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An Experimental Animal Model for Head and Neck Lymphedema

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Purpose: Head and neck lymphedema (HNL) is a disfiguring disease affecting over 75% of patients treated for head and neck cancer. Animal models of lymphedema are used to test pharmacologic and microsurgical therapies, which can offer improved outcomes compared to standard conservative therapies. However, no animal model for HNL has been described in the literature to date. The purpose of this study is to describe the first reproducible rat model for HNL.

Methods: Thirty-six (36) rats were split into 2 groups: 1) 18 experimental animals received combined lymphatic injury consisting of cervical lymph node dissection followed by irradiation, 2) 18 control animals received sham surgery. Outcomes measured at postoperative days 15, 30 and 60 included neck circumference, cheek-to-cheek distance, and fat volume within the head and neck region as measured by magnetic resonance imaging (MRI). Lymphatic drainage was measured at day 60 via indocyanine green (ICG) lymphography, after which animals were sacrificed for histological analysis.

Results: Postsurgical lymphedema was observed 94% of the time in experimental animals (17/18). Compared to controls, experimental animals experienced significantly more growth at all timepoints as measured by neck circumference (12% change at final timepoint, $P < 0.0001$), cheek-to-cheek distance (10% change at final timepoint, $P < 0.001$), and fat volume (18% change at final timepoint, $P < 0.05$). Experimental animals had significantly slower lymphatic drainage than control animals as measured by ICG clearance ($P < 0.05$). Histological analysis of experimental animals revealed 107% greater hypodermal thickness ($P < 0.0001$) and 57% greater dermal thickness ($P < 0.05$) compared to controls, indicating subcutaneous tissue expansion.

Conclusion: Experimental animals receiving combined lymphatic injury developed changes consistent with postsurgical HNL, as evidenced by significant growth in all head and neck measures, slower lymphatic drainage, and subcutaneous tissue expansion compared to control animals. In conclusion, we demonstrate that combined lymphatic injury in rats leads to a reproducible model of HNL.