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Official Title: Standardization of Indocyanine Green Lymphography Protocol With Exercise for Lymphedema Assessment

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Exercise-Enhanced ICG Lymphography

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Protocol Version (SAP associated with)

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Abbreviations and definitions

Indocyanine Green ICG

SD Standard deviation

SPSS Statistical package for the social sciences

Background:

Indocyanine green (ICG) lymphography is a non-radioactive, fluorophore-based imaging modality that provides functional imaging of the lymphatic system. With specificity comparable to and sensitivity superior to technetium99-based lymphoscintigraphy, the conventional diagnostic gold standard, ICG lymphography has been increasingly relied upon to diagnose extremity lymphedema. The diagnosis of lymphedema is confirmed when the pathologic dermal backflow patterns are seen. In addition to providing a definitive diagnosis, the

types/distribution of the dermal backflow patterns presently allows the determination of disease

severity. Since the dermal backflow patterns emerge in a delayed fashion and, after their initial emergence, they continually evolve until reaching a steady-state, or plateau, a delayed scan at the time of plateau is necessary to achieve an accurate representation

of the disease. Exercise has been shown to accelerate lymphatic drainage.

Study Objectives:

To determine if controlled exercise could shorten the time it takes for ICG lymphography to reach a plateau, and to create a standardized protocol to increase the efficiency and reliability of

ICG lymphography to diagnose extremity lymphedema.

Study Methods:

Design: non-randomized controlled trial

Recruitment:

All lymphedema patients presented to our lymphedema reconstruction center over a 6-month period and those who met inclusion criteria were recruited into the study.

Inclusion criteria: 18 years or older, having voluntarily agreed to participate in the study, and being suspected to have lymphedema or previously diagnosed with lymphedema.

Exclusion criteria: allergy to iodine, women who were pregnant or nursing, having heart/lung/joint conditions that would prevent exercising.

Exercise protocol:

Patients presented for a one time visit. Following standard ICG injections, patients were

exercised on a recumbent cross-trainer at five-minute intervals at specific, controlled intensity. Delayed scanning was performed following each exercise interval, and sequential changes of lymphographic patterns were recorded. The cycle of exercise/scan continued until achieving a plateau, or when no further lymphographic changes were observed for two consecutive cycles. Following the point of the plateau, further delayed scanning was performed every hour to identify the time point when the lymphographic patterns started to recede. Twenty-three limbs in 9 patients (10 arms, 13 legs) with unilateral and bilateral lymphedema were studied. Campisi criteria were used to clinically stage disease severity.

Statistical analysis (SAP version: 2.0)

All patients who participated in the study were included in the analysis and the analysis compared the individuals' affected limbs to the unaffected limbs. Video footage of indocyanine green lymphography was independently reviewed by three experienced ICG lymphographers to identify time points of ICG plateau and regression. SPSS was used to perform the data analysis using a significance level of 0.05 and a confidence interval of 95%. Descriptive analysis generated frequencies of the study variables, and comparisons of categorical variables were performed using the chi-square test.