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A New Indocyanine Green Lymphography Protocol for Assessment of Lymphedema in the Head and Neck

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Abstract

Head and neck cancer and its treatment may result in lymphedema, however, no specific imaging criteria have been assigned to diagnose this condition. This study reports an ICG lymphography protocol for investigating changes in individuals experiencing swelling post-neck dissection. ICG lymphography was performed in 10 healthy participants and 16 individuals who complained of facial or neck swelling following treatment for head and neck cancer. Four ICG injection sites were proposed to demonstrate 3 lymphatic territories drainining to upper cervical, submandibular, and submental nodes. In healthy controls, 3 lymphatic drainage pathways were demonstrated in the ipsilateral neck. In individuals post-neck dissection, dermal backflow was present and 2 additional drainage pathways were visualized to the paraspinal and axillary regions. This study proposes an anatomy-based protocol for ICG lymphography and interpretations of imaging findings in patients post-neck dissection surgery. ICG lymphography offers a diagnostic imaging tool for head and neck lymphedema.

Keywords

head and neck cancer, indocyanine green, lymphedema, lymphography, neck dissection

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Head and neck cancer survivors can additionally face the compounding challenges of lymphedema in the head and neck region.[1] Research suggests that the prevalence of head and neck lymphedema is as high as 90% following treatment for head and neck cancer with over half of those patients developing fibrosis.[2] However, head and neck lymphedema is underdiagnosed because there are currently no specific imaging criteria assigned to diagnose head and neck lymphedema.

This study reports an ICG lymphography protocol for investigating changes in the superficial lymphatics in individuals experiencing swelling post-neck dissection. It aims to define tracer injection sites, interpret imaging findings and consider potential clinical applications for the use of the procedure.

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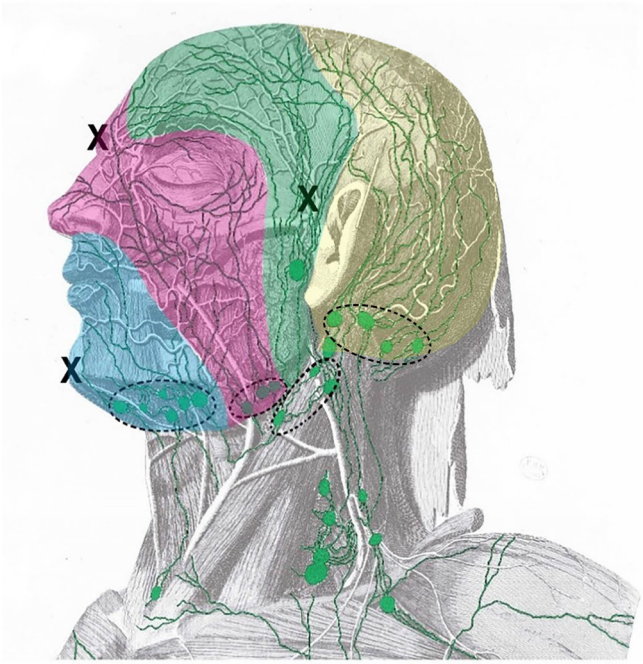

Figure 1. A drawing of the lymphatic system by Mascagni.[2] Color of the lymphatic territories: submental (blue), submandibular (purple), upper cervical (green), and occipital (yellow), were added by the author. X represents ICG injection sites.

Materials and Methods

ICG lymphography was performed in individuals who had undergone neck dissection for head and neck cancer and had sought lymphedema treatment due to facial or neck swelling at the Macquarie Lymphedema Clinic, between May 2022 and August 2023. In addition, healthy participants were recruited to provide control images. All subjects consented to clinical photography in addition to other data collection. The study was approved by the institutional Human Research Ethics Committee (HREC) review committee at Macquarie University (approval number 520251119844648).

ICG injection sites

Previous anatomical studies allowed us to demarcate the skin into lymphatic territories (lymphosomes) corresponding to groups of sentinel lymph nodes.[3,4] The lymphatics in the head are divided into 4 lymphosomes on each side draining to occipital, upper cervical, submandibular, and submental lymph nodes (**Figure 1**). Given that hair-bearing scalp is unsuitable for ICG lymphographic assessment, 4 ICG injection sites were proposed to demonstrate 3 lymphosomes (**Figure 1**).

Figure 2. ICG image of a healthy control participant. Photos with lymphatic mapping (top) and ICG images (bottom).

ICG Imaging Procedure

The participant was positioned supine. After sterilization of the skin, a cryo-numbing device (Exocool, Exocool Co., Ltd.) was applied to the injection site for 5 seconds to alleviate needle discomfort. Using a 33 G needle and 1 mL lure-lock syringe, 0.1 mL ICG solution (25 mg ICG with 10 mL of saline) was injected subcutaneously at each site.

After an initial observation period of 5 minutes, the examination table was placed in a head up position to place the participant in a semi-seated position facilitating the movement of ICG dye by gravity. Imaging parameters recorded during the procedure included: locations of lymphatic vessels, demarcated areas of dermal backflow, direction of ICG movement, location of lymph nodes, and location of final drainage region. This information was marked directly on the individual's skin with color markers.

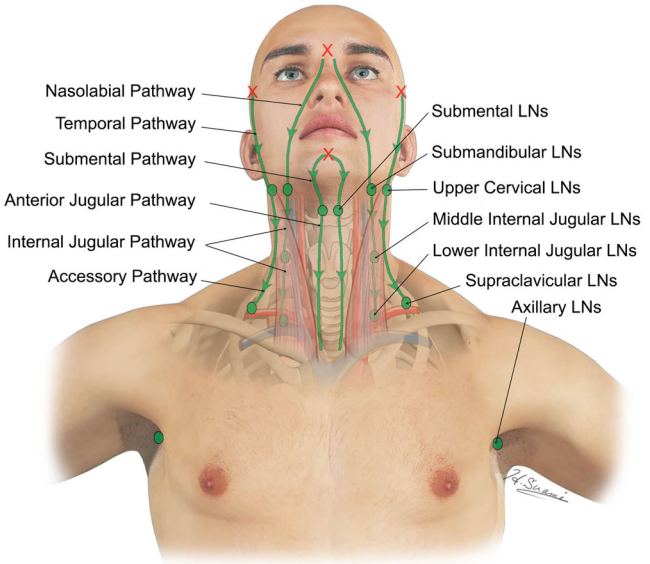

Figure 3. Schematic diagram of lymphatic pathways in the head and neck with ICG lymