

REFINEMENT OF A RODENT MODEL OF PERIPHERAL LYMPHEDEMA**L. Lee-Donaldson, M.H. Witte, M. Bernas, C.L. Witte, D. Way, B. Stea**

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ABSTRACT

A reliable, inexpensive experimental counterpart of peripheral lymphedema has been notoriously difficult to reproduce thereby stifling basic and clinical research into this frustrating clinical condition. Accordingly, in 45 adult Wistar-Fuzzy rats, we attempted to produce sustained hindlimb lymphedema by either groin nodal/lymphatic microsurgical ablation (S) (guided by visual blue dye lymphography) or limited field-groin irradiation (R) alone (4500 rads) or combined S followed by R or R followed by S with an additional non-manipulated group serving as controls. Observations were made for 30-100 days thereafter. Hindlimb volumes were determined serially using the truncated cone formula based on multiple circumferential measurements at standardized intervals along the affected hindlimb and the findings compared with similar measurements in the contralateral non-manipulated hindlimb. In randomly selected rats from each group, lymphatic drainage was assessed by lymphangioscintigraphy (LAS), soft tissue swelling by magnetic resonance imaging (MRI), and edema fluid total protein content by refractometry. Whereas S or R alone produced only transient or mild hindlimb edema without associated morbidity or mortality, S-R or R-S induced moderate to severe sustained protein-rich hindlimb lymphedema associated with 9-13% early mortality and notable late local limb morbidity. Lymphatic obstruction was documented by sustained maintenance of increased hindlimb volume, subcutaneous fluid accumulation (MRI), and impaired lymphatic drainage (LAS). This reproducible rodent model of secondary lymphedema reliably simulates a stable clinical condition for a window of up to 100 days and should thereby facilitate standardized testing of therapeutic/preventive protocols and basic research into lymphatic dynamics in secondary lymphedema.