2026 NEW YORK REGIONAL SOCIETY OF PLASTIC SURGEONS ANNUAL RESIDENTS' NIGHT RESEARCH COMPETITION

MONDAY, APRIL 20, 2026
NEW YORK ACADEMY OF MEDICINE

ABSTRACT SUBMISSION TITLE: *A Humanized Murine Model Demonstrates Improved Fat Graft Retention and Translational Relevance*

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Abstract Text:

PURPOSE:

Autologous fat grafting (AFG) is widely used in breast reconstruction, yet long-term volume retention remains variable and incompletely understood. While technical factors influence graft survival, preclinical studies predominantly rely on athymic models lacking adaptive immunity, and the contribution of the host immune microenvironment remains poorly characterized. We utilized a humanized murine model to better approximate clinical fat graft retention in the setting of a functional human immune system.

METHODS:

Donor-matched human lipoaspirate was implanted into athymic (n=7) and humanized (n=7) mice engrafted with human $CD34^{+}$ hematopoietic stem cells. Volume retention was quantified at 12 weeks using MRI-based volumetric analysis normalized to injected volume, with adjustment for interval weight change. Donor-matched comparisons were

performed between murine models and, in a subset (n=4), compared to corresponding clinical retention.

RESULTS:

Humanized mice demonstrated significantly greater mean 12-week fat graft retention compared to athymic controls (44.4% vs. 21.8%; mean difference +14.3%, p=0.035), which remained significant after adjustment for interval weight change. Mean clinical retention in the donor subset was 67.9%. Both murine models underestimated clinical retention; however, the humanized model demonstrated lower mean absolute error than the athymic model (30% vs. 40%, p=0.25). Exploratory contrast-enhanced imaging demonstrated increased signal intensity in humanized grafts, suggesting enhanced perfusion and graft integration.

CONCLUSIONS:

The humanized murine model demonstrates improved fat graft retention and more closely reflects clinical outcomes, supporting a role for the immune microenvironment and inflammatory remodeling in graft survival. These findings suggest that optimizing fat graft retention will require consideration of both technical and host-specific factors. Ongoing work will evaluate angiogenesis and immune cell integration to define underlying mechanisms.