Poster Session I (cont.)

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CHARACTERIZATION OF TISSUE ENGINEERED TRACHEAL GRAFTS IN AN OVINE MODEL

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Purpose:
Tracheal agenesis and tracheal clefts are rare but life-threatening congenital defects with limited therapeutic options. Development of a tissue-engineered tracheal graft (TETG) holds the promise of an autologous airway conduit with the ability to grow and self-repair over the course of a patient's life. To this end, we evaluated efficiency of seeding bone marrow-derived mononuclear cells on a polymeric scaffold and evaluated the effect of cell seeding on graft performance in an ovine model (*Ovis aries*).

Methods:
Autologous bone marrow was aspirated from juvenile sheep isolated by either centrifugation or filtration. Seeding efficiency of high porosity (HP, n=2) and normal porosity (NP, n=6) electrospun polyethylene terephthalate and polyurethane tracheal grafts were characterized by cell counts, DNA quantitation, and histology. Sheep received unseeded (n=2) or seeded (n=4) NP grafts as tracheal interposition grafts. Animals were survived until an end-point of 14 or 42 days.

Results:
Seeding efficiency of NP grafts (60-75%) was markedly increased when compared to HP grafts (20-29%) by cell counts and DNA analysis (NP: 249.4 ± 6.66 $x10^3$ cells/mm^2, HP: 97.4 ± 20.99 $x10^3$ cells/mm^2; $p<0.04$). After implantation, epithelial cells were demonstrated on the TETG lumen by cytology. Three animals were terminated early due to respiratory complications at day 30 (unseeded), 34 (seeded), and 36 (unseeded). All animals had tracheal stenosis at autopsy. Histology of TETG explants demonstrated epithelial migration, hyperplasia, and wound healing at the sites of anastomoses.

Conclusion:
We present the first large animal study demonstrating the feasibility of using mononuclear-seeded polymeric scaffolds for implantation as tracheal interposition grafts. These grafts function as airway conduits up to 6 weeks after implantation, and induce neotissue formation, but are limited by the formation of stenosis. These results provide the foundation for development of a novel tracheal graft for use in the repair of major congenital tracheal defects.

Notes: