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PURPOSE: Murine models are commonly employed to simulate aspects of human adipose physiology. Tremendous advances in our understanding of human obesity and endocrinology have been made possible by comparative studies in mice. However, fat depots — both within and between species — differ dramatically in their transcriptional properties. Understanding the fundamental differences between human and mouse adipose tissue, and thus the inherent limitations of murine models, begins with comparing their basic architecture. This study employs whole tissue mounting and confocal microscopy to characterize the three-dimensional architecture of the mouse inguinal fat pad, and two significant human fat depots, the lower abdomen and gluteofemoral regions.

METHODS: Abdominal and gluteofemoral adipose tissue specimens were obtained from three operative patients each, in accordance with Stanford Institutional Review Board policy. The patients ranged in age from 35 to 60 years and had no significant prior medical history. Bilateral inguinal fat pads were harvested from three Crl:CD1-Foxn1nu CD-1 Nude mice. The human samples were incubated in Human CD34 PE-Cy 5.5 Conjugate and Phosphate Buffered Saline (PBS) for 24 hours. Similarly, the mouse inguinal fat pad samples were incubated in purified anti-mouse CD34 antibody and PBS for 24 hours. The mouse and human specimens were separately incubated in a staining master mix containing Isolectin endothelial cell stain, LipidTox adipocyte stain (Thermo Fisher Scientific; Waltham, MA), and Hoechst nuclear stain for two hours and then whole-mounted. Laser scanning confocal microscopy was performed using the Leica TCS SP8 X. Three-dimensional volume rendering and analysis was performed on Imaris software (Bitplane AG; Zurich CH).

RESULTS: In general, there are significantly more vessels per adipocyte in mouse compared to human abdominal or gluteofemoral fat (p < 0.05). Quantification of ASC as normalized to adipocyte number shows similar ASC density between species (p = 0.31). Moreover, the ratio of ASC to blood vessels is significantly reduced in mouse compared to human fat (p < 0.05); however, the mean distance between ASC and blood vessels in human fat is significantly greater compared to mouse (p < 0.05). Expectedly, human adipocytes were generally larger and more heterogeneous in size. Frequency distribution of adipocyte volume in mouse and human samples demonstrates significantly greater diversity in human tissue (p < 0.05).

CONCLUSION: The basic architecture of human adipose tissue differs significantly from that of mice. These differences likely confer variance in functional properties between the two sources. Thus, caution should be exercised when drawing parallels between the two species, particularly when designing murine models of human disease.

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Proximal and Distal Recipient Vessels Are Associated with Equivalent Outcomes in Lower Extremity Trauma Free Flap Reconstruction: A 312 Patient Series and Systematic Review

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PURPOSE: Recipient vessels proximal to the zone of injury have traditionally been preferred in traumatic lower extremity free flap reconstruction. This is due to presumed changes in the caliber and quality of vessels within and distal to the site of trauma that may result in less favorable outcomes and higher rates of flap failure. However, more recent data have shown mixed outcomes when performing anastomoses distal to the zone of injury. This study investigates the impact of lower extremity recipient vessel location on free flap outcomes.
Timming of Traumatic Lower Extremity Free Flap Reconstruction: Does Time to Coverage Impact Outcomes?

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Purpose: Microvascular free-tissue transfer is commonly used for the reconstruction of traumatic lower extremity injuries, particularly in cases of open fractures with substantial associated soft-tissue defects. Initial outcomes studies in the late 1970s and early 1980s established the principle of early flap coverage in an effort to minimize fibrosis, edema, and infection that may complicate repair. However, this has been challenged by several more recent studies that suggest reconstruction can be performed beyond this early window with comparable outcomes. Additionally, clinical and logistical factors—including associated injuries and patient transport—often preclude immediate reconstruction. The aim of this study was to determine whether reconstructive timing influences outcomes and complication rates in traumatic lower extremity free flap repair.

Methods: Retrospective review of our institutional flap registry from 1979–2016 identified 806 lower extremity free flaps; 393 soft tissue free flaps for Gustilo IIIB/C coverage met inclusion criteria. Patients were stratified based on clinically relevant intervals between injury and free flap coverage: 0–10 days, 11–90 days, and >90 days. Demographics, flap characteristics, and outcomes were compared between groups using Chi-square and one-way ANOVA. Multivariate logistic regression was performed to control for variables with significant differences between groups on univariate analysis as well as clinically relevant variables, including timing within cohort (1976–1996 vs. 1997–2006), arterial injury, flap type and size, and use of vein grafts. Primary outcomes assessed included total and partial flap failure (9.3% vs. 9.3%; p=0.815) or partial flap failure (7.4% vs. 11.9%; p=0.978) compared to proximal anastomoses when controlling for confounding variables, such as presence of arterial injury, flap type, and time from injury to coverage. Furthermore, distal anastomoses were not associated with increased rates of operative take backs (19.6%) compared to proximal anastomoses (23.8%; p=0.356). The rates of arterial (p=0.469) and venous complications (p=0.348) were similar between proximal and distal groups. Systematic review yielded 11 articles with 1245 proximal and 127 distal anastomoses for comparison. Pooled analysis of all studies (p=0.58) and weighted comparative analysis of direct comparison studies (p=0.39) found no difference in flap failure rates between proximal and distal groups.

Conclusion: There was no statistically significant difference in complication or flap failure rates for anastomoses performed proximal to the zone of injury. These findings suggest that as long as the recipient vessels are outside the zone of injury, selection should be based on pedicle length, ease of vessel exposure, and adequate inflow/outflow rather than simply a proximal or distal orientation relative to the injury.

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