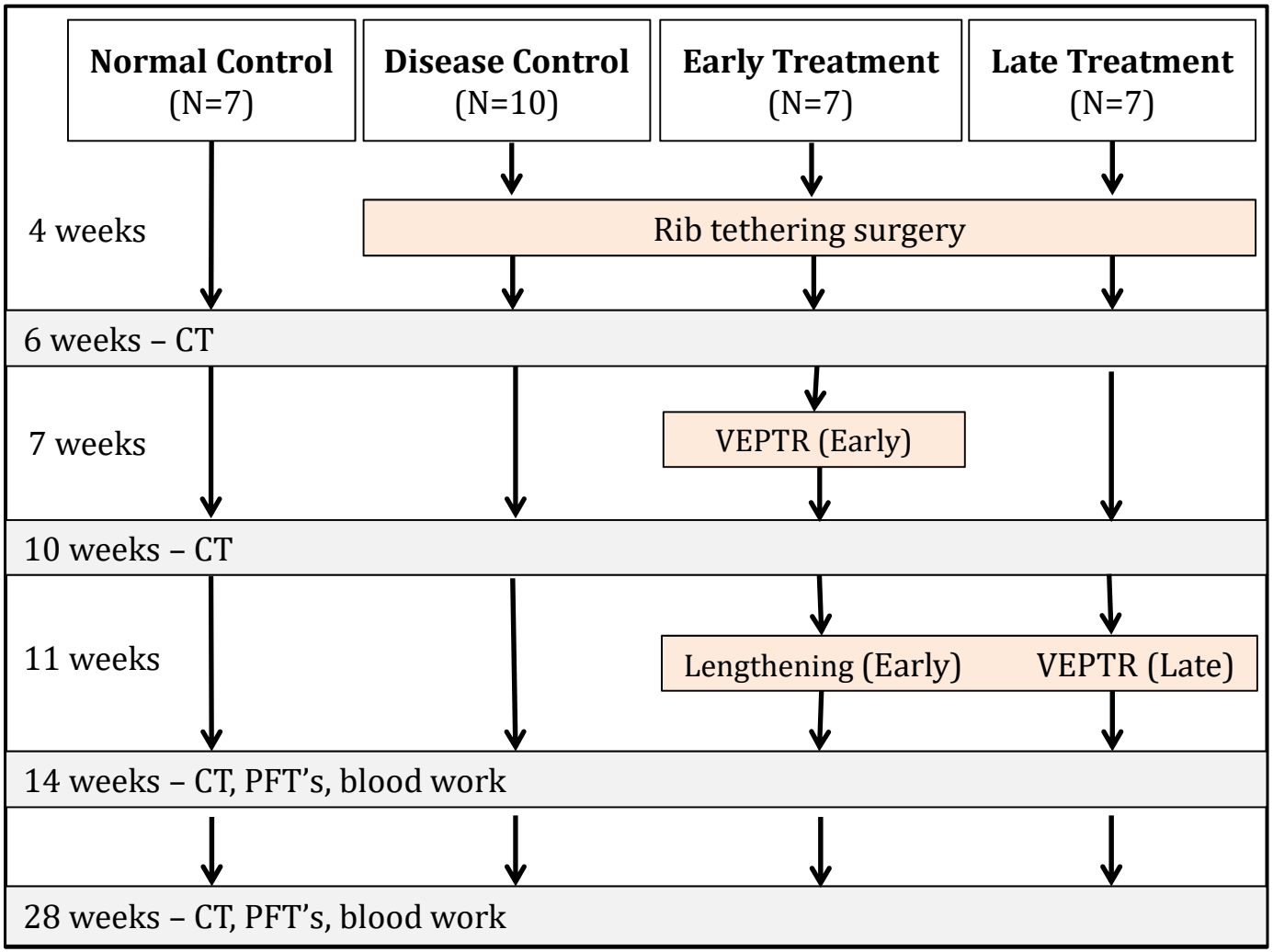
- Using improved Rabbit Model for TIS
  - Evaluate effect of *early vs. late* treatment of TIS by expansion thoracoplasty on correcting spinal deformity, expanding thoracic volume, improving lung growth and respiratory function compared to untreated and healthy control rabbits

Hypothesis

Efficacy of expansion thoracoplasty and sequential lengthening of the constricted hemithorax *depend on the timing of the intervention relative to the growth remaining for the lung, spine and rib cage*

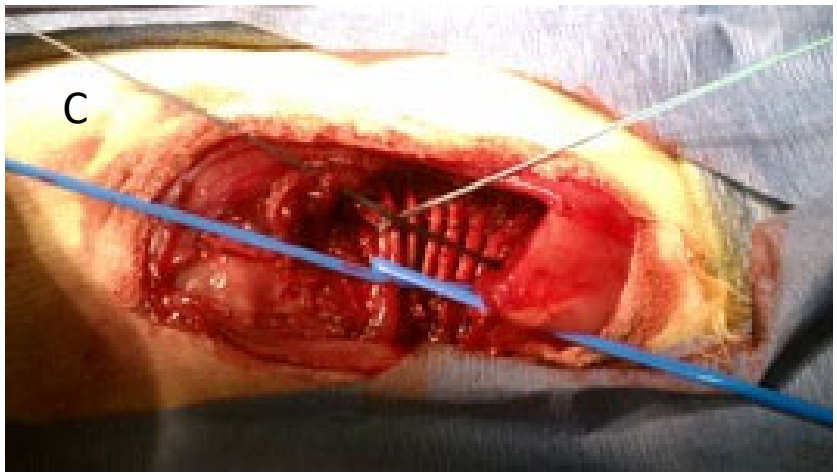


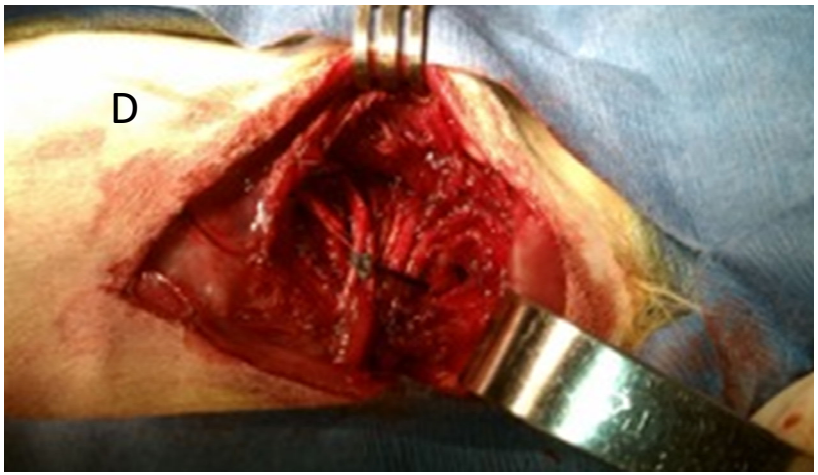
Experimental Design



Rabbits skeletally mature by 28 weeks, growth decreases exponentially after 14 wks
Pulmonary development continues in healthy rabbits through skeletal maturity

Surgical Technique: Unilateral Rib Tether (Right Hemithorax)
Performed @ age 4wks to induce TIS





3D Deformity of Spine/Thorax Induced with Growth

SEVERE

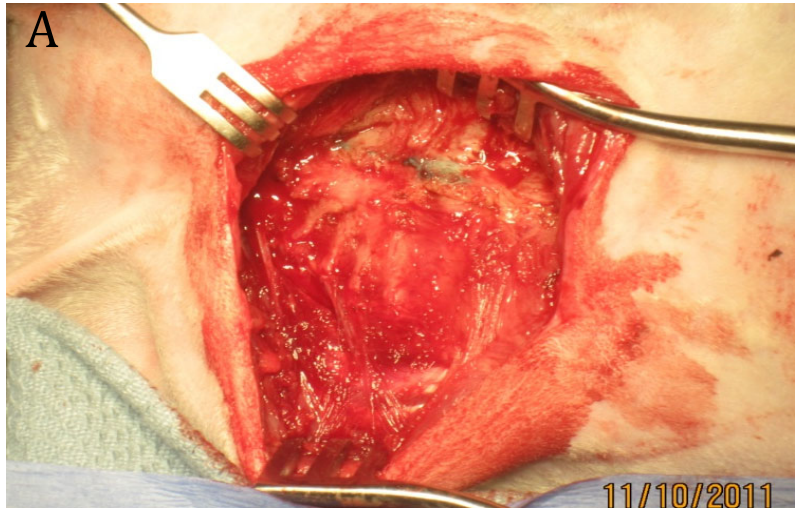
MODERATE

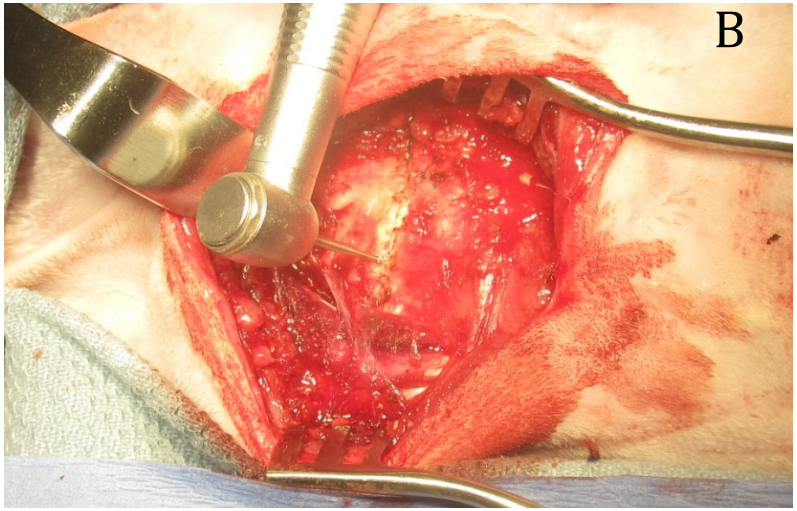
- **Variability in disease**
  - Severe TIS (Scoliosis >40°)
  - Moderate TIS (Scoliosis<40°)

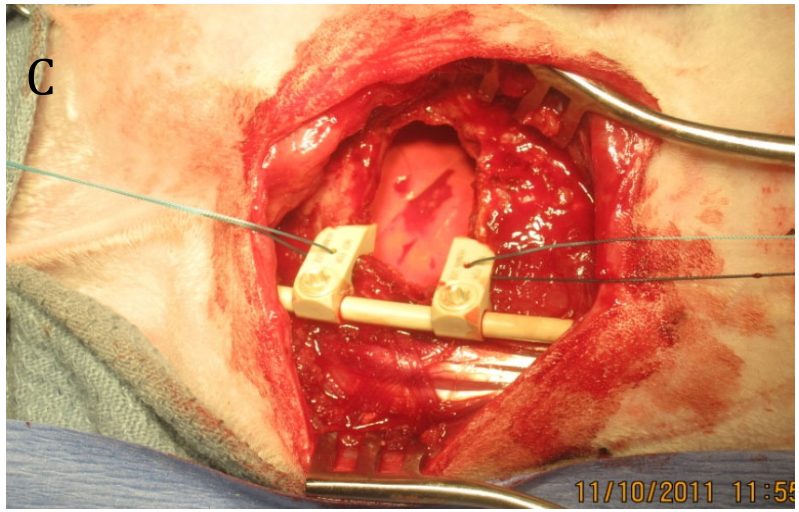
Expansion Thoracoplasty:

