# Optimized Surgical Approach for Applying Mechanical Force to Murine Models to Simulate Human Hypertrophic Scar Formation

**Paschalia M. Mountziaris, MD, PhD**; James Kenney, BS; C. Michael DiPersio, PhD; Livingston Van De Water, PhD; Ashit Patel, MBChB; Malcolm Z. Roth, MD

**Disclosure/Financial Support:** Ongoing work in this area is supported by the Plastic Surgery Foundation (Pilot Research Grant Award Number 415339, to Dr. Paschalia M. Mountziaris). None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this work.

**INTRODUCTION:** Aberrations in the tightly regulated biological process of wound healing can lead to hypertrophic scars. In vivo hypertrophic scarring models are limited by the loose-skinned nature of rodents, such that wound healing significantly differs from that in humans. We present several crucial modifications to a previously described mechanical loading technique, which produce reliable and robust hypertrophic scars in murine models.

**MATERIALS AND METHODS**: Incisional wounds were made on the backs of 6- to 11-week-old epidermal-specific integrin knockout and wild type mice. A mechanical loading device was mounted, and the impact of several factors was analyzed, including: device type (distractor, stent), incision orientation (transverse, longitudinal) and suture material (nylon, stainless steel, adhesive skin glue). In the case of the distractor, the device was incrementally tightened for 10 days to maintain mechanical stress. Wound sites were harvested at intervals and analyzed via histology and immunohistochemistry.

**RESULTS**: All factors significantly affected the observed wound healing response. Incision orientation had a notable impact in smaller transgenic mice. Suture material significantly affected animal tolerance of the device over the 10 days necessary to induce hypertrophic scar formation. With the optimal combination of factors, consistent robust scarring was observed, similar to that in human hypertrophic scars.

**CONCLUSION:** Our results demonstrate a modified, optimal method to induce hypertrophic scarring in both wild type and transgenic mice, enabling *in vivo* studies of the pathophysiology of this process. Such studies hold the promise of identifying putative targets to prevent or reverse disfiguring hypertrophic scar formation.