Anti-Sclerostin (Scl-Ab) Increases Bone Mass and Fusion Volume in a Rat Posterolateral Spinal Fusion Model

1,2Shaffer, AD; 1Shonuga OA; 3Hirsch, BP; 4Cunningham M; 5Li, CY; 4Ke HZ; 4Lane JM
1 – Hospital for Special Surgery, New York, NY, 2 – Weill Cornell Medical College, New York, NY, 3 – University of Miami, Miami, FL, 4 – Amgen, Thousand Oaks, CA

Introduction
Spinal fusion is a commonly performed procedure indicated for a range of injuries and medical conditions. Spinal fusion pseudarthrosis rates range from 5 to 40% [1-4] and failure of fusion is associated with a host of complications as well as continued pain and morbidity. The implications of spinal fusion pseudarthrosis include additional pain, increased medication requirements, more restricted mobility, ultimately requiring additional costly procedures and longer hospital stays.

Biologic adjuncts to spinal fusion currently include autologous and allogenic bone graft and recombinant bone morphogenetic proteins, which amongst several biologic effects target the Wnt pathway in the process of making bone. Currently under investigation are several additional classes of biologic adjuncts that target the Wnt signaling pathway in an osteocyte specific manner leading to increased bone formation in the setting of fracture healing. The effects of a novel monoclonal antibody to a Wnt-specific protein Sclerostin are currently being evaluated in multiple domains of fracture healing. The objective of this study was to evaluate the effect that twice-weekly subcutaneous injection of Sclerostin antibody (Scl-Ab) had on fusion rate and mass in a rat spinal fusion model.

Methods
60 male 10 wk old Lewis rats underwent posterolateral intertransverse process spine fusion between L4 and L5 with 0.2g of morselized bone graft from a donor rat and randomized prior to surgery into two groups (n=30/group). Rats were started on a twice-weekly regimen of subcutaneously injected saline or 25 mg/kg Scl-Ab (Amgen, Inc., Thousand Oaks, CA) on post-op day 2 that continued until sacrifice at six wks postoperatively. At sacrifice spines were harvested en-bloc from sacrum to L1 and cleaned of soft tissue. Sixty harvested spines were frozen and underwent microCT (uCT) imaging. Thawed spines were evaluated for gross motion by manual palpation by three blinded authors, with fusion defined as no motion and scored by consensus. uCT imaging was evaluated for bone mineral density, total bone mass in the posterolateral spinal elements and fusion callus volume. The HSS Institutional Animal Care and Use Committee approved the animal study.

Results
Manual palpation revealed no statistically significant differences between the two groups, Scl-Ab and saline, with fusion rates by manual palpation of 61% and 60% respectively (p = 0.92). uCT imaging revealed significantly increased posterolateral element bone mass in the spines of animals treated with Scl-Ab with mean bone mass of 442569 ± 82820 mg HA and 29453 ± 29912 mg HA in spines treated with Scl-Ab and saline respectively (p < 0.001). The mean fusion callus volume in Scl-Ab treated animals was increased over saline treated animals (524 ± 96 cm³ vs 362 ± 34 cm³ p < 0.001). Additionally, fusion callus bone mineral density in Scl-Ab treated animals was increased over saline treated animals (842 ± 16 mg HA / cm³ vs. 813 ± 14 mg HA / cm³) p < 0.001). Overall fusion callus mass was also significantly increased in spines treated with Scl-Ab over saline with mean bone mass of 169032 ± 6421 mg HA and 88208 ± 3578 mg HA respectively (p < 0.001).

Conclusions
Scl-Ab is an easily administered, effective adjunct for spinal fusion in a rat model. Sclerostin dramatically increased bone mass in the posterolateral spinous elements and fusion callus volume. While greater fusion rate was not seen, the increase in fusion mass may translate to improved fusion quality clinically and lower instrumentation failure in instrumented human fusions, since greater bone density and growth is associated with lower rates of pseudarthrosis and instrumentation failure in spinal fusion. Further studies are warranted.

Significance
Spinal fusion is a commonly performed procedure that improves pain and function but failure of spinal fusion can be a costly problem both in human and economic terms. Discovery of novel biologic agents can lead to new perioperative prophylactic regimens to avoid nonunion.

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