THE HARTWELL FOUNDATION

2012 Individual Biomedical Research Award

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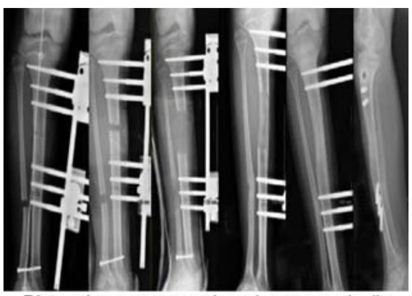
Bone Growth Following Periosteal Resection: Utilization of a Novel Bio-Delivery System to Regulate the Expansion of the Growth Plate

Approximately 40,000 children in the U.S. suffer from conditions of abnormal skeletal growth, including limb deformities, limb length discrepancies, scoliosis, and even hip dysplasia. While these conditions are not terminal, they cause significant physical impairment that interferes with normal childhood. Many treatments aimed at deformity correction rely upon surgical sawing and realigning bones (osteotomy), while the most commonly performed surgery to lengthen a limb involves cutting the bone and gradually pulling it apart. This requires the child to have pins protruding through their skin, connected to a distraction device, where they remain for up to six months. These gruesome procedures are associated with significant morbidity and complications, and alternative approaches are desperately needed. One of the most promising techniques being pursued is called periosteal resection, which involves the surgical release of the dense fibrous membrane covering the bone surface (periosteum) from the underlying bone. The periosteum mechanically exerts a compressive force to restrict growth near the ends of the long bones (growth plate). Unfortunately, the practical application of periosteal resection is inconsistent. To address this need, Matt offers a hypothesis that the observed growth acceleration following resection occurs because of the removal of both a mechanical constraint and a natural growth inhibitor. Using a rabbit animal model, he proposes to overcome inconsistency in periosteal resection of the tibia by surgically implanting a specially designed artificial and biologically active membrane under the periosteum to encourage bone growth. The insertion of the membrane will effectively block the growth-retarding mechanical properties of the intact periosteum, physically impede the persistent presence of periosteal growth inhibitor (PTHrP, parathyroid related protein), and simultaneously deliver to the underlying bone a cytokine transforming growth factor (TGFβ-1). If this approach to accelerate bone growth is successful, the result will revolutionize children's orthopedics by decreasing the need for surgical limb lengthening and corrective osteotomies, while providing practical benefits like substantially reduced post-operative pain and elimination of post-operative weight bearing restrictions.



Distraction osteogenesis --- bones surgically lengthened independent of the growth plate