In vivo Evaluation of an Autologous graft and two Acellular Human Dermal Matrices

J. Faleris, R. Hernandez
RTI Biologics, Inc. Alachua, FL 32615

Purpose: Autologous grafts are used for soft tissue augmentation and are frequently considered the gold standard. However, acellular biologic matrices have been used as a substitute to reduce the autograft co-morbidities. Recent studies have shown that alterations in the inflammatory response may change the wound healing continuum to reduce scarring or healing time [1]. Various methods of biologic matrix decellularization may alter the host inflammatory response and consequently wound healing. Tutoplast® processed cadaveric human dermis (RTI Biologics; Alachua, FL) is a collagen matrix with an intact basement membrane (BM). Production of this acellular dermal matrix (ADM) yields matrices consisting of the superior and inferior dermal regions. An *in vivo* characterization was conducted to compare the inflammatory response and vascularization of the ADM superior region and inferior region matrices.

Methods: Cadaveric human dermis was procured and processed through Tutoplast®, including terminal γ-irradiation to produce the ADM samples. Test samples also included an autologous group, Table 1.

Group	Description
A	Autologous muscle sample
ADM-SR*	ADM superior region orientation reticular dermis juxtaposition skeletal muscle
ADM-SB*	ADM superior region orientation basement membrane juxtaposition skeletal muscle
ADM-IR*	ADM inferior region orientation non-specific

Table 1. Sample groups, *Donors matched in each rat.

Post-Tutoplast processing ADM tissue was paraffin and methylmethacrylate embedded, sectioned and evaluated to examine cellularity and characterize the extracellular matrix components. Thirty-six samples measuring 1.0x1.5 cm were sutured to the skeletal muscle in 12 Sprague Dawley rats. Histologies from 3, 7, 14, and 28 day sacrifices (four implants per rat, three rats per timepoint) were semi-quantitatively scored by an independent pathologist to evaluate and compare all groups for inflammatory response, neovascularization and remaining implant dimensions (0-4 scale; 0=none, 1=minimal, 2=mild, 3=moderate, 4=marked).

Results: Immunohistochemistry showed an intact BM present in the ADM-SR and ADM-SB at the dermal-epidermal junction and vascular channels and absence of cellular debris. The ADM-IR had an intact BM only in the vascular channel remnants. The *in vivo* cellular infiltration of autograft implants provoked the highest host response, characterized as acute and chronic inflammation resulting in scar tissue, Fig. 1 and 3. An increase and subsequent significant reduction in vascularization over time is consistent with these findings, Fig. 2. The ADM samples showed no biologically significant differences between groups. The ADMs were initially infiltrated with mononuclear cells and polymorphonuclear cells. At 28 days, ADM displayed a narrow band of fibrosis around the implant with sustained infiltration of fibroblasts and mononuclear cells, Fig. 1. ADM-SB was the last implant to show signs of vascularization, Fig 2. At 28 days, vascularization scores of all ADM groups showed no biologically significant differences.

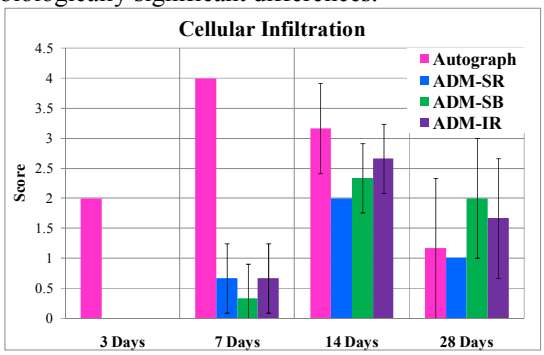

Figure 1: Cellular infiltration of all implants over time.

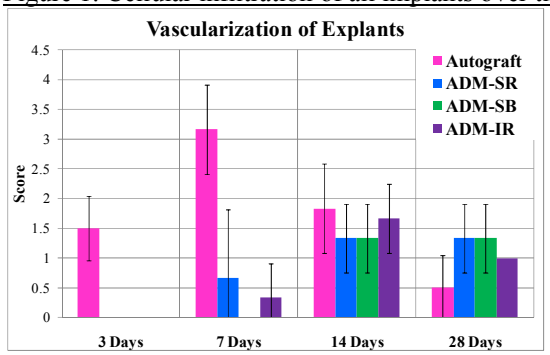

Figure 2. Vascularization of all implants over time.

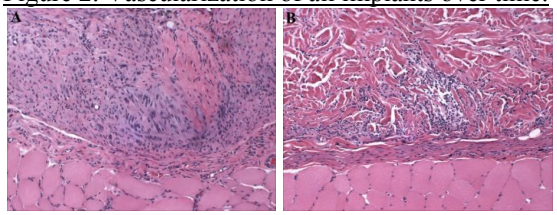

Figure 3. Autologous (A) and ADM (B) at 28 days. H&E, 100X magnification.

Discussion: The ADM samples, independent of dermal region or orientation showed no biologically significant differences; however, the vascularization and inflammation trend of the ADM-IR group appears similar to the autologous group with respect to a reduced vascularization score at 28 days and early cellular infiltration. The primary cause of increased inflammatory response and scar formation appeared to be the presence of graft cellular material. Reduced inflammatory response in all ADM samples may correlate with higher vascularization scores at 28 days and subsequent reduced scar formation comparatively to the autologous group. Additional studies are required to determine how the presence and implant orientation of the BM relates to the *in vivo* inflammatory cell differentiation, cytokine production and tissue remodeling.

References: 1 (Wilgus TA. Pharm Res. 2008; 58: 112-116.)