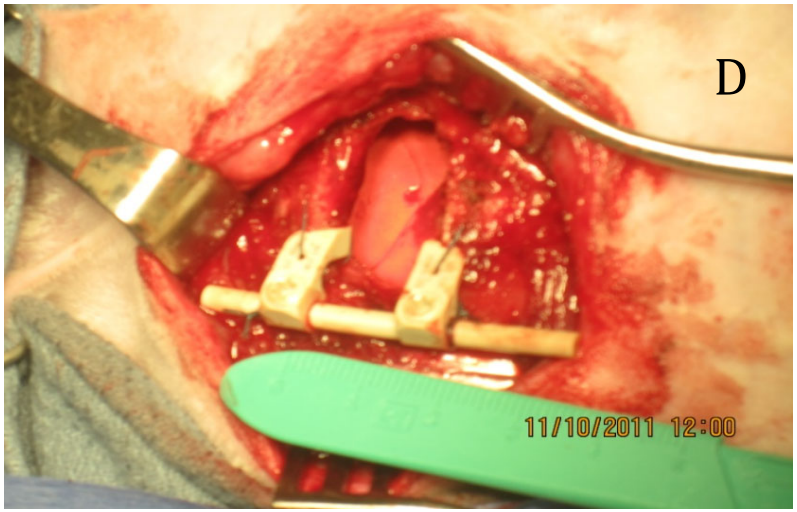
Performed @ 7 wks (Early) and 11 wks (Late)

Early group - repeat lengthening rib distracter @ 11 wks

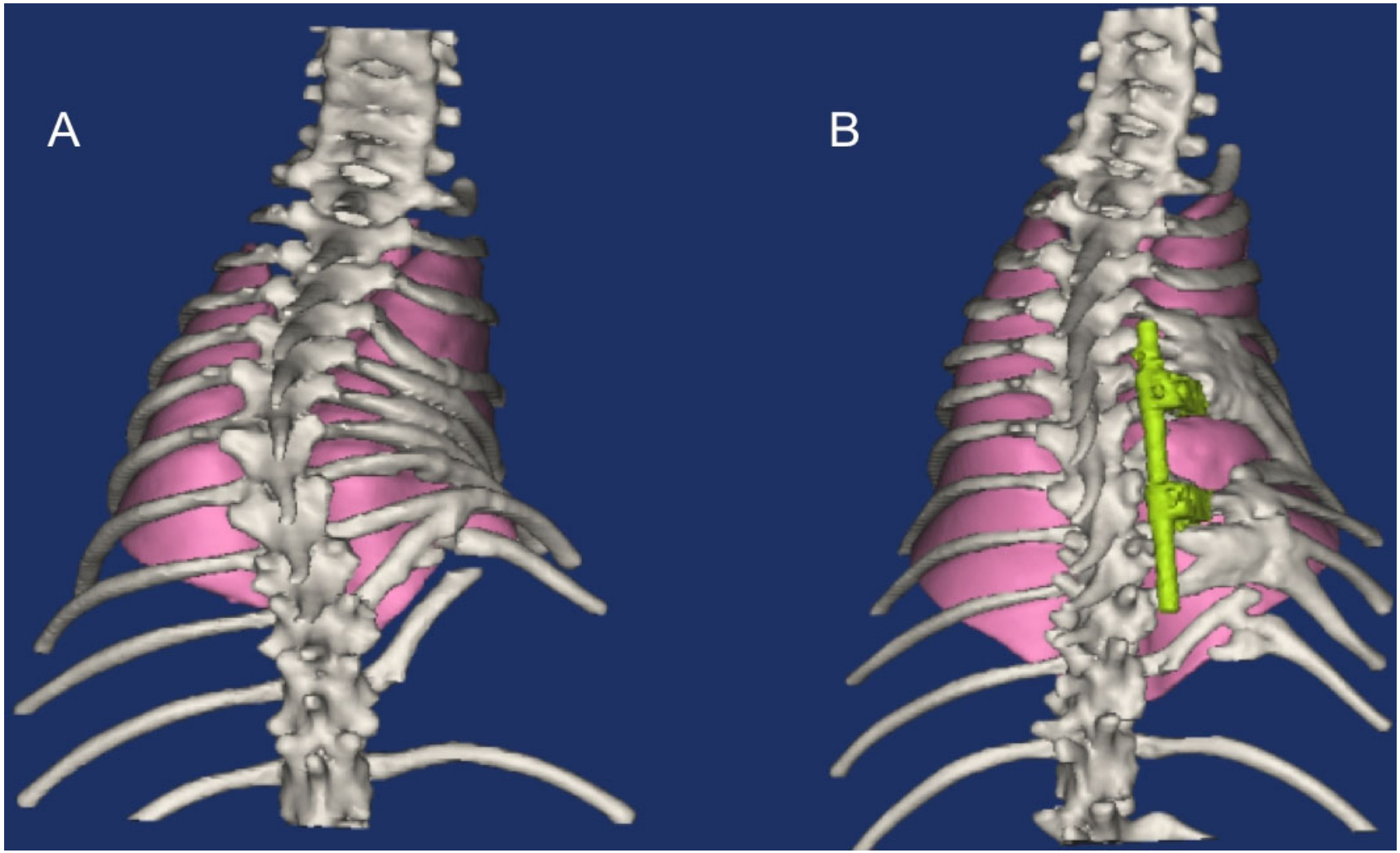






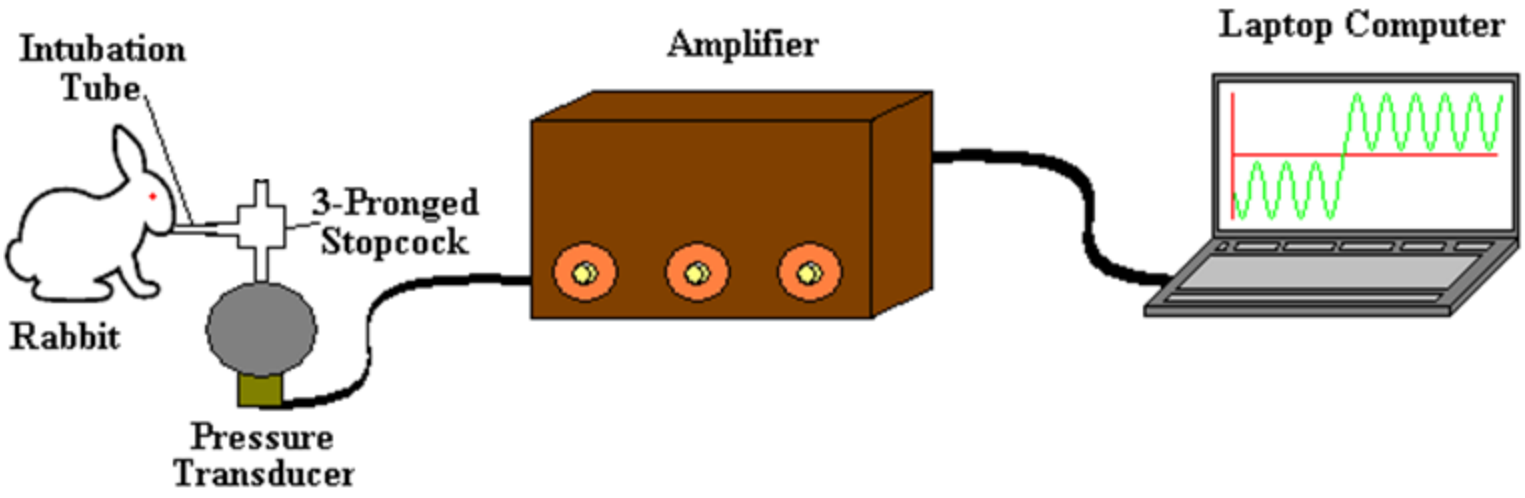


Expansion Thoracoplasty



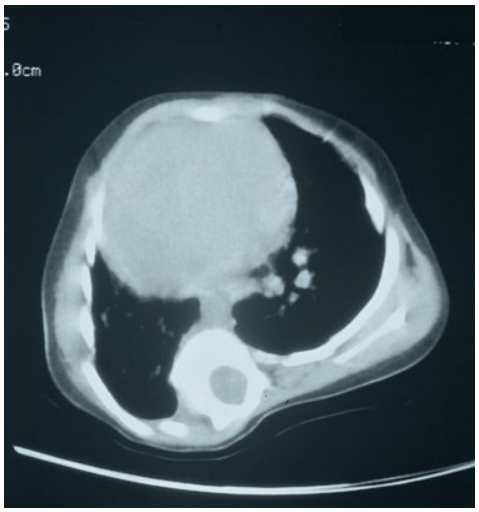
CT Imaging Protocol Lung/Thorax

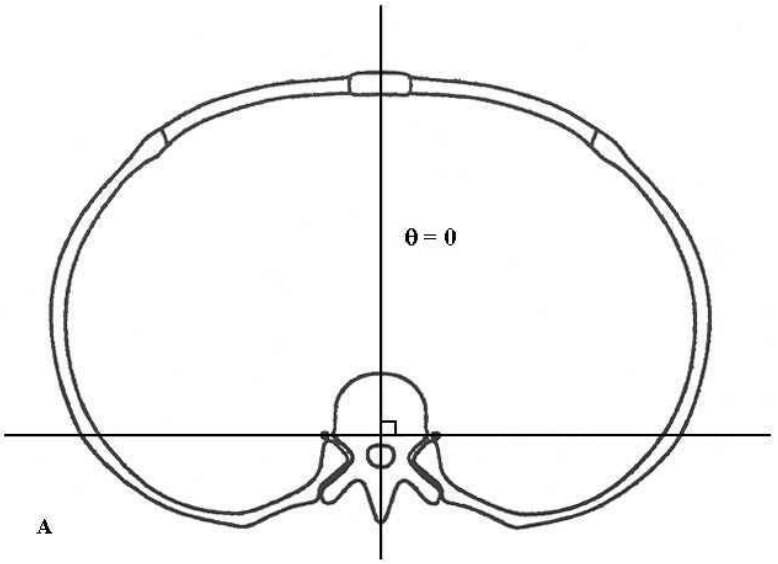
- CT scans: 6, 10, 14, & 28 weeks of age
  - Rabbits anesthetized, mechanically ventilated
  - Hyperventilated to induce apnea
  - "Breath-hold" on 3rd breath
    - ETT pressure maintained at 0, 5, 15, & 25 cm H_2O

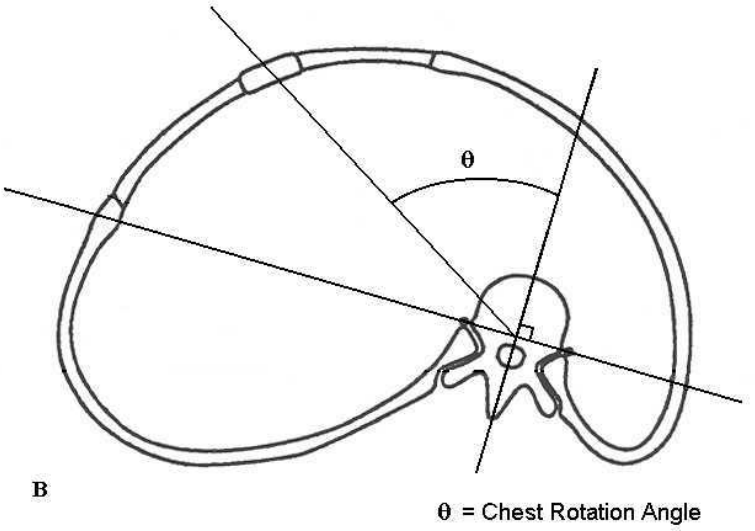


Calculation of Chest Rotation Angle

- Measured sequentially, transaxial images T1 - T13
- Describes distortion of thorax ("windswept thorax")

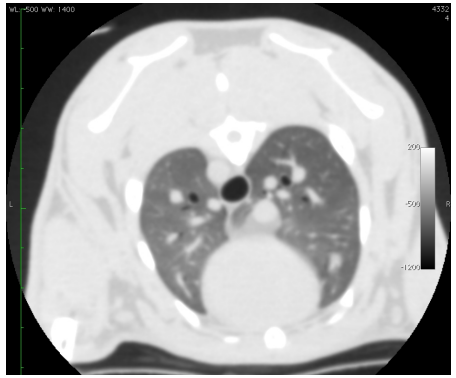


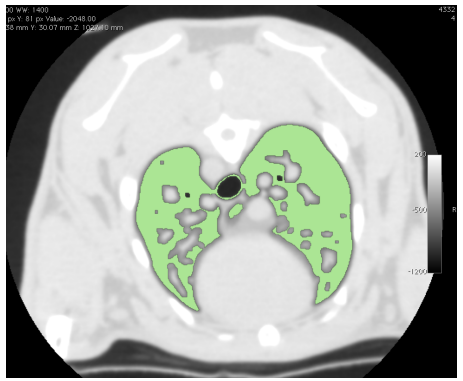




Calculation of Lung Mass and Volume from CT

- **Segment Lung**:
  - Based on tissue density threshold
  - Manually remove esophagus and trachea
  - Obtain total lung volume @ sequential "breath hold" pressures 0-25 cmH_2O
  - Separate left and right lungs
- **Hounsfield unit(HU) linearly related to density**
  - HU = 0 equivalent to H_2O
  - HU = -1000 equivalent to air
  - Lung tissue density equivalent to water ~ 1g/mL. Air density negligible ~0g/mL.
  - $\rho_{voxel} = 1 + (HU/1000)$



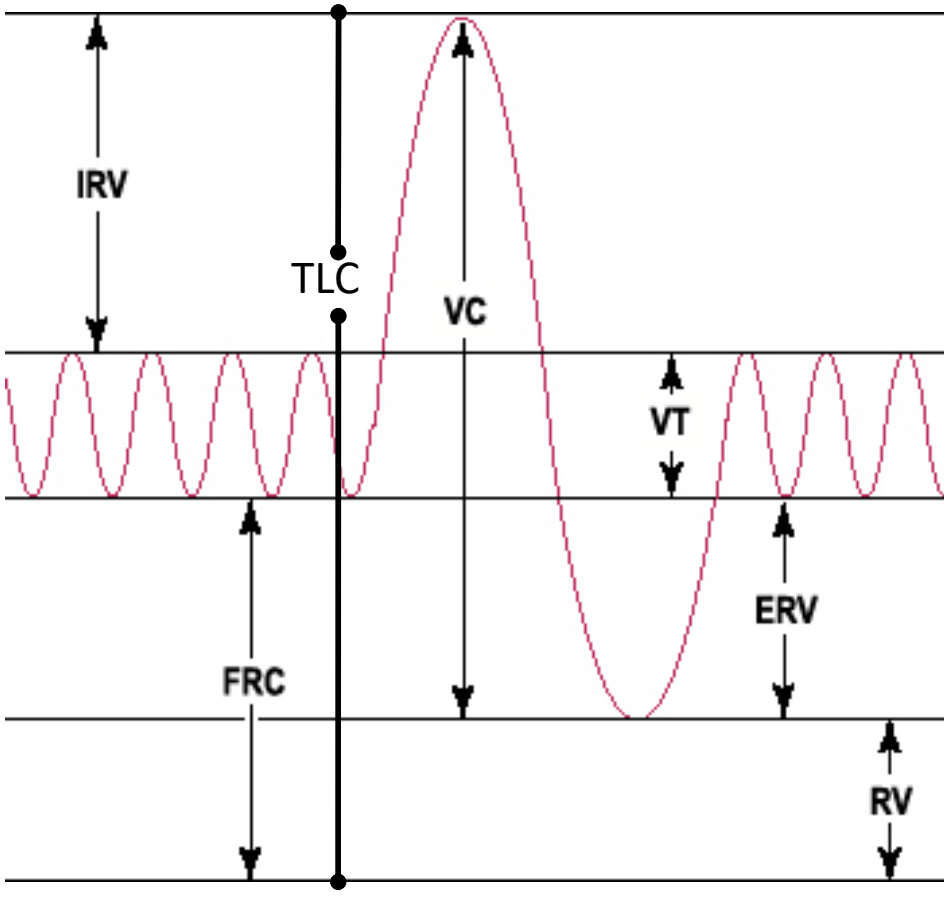


- **Calculations:**

$$V_{air} = \sum_{n=1}^{N} (-HU/1000) \cdot V_{pixel} \qquad M_{lungs} = \sum_{n=1}^{N} ((1 + HU/1000)) \cdot V_{pixel}$$

Lung Volume Measures

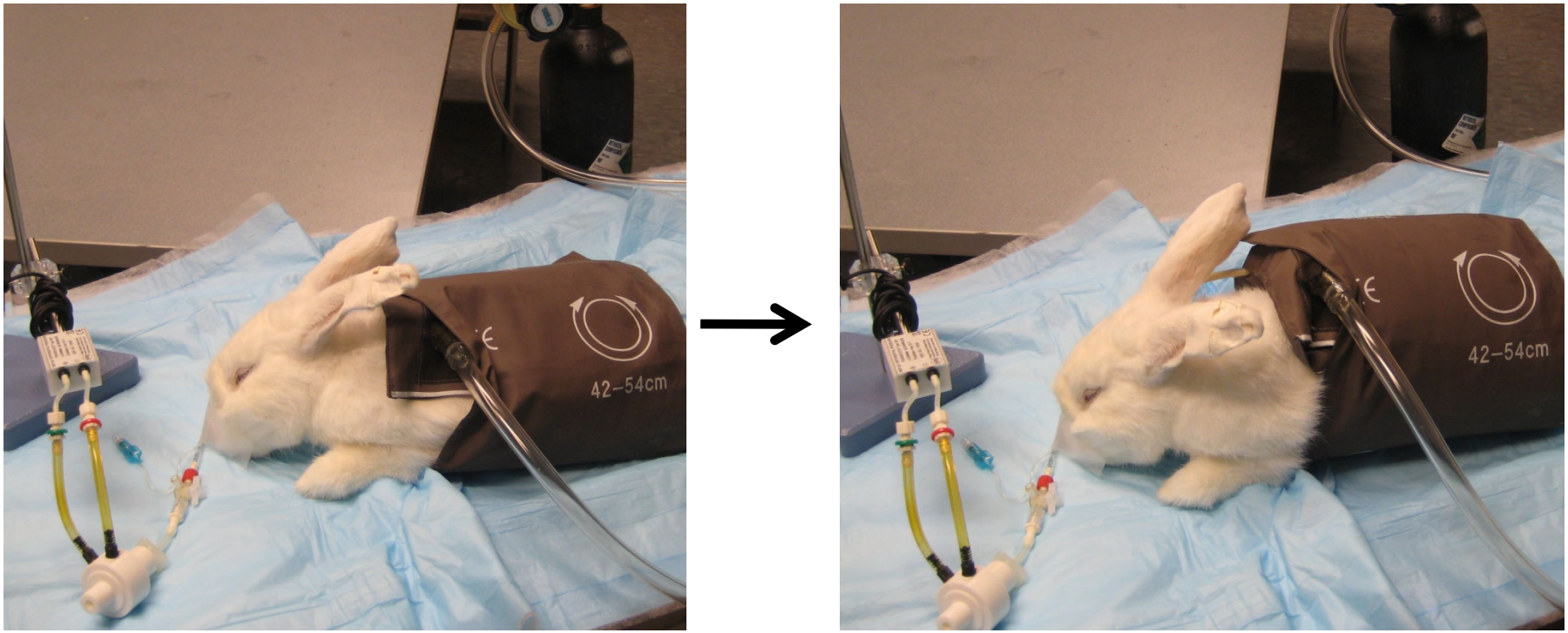
- CT based measures
  - **TLC** : Aerated lung volume measured @ 25 cmH_20 static ETT press.
  - **FRC** : Aerated lung volume measured @ 0 cm H_2O static ETT press.
- PFT
  - **VC**: Raised Volume Rapid Thoracoabdominal Compression (RVRTC)



