INTRODUCTION:
Thoracic Insufficiency Syndrome (TIS) is defined as the inability of the thorax to support normal respiration or lung growth in patients with congenital or acquired deformities of the ribs and spine. Recently, a series of children with TIS as a consequence of congenital scoliosis and fused ribs were treated by expansion thoracoplasty using a Vertical Expandable Prosthetic Titanium Rib (VEPTR) implant (Synthes, West Chester, PA). This device addresses indirectly the thoracic hypoplasia caused by the fused ribs by expanding the constricted hemithorax, and addresses indirectly the scoliosis by distracting the concavity of the spinal deformity. In spite of the clinical success of this treatment, it remains unknown how this procedure affects lung growth and development. The specific aims of this in vivo pilot study were to develop an animal model of TIS and to use this model to evaluate how expansion thoracoplasty affects thoracic volume, lung volume, respiratory mechanics, alveolar morphology and spine deformity during growth and development.

METHODS:
After receiving IACUC approval, ten 4-week old female New Zealand white rabbits were divided into three groups: Normal Controls (n=3), Disease Controls (n=3), and VEPTR Treated (n=4). At 5 weeks, a constricted left hemithorax was created in 7 rabbits by tethering left ribs 4-8 to induce a postnatal pulmonary hypoplasia of the left lung and scoliosis. By 8 weeks, the rib fusions resulted in a constricted left hemithorax and scoliosis which were confirmed radiographically. At 10 weeks, thoracostomy through the fused ribs using a high speed burr and implantation of a mini-VEPTR device at the apex of the concavity were performed on 4 of the 7 rabbits to expand the constricted left hemithorax. The remaining 3 rabbits with fused ribs comprised the Disease Control group. At 18 weeks, growth of the spine and thorax were assessed using sequential transaxial CT scans of the entire thorax. Ventilated lung volumes were calculated by segmenting CT images according to established thresholds (in Hounsfield units) for aerated lung tissue and summing the voxels. Functional residual capacity (FRC) volumes were measured by plethysmography. At 24 weeks, all rabbits were ventilated on pure O2 for 10 minutes prior to euthanasia. The lungs and heart were excised and the lungs infiltrated with formalin at 25 mm Hg for 48 hours. Total lung volumes were measured using Archimedes’ Principle before being prepared for quantitative histologic analysis of alveolar morphology. Measures of pulmonary function, spine, and rib cage deformity were related to one another across the groups using ANOVA and Fisher’s probable least significant difference.

RESULTS:
All rabbits thrived; there were no differences in the weights of the rabbits (F=0.99, p=0.42). Unilateral rib tethering produced a convex right scoliosis in Disease Controls (14°) while the VEPTR Treated rabbits developed a convex left scoliosis (16°) after expansion thoracoplasty, indicating that the scoliosis was overcorrected by expansion thoracoplasty (Fig. 1a). No significant differences in total lung volume measured by CT normalized by the weight of the rabbit were noted among the groups at 18 weeks; normalized total lung volumes measured by Archimedes’ Principle were not significantly different among the groups at 24 weeks. However, the % ratio of left lung volume to total lung volume revealed that both Disease Control and VEPTR Treated rabbits, and that the contralateral lung hypertrophied (compared to Normal) to compensate for the constricted left lung to maintain total lung volumes nearly equal among groups. Expansion thoracoplasty with the VEPTR increased the volume of the left hemithorax but did not restore the ipsilateral lung volume to Normal. Compared to Normal Controls, the left lung volume of the Disease Control group was 12% smaller while the left lung volume of the VEPTR Treated rabbits was 3% smaller. Compared to Normal, the right lung volume of the Disease Control group was 17% greater while the right lung volume of the VEPTR Treated rabbits was 23% greater, suggesting that the entire thorax was lengthened by the procedure. FRC volumes normalized by weight were similar to aerated lung volumes measured by CT; FRC for Disease Controls was 46% that of the Normal Controls, while FRC for VEPTR Treated rabbits improved to 66% that of Normal Controls.

DISCUSSION:
This rabbit model appears to provide an accessible prototype of TIS and a means to investigate how distraction thoracoplasty might mitigate postnatal pulmonary hypoplasia. These data suggest that expansion thoracoplasty reduced the scoliosis and increased the volume of the constricted hemithorax induced by unilateral rib tethering, but the increase in the volume of the ipsilateral lung was small. In this model, compensatory hypertrophy of the contralateral lung occurred to maintain total lung volumes at normal, a phenomenon observed clinically in young children after pneumonectomy. It is possible that the lack of improved lung growth after thoracostomy and VEPTR implantation was idiopathic and that the trauma from the second surgery at 10 weeks injured the lung so that it could not grow into the expanded hemithorax. Alternatively, if distraction thoracoplasty allows partial reversal of inhibited lung growth in proportion to the lung growth remaining, then distraction thoracoplasty in 10 week old rabbits (who are mature by 24 weeks) may be too late to significantly influence lung growth and development. Even though there was no significant increase in alveolar number or alveolar volume, distraction thoracoplasty may improve respiratory function by preventing the emphysematous changes seen in congenital diaphragmatic hernia patients (i.e. a prenatal condition that produces pulmonary hypoplasia). In contrast, lung tissue from VEPTR Treated rabbits demonstrated increased vascularity and near normal air space fractions. However, there was no significant increase in the number or density of alveoli for the VEPTR Treated rabbits, indicating that there was no additional lung growth in these rabbits.


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