Department of Surgery
2026 Research Day
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Title: Optimizing Microvascular Architecture to Promote Early Inosculation of Engineered Human Skin Grafts

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Background
Rapid vascular connection between host and graft vessels is essential for successful skin graft integration. However, many engineered and acellular skin substitutes fail to establish early perfusion, resulting in ischemia, delayed healing, and graft failure. Although pre-vascularized tissue constructs have been proposed to accelerate vascular integration, the microvascular features that enable efficient host–graft inosculation remain poorly defined. Emerging evidence suggests that vascular organization and maturation state, rather than vessel density alone, may determine integration capacity. We hypothesize that engineered human skin constructs reach a specific microvascular maturation state that optimally supports early inosculation with host vasculature**.**

Methods: Engineered human skin constructs containing a pre-vascularized dermal compartment composed of endothelial cells, fibroblasts, and dental pulp stem cells embedded within collagen–fibrin matrices were generated and cultured under air–liquid interface conditions. Constructs were evaluated at defined in vitro maturation stages corresponding to early, intermediate, and late microvascular network states. After characterization, constructs from each stage were implanted into full-thickness dorsal wounds in SCID hairless outbred (SHO) mice to assess early host–graft vascular integration.

Results: Preliminary data demonstrate that engineered skin constructs develop organized microvascular networks *in vitro* with architecture that evolves over time. Although early constructs exhibited the highest vessel density, constructs implanted at an intermediate maturation stage showed the greatest dermal organization and evidence of host–graft vascular inosculation in vivo. These findings indicate that maximal vessel density alone does not predict successful integration and instead identify an intermediate vascular network state as optimal for early host–graft vascular connection.

Conclusions: These findings suggest that early graft integration depends on achieving an optimal microvascular architectural state prior to implantation. Defining the structural features that promote rapid inosculation may enable the design of engineered skin grafts with improved survival and integration. Preservation of this vascular architecture through decellularization may further enable development of off-the-shelf skin substitutes capable of guiding host-driven vascularization.