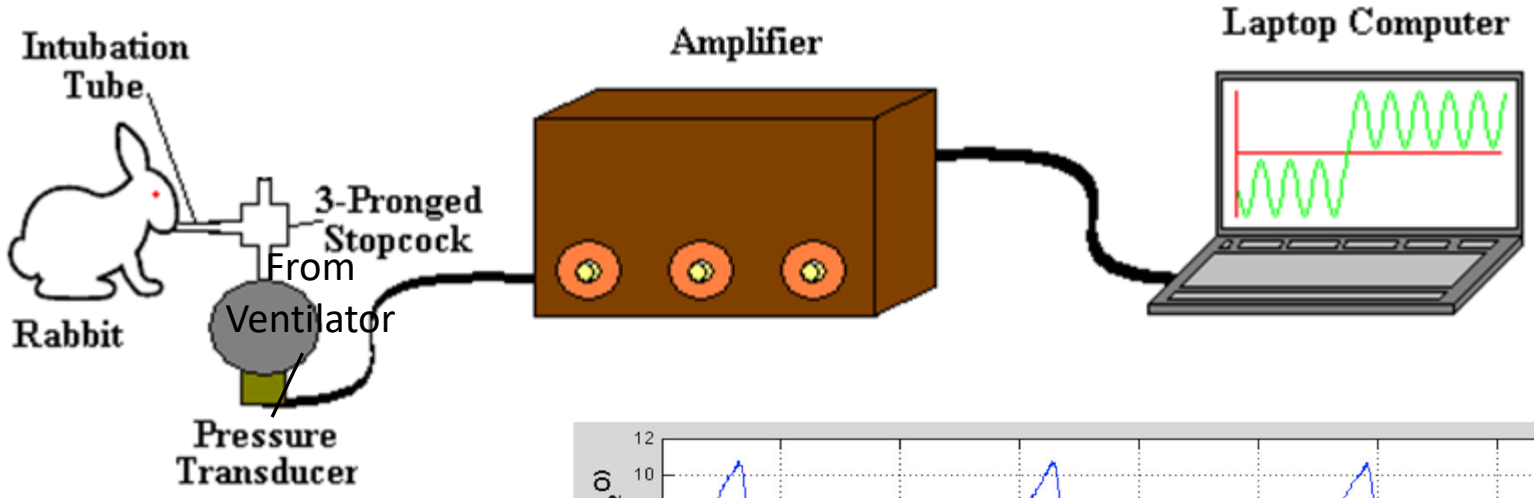
Respiratory Volumes

Vital Capacity & Residual Volume

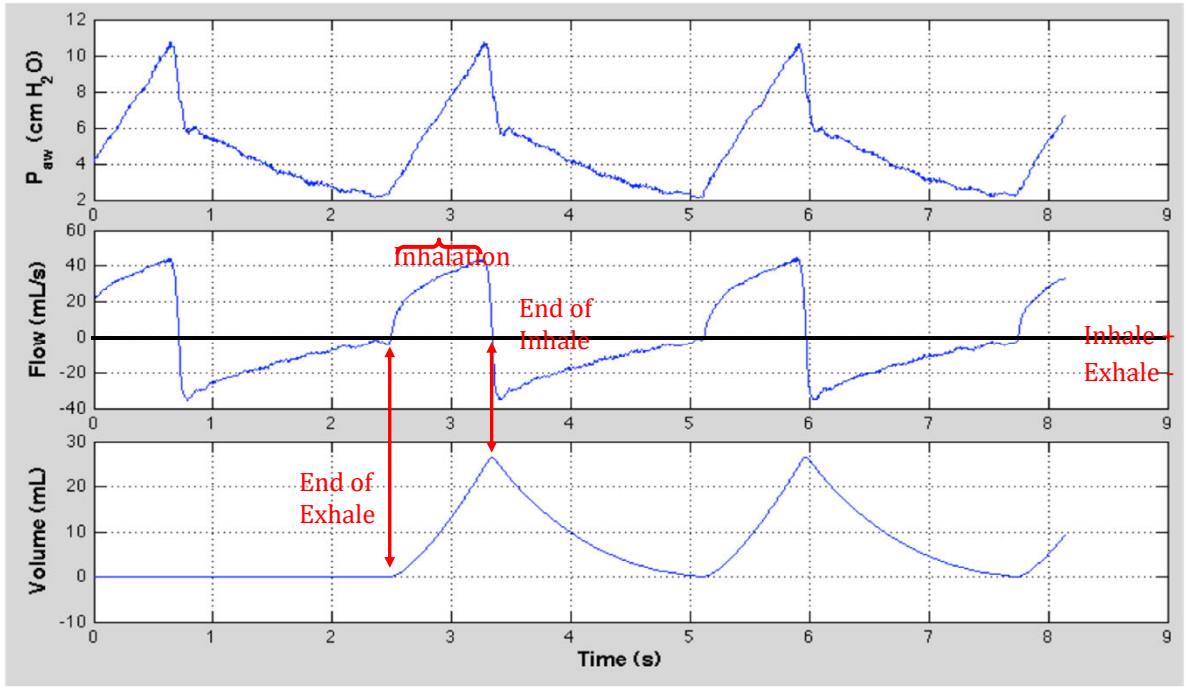
- Raised Volume Rapid Thoracoabdominal Compression (RVRTC)
  - Similar to forced expiration test in infants
  - Lungs forcefully deflated from TLC to RV
- Protocol: Anesthetized/Ventilated rabbit
  - Lungs inflated to 25 cmH_2O (TLC)
  - Thoracoabdominal air bladder rapidly raised to 60 cmH_2O
  - Expired air volume recorded (VC)



Respiratory Compliance Measurement

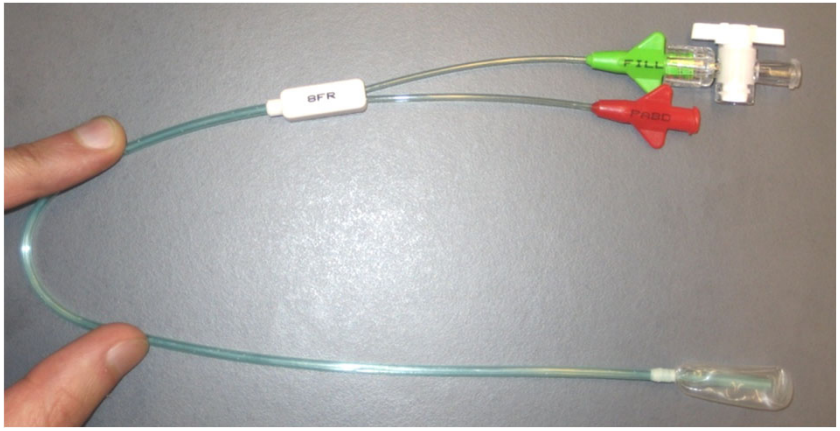


- Compliance = $\Delta V_{Lungs}/\Delta P_{airway}$
- Δ volume after inflating lung to 25cmH_2O

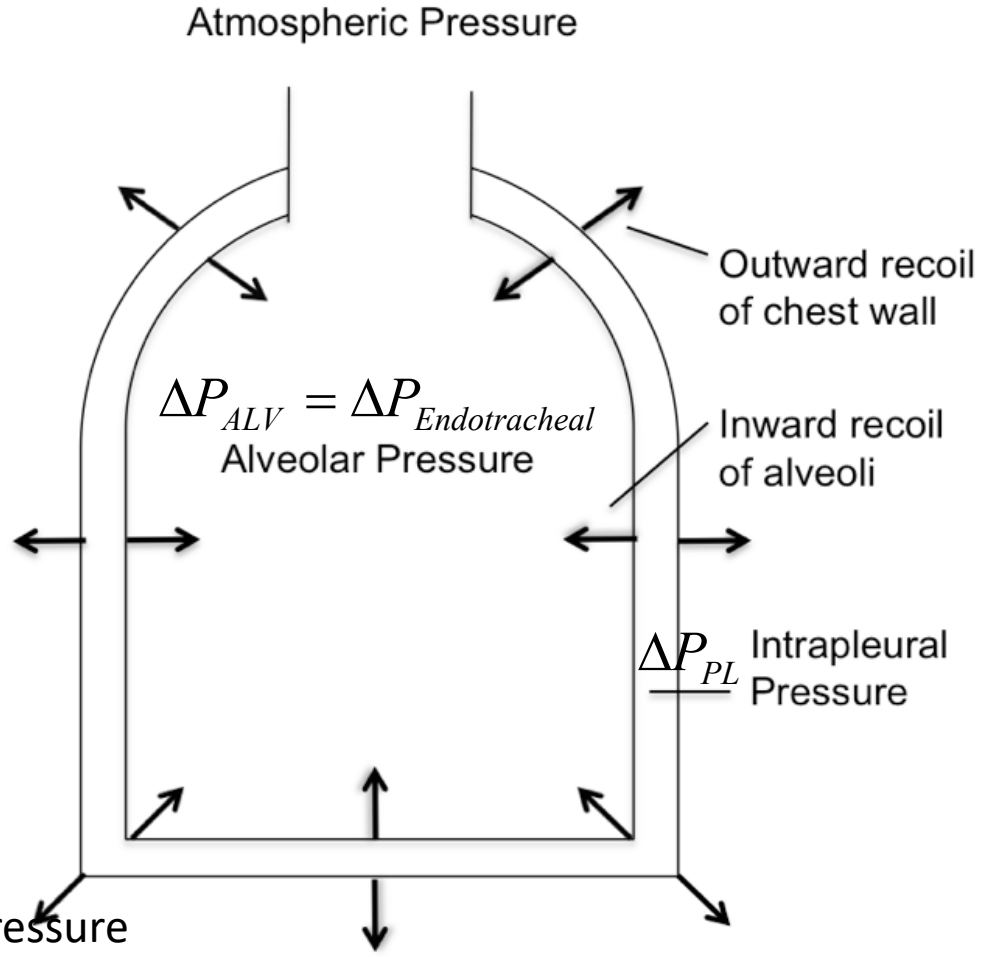


Partitioned Compliance

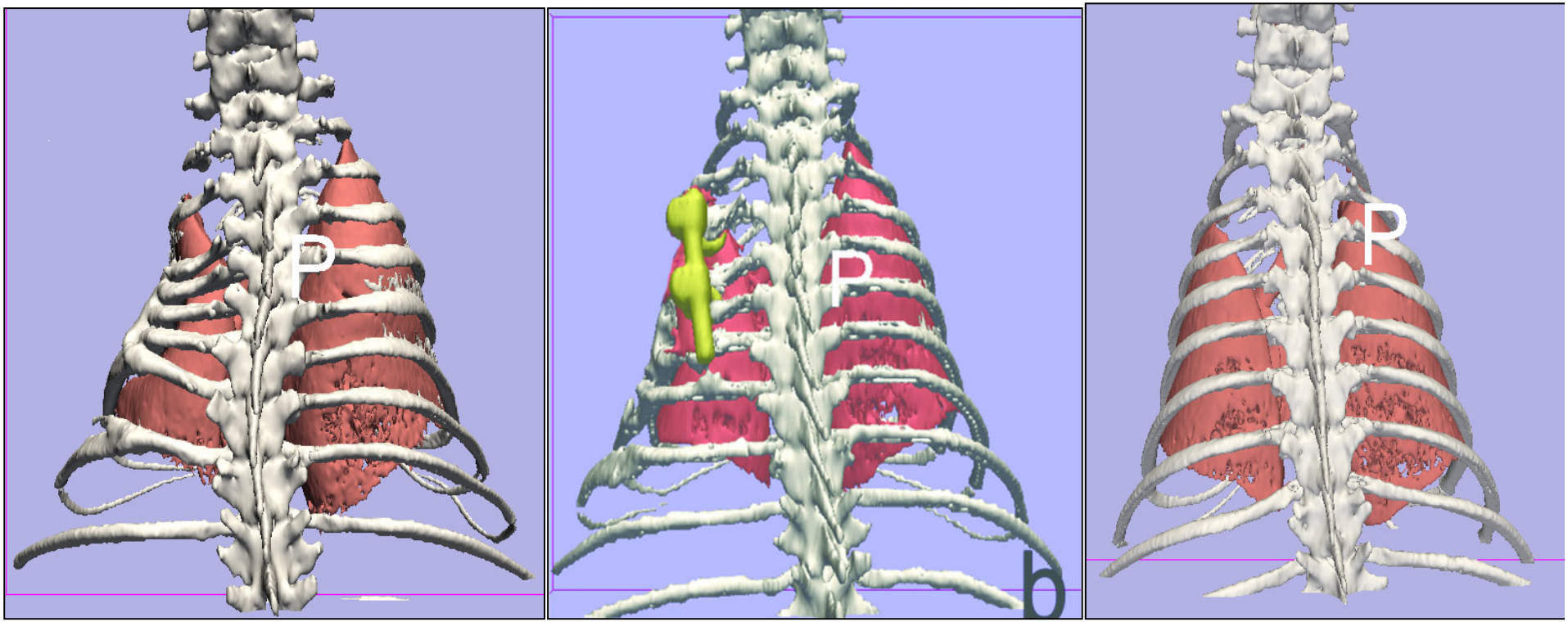
- Chest wall $C_{CW} = \frac{\Delta V_L}{\Delta P_{PL}}$
- Lung $C_L = \frac{\Delta V_L}{\Delta P_{ALV} - \Delta P_{PL}}$
- Total Resp. $C_R = \frac{\Delta V_L}{\Delta P_{ALV}}$



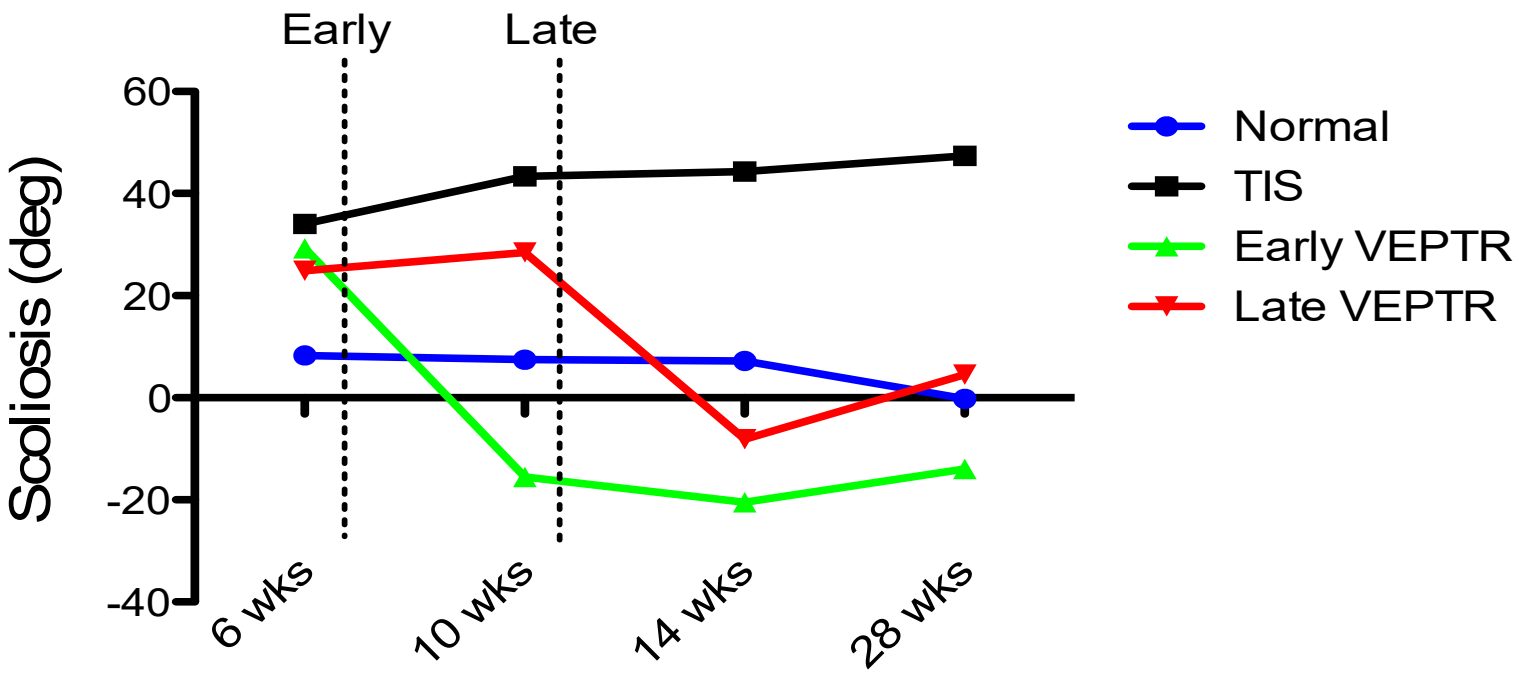
Pediatric esophageal balloon ≅ intrapleural pressure



RESULTS



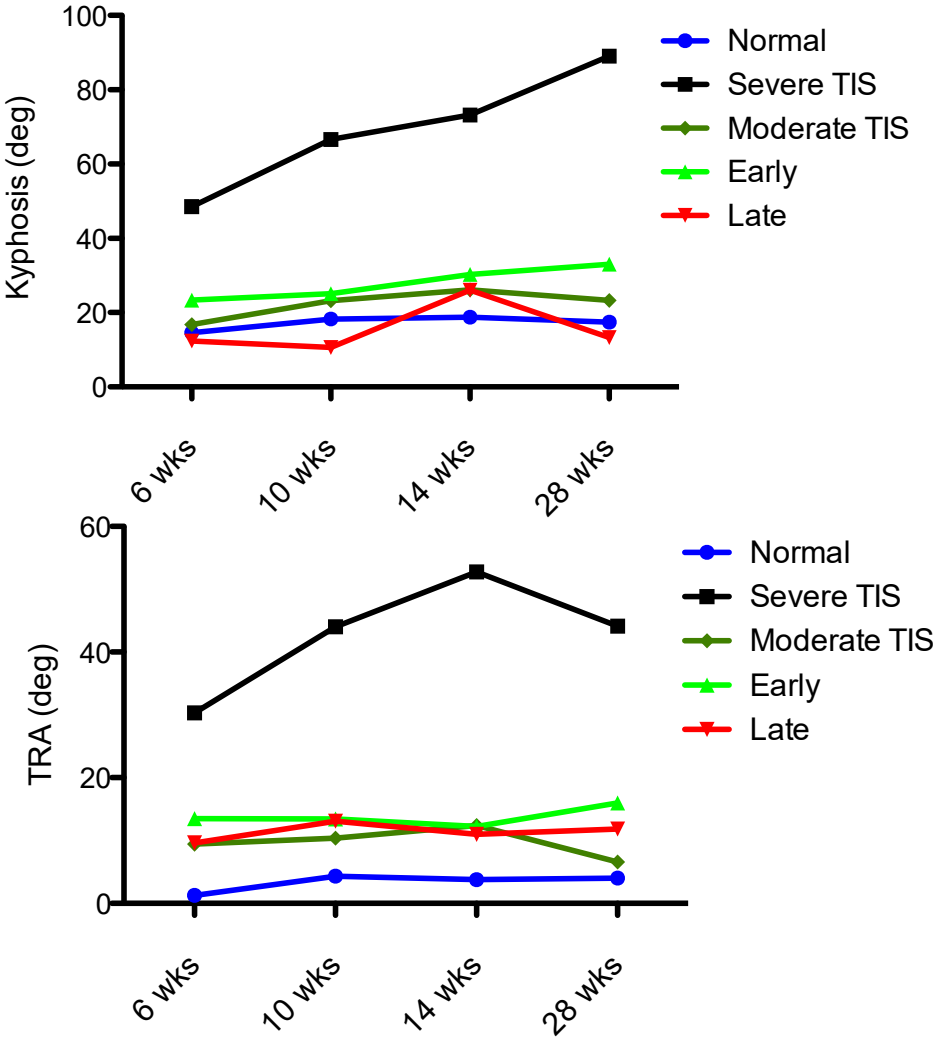
Resultant Spinal Deformity: Scoliosis



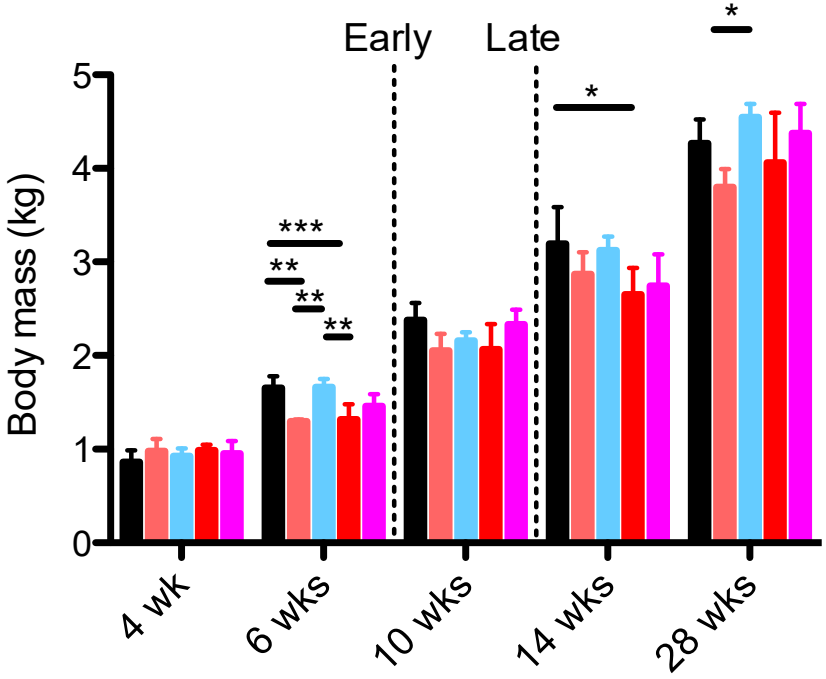
- 2 weeks after rib tethering, rabbits achieved average scoliosis of 27.7°
- Scoliosis progressed in TIS group to ~40° by age 14 weeks
- Compared to TIS, scoliosis less ($p<0.001$) Normal & treated rabbits @ 14 & 28 wks
- Scoliosis overcorrected in treated rabbits
- Completion of growth, anti-scoliosis improved 7° for Early & 18° for Late Treatment

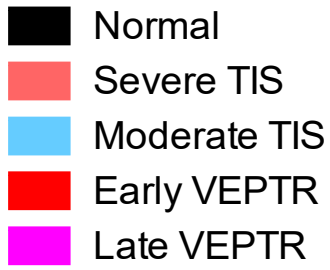
Resultant Spinal Deformity: Kyphosis and Trunk Rotation

- Unilateral Rib tethering induced kyphosis and “windswept” thorax in severe TIS group
- Expansion thoracoplasty (Early or Late) significantly reduced 3D spinal deformity



Change in Body Mass with Somatic Growth



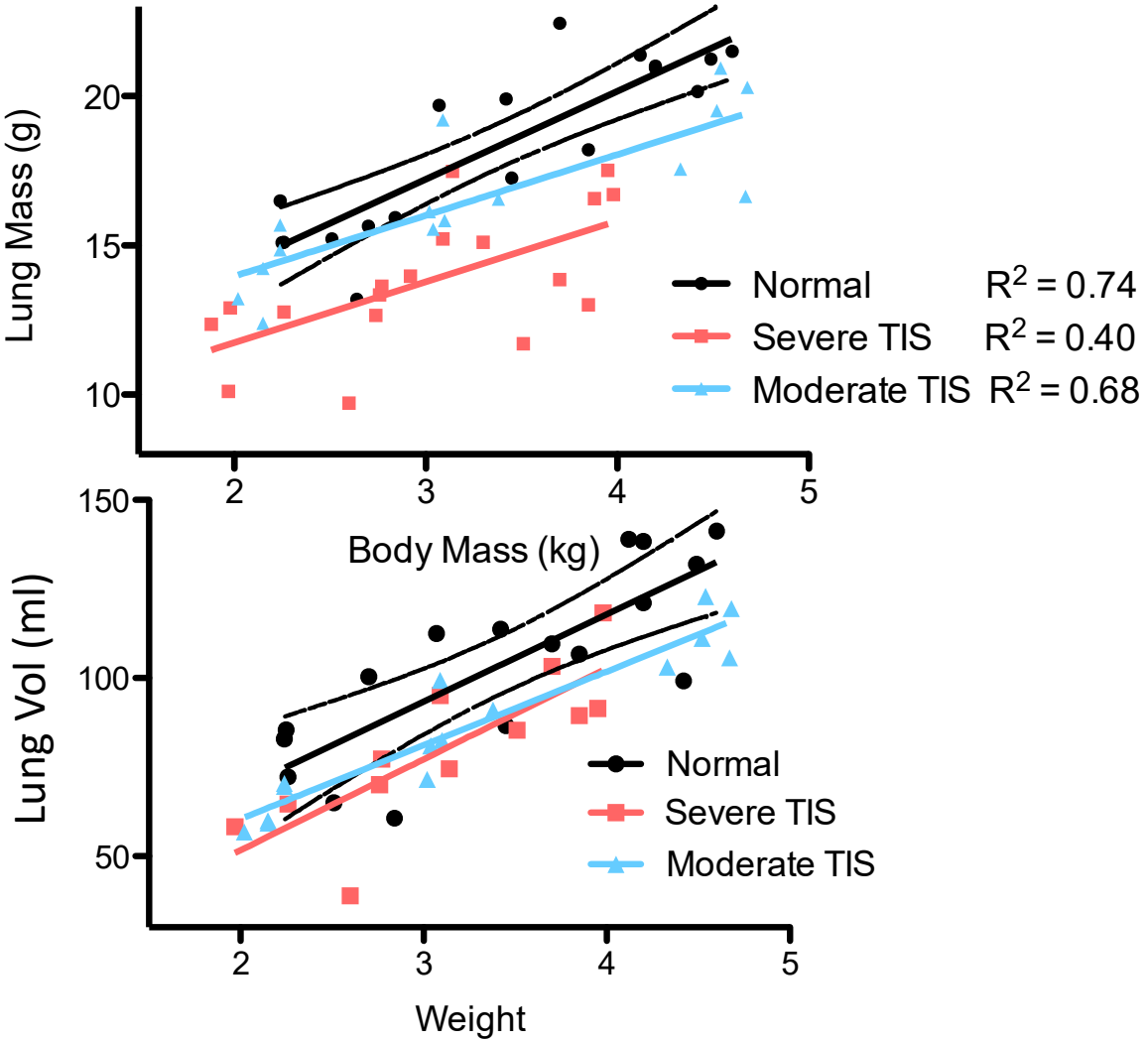


* - p<0.05, ** - p<0.01, *** - p<0.001.
ANOVA with Bonferroni post-hoc analysis

- @ 6 wks, prior to expansion thoracoplasty, Normal and Moderate TIS rabbits weigh more than rabbits with Severe TIS and TIS rabbits assigned to thoracoplasty groups
- @14 wks, Early thoracoplasty rabbits (*expansion X2*) weigh less than normal
- @28 wks, severe TIS rabbits weigh less than moderately affected TIS rabbits

Growth of Lung (Mass and Volume) Relative to Somatic Growth (Body Mass)

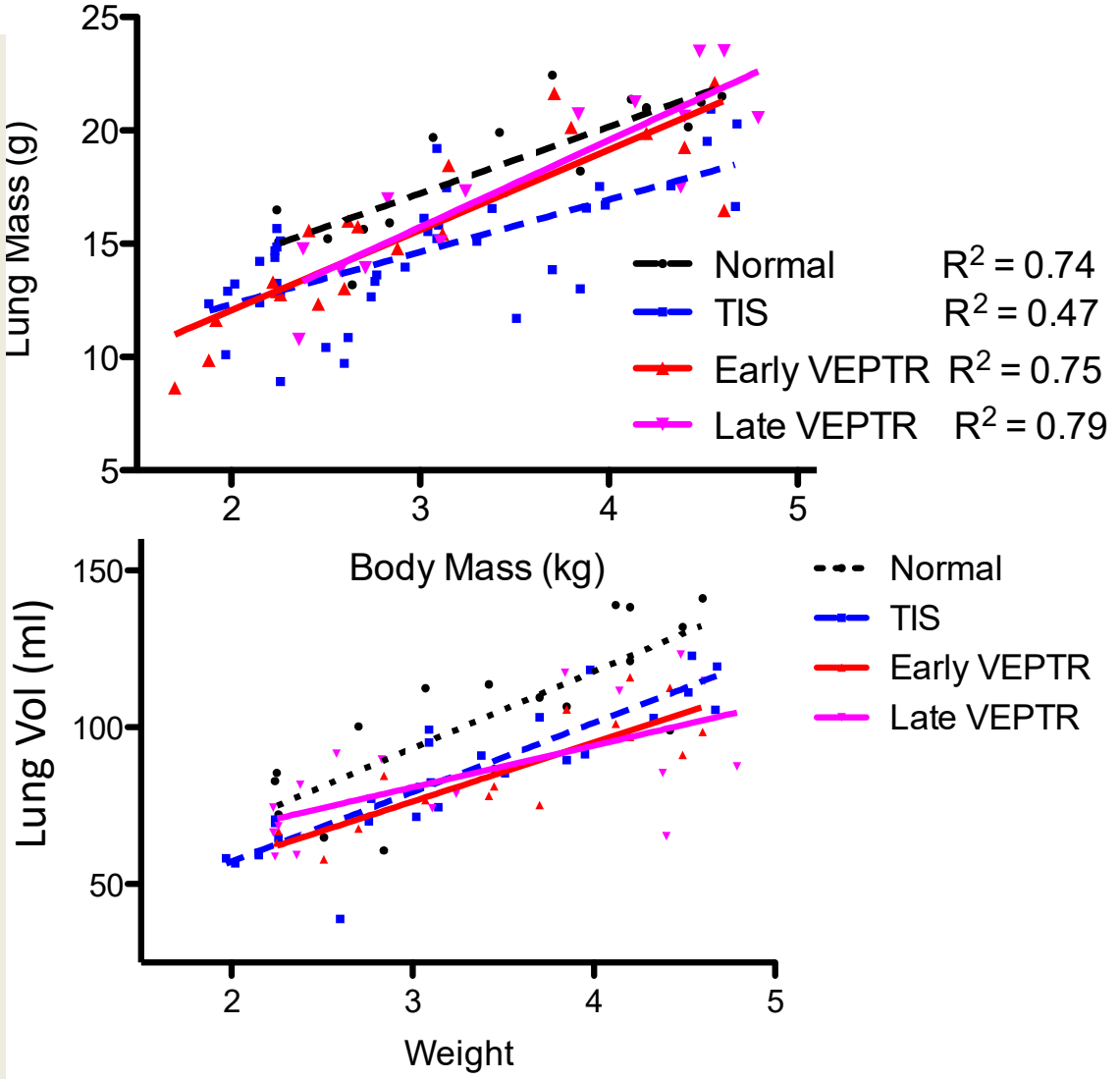
- Rate of lung growth (measured by mass or volume) relative to somatic growth is significantly less than normal for rabbits with moderate and severe TIS



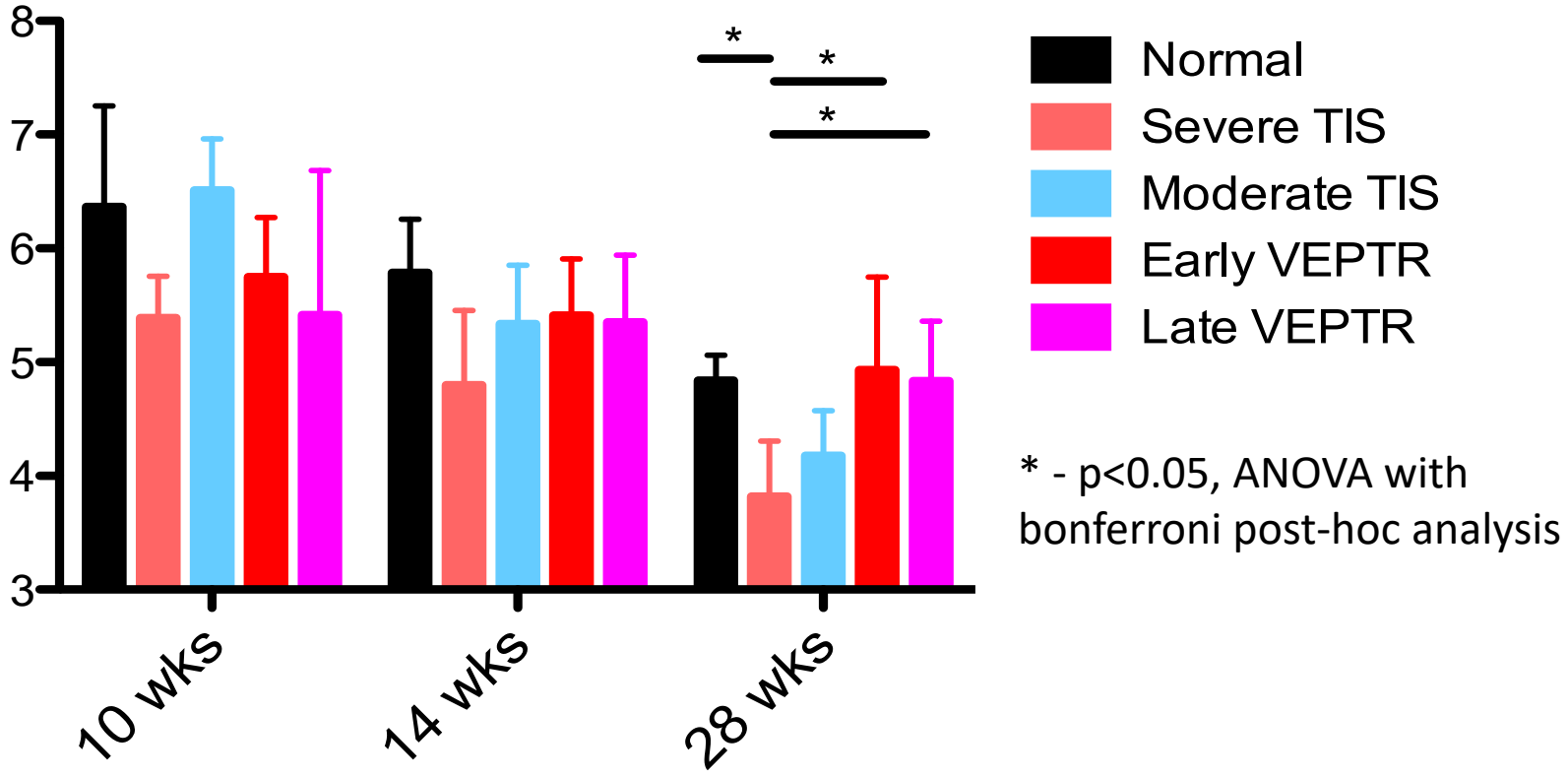
Response to Early and Late Thoracoplasty

Lung Growth (Mass & Volume) Relative to Somatic Growth (Body Mass)

- Thoracoplasty **improves** rate of lung growth relative to somatic growth when lung growth measured by *mass*
- Thoracoplasty **less effective** when lung growth measured by aerated *lung volume*
  - ➢ suggests that while there is more lung parenchyma, may not be functional lung tissue

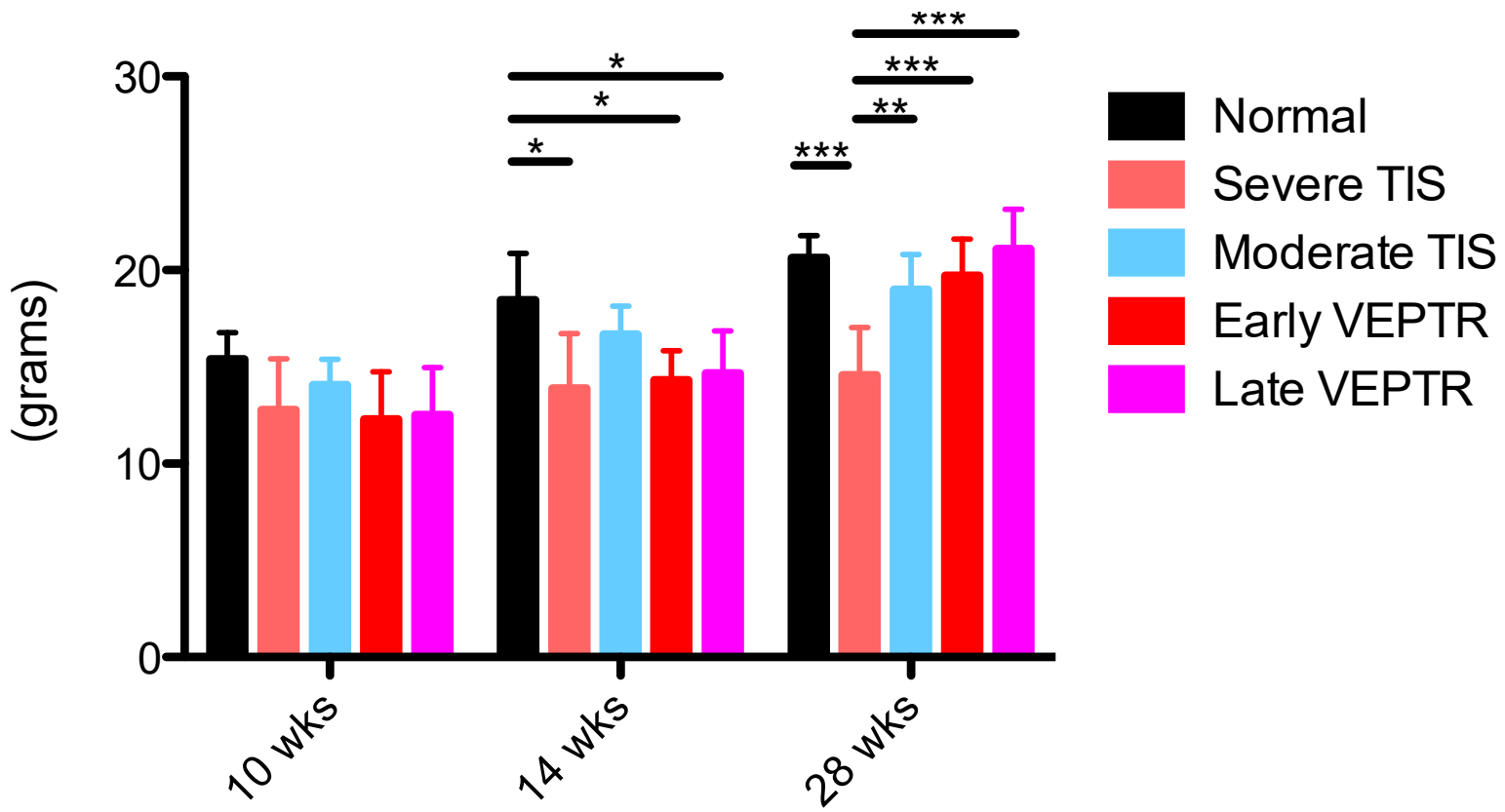


Lung/Body Mass Ratio



- Rabbits with severe TIS - Lung Mass relative to Body Mass significantly *less* than normal
- By completion of growth, Lung Mass relative to Body Mass significantly *improved* for thoracoplasty groups (Early & Late)

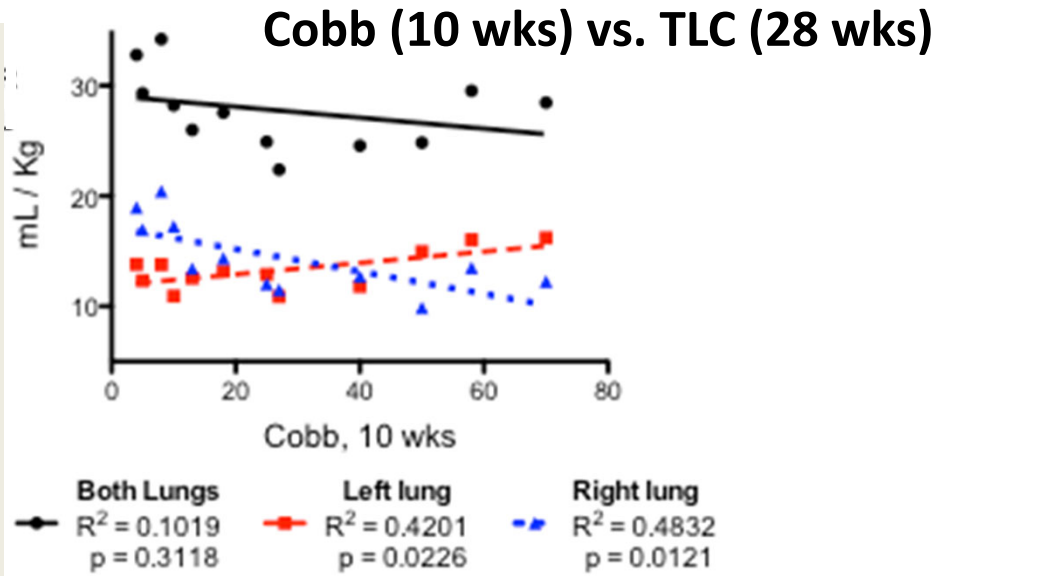
Lung mass

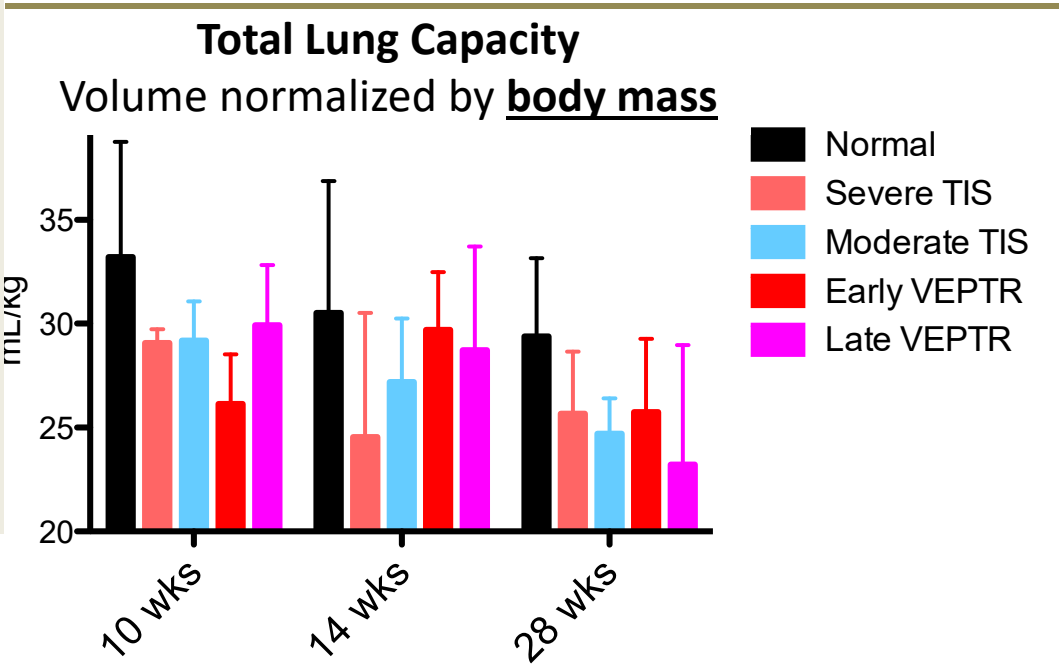


* - p<0.05, ** -p<0.01, *** -p<0.001. ANOVA with bonferroni post-hoc analysis

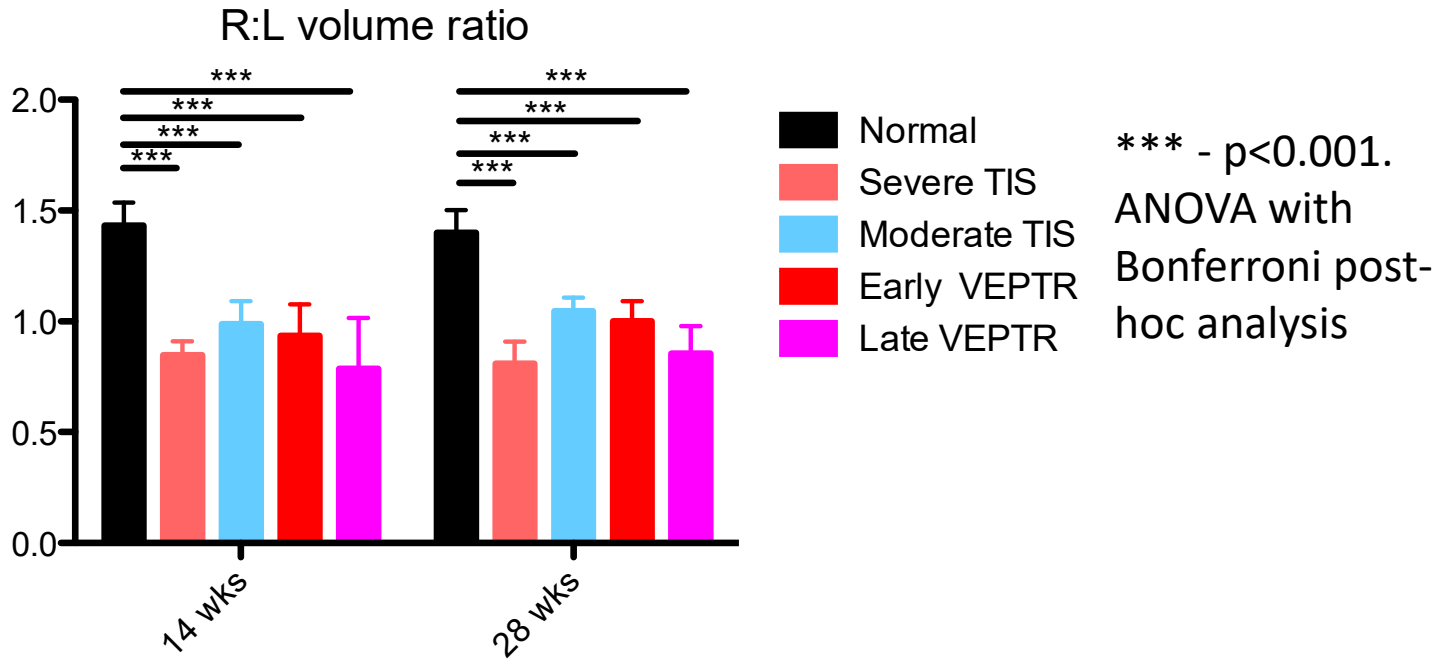
Total Lung Capacity

- Cobb @ 10 wks predicted ~45% variation R & L Lung TLC @ 28 wks
- Growth Right lung inhibited, left lung hypertrophied (compensation)
- TIS rabbits - TLC reduced relative to Normal
- TLC of Rabbits undergoing Thoracoplasty Early tended to be better than Late but NOT equivalent to Normal





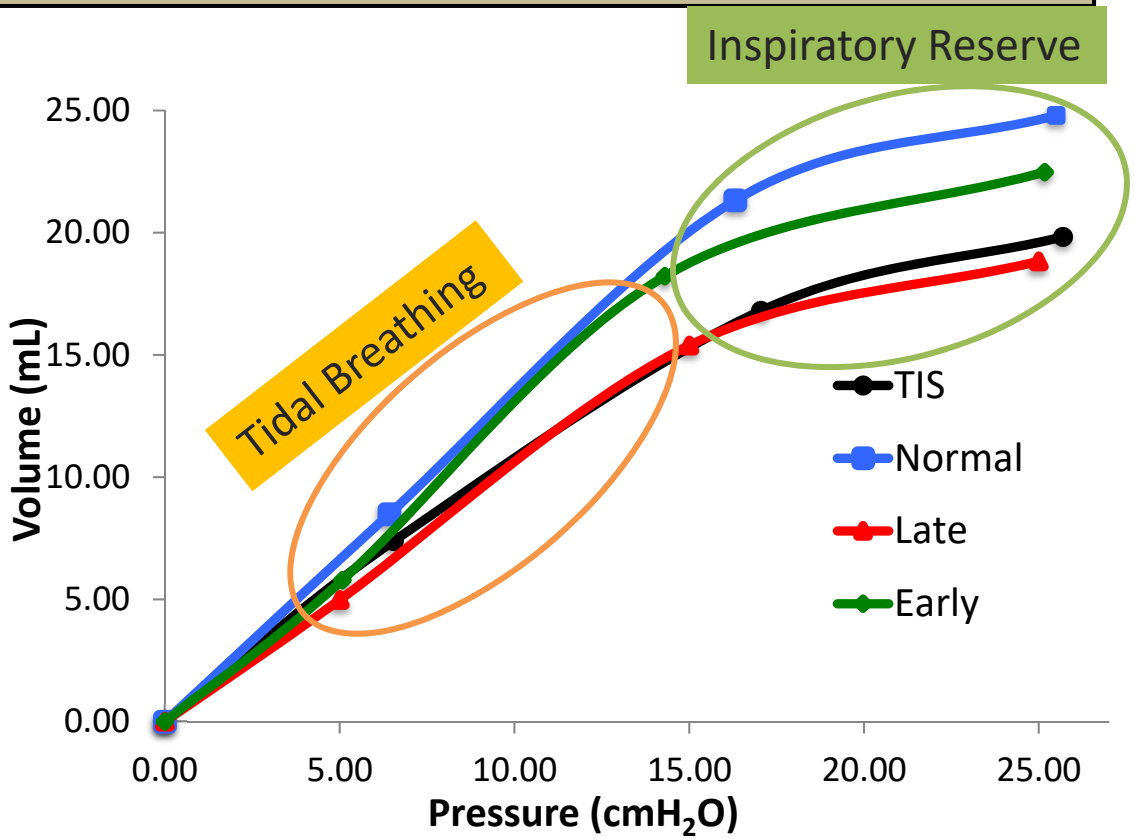
Right : Left Lung Volume Ratio



- Normal - Volume right lung ~40% > than left
- In contrast, R:L lung volume ratio < Normal ($p<0.01$) for TIS, Early and Late thoracoplasty rabbits
- Severe TIS - R:L lung volume ratio < 1
- Reflects constricted growth of right lung and compensatory hypertrophy of left lung

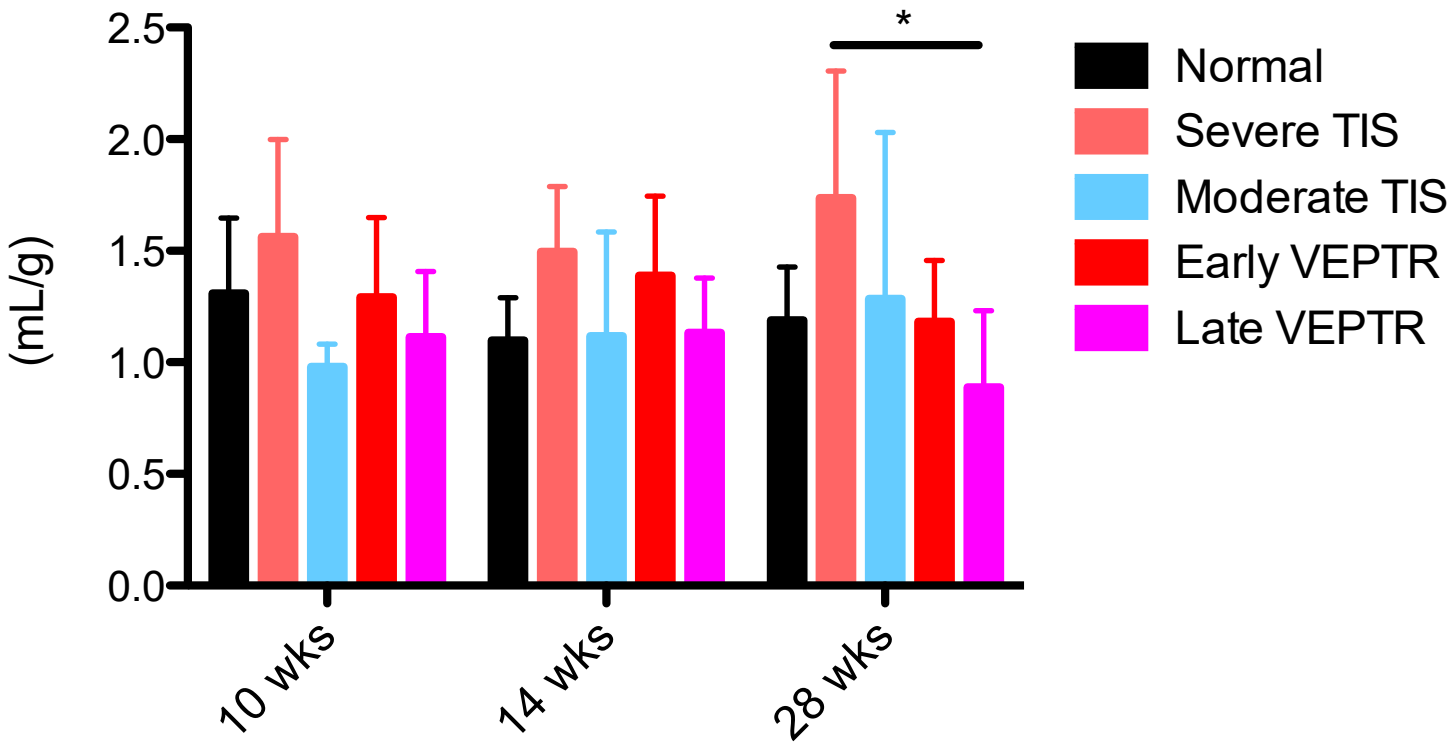
Respiratory Compliance

- Compliance calculated for 3 phases inspiration:
  - 0-5 cmH_2O: alveoli initially expand
  - 5-15 cmH_2O: tidal breathing
  - 15-20 cmH_2O: alveoli approach max distension
- Compliance during tidal breathing compared:
  - **Early Thoracoplasty equivalent to Normal and significantly greater than that of TIS rabbits ($p<0.01$)**
  - **Late Thoracoplasty not significantly different from TIS**



	Respiratory Compliance		
Insp. Press	TIS	Early	Late
0 to 5 cm	91%	88%	77%
5 to 15 cm	**69%**	**105%**	80%
15 to 25 cm	93%	102%	92%

Functional Residual Capacity



Volumes normalized by lung mass

* - $p<0.05$. ANOVA with Bonferroni post-hoc analysis

Discussion

- Tethering right hemithorax of 4 wk old rabbits reproduced 3D spine deformity, thoracic dysplasia, pulmonary hypoplasia and restricted lung function exhibited by TIS patients; did not recreate failure to thrive clinically observed
- Kyphoscoliosis significantly improved by expansion thoracoplasty whether performed early or late (anti-scoliosis tended to resolve)
- Persistence of R:L lung volume ratio < 1.4 suggests that expansion thoracoplasty, early or late does not “cure” hypoplastic right lung.
  - Recovered lung volume primarily by distraction of entire thorax + compensatory hypertrophy of contralateral left lung
- Expanded thorax remains relatively rigid, but lung itself is less restricted (more compliant) in Early Thoracoplasty rabbits
- Further evaluation using additional measures of pulmonary function necessary to understand affect of expansion thoracoplasty on vital capacity, dynamic elastance, O_2:CO_2 exchange and micro-anatomy

Conclusion

- **Hypothesis supported** - benefits of expansion thoracoplasty followed by serial distractions of the constricted hemithorax depend on timing of treatment relative to the remaining growth of the lung, spine and thorax.
- When expansion thoracoplasty performed earlier followed by subsequent distraction of hemithorax to simulate longitudinal growth of the thorax there was greater improvement in pulmonary function
- However early onset kyphoscoliosis induced by the unilateral chest wall deformity was corrected by expansion thoracoplasty performed either early or late

Thank you

Brian.Snyder@childrens.harvard.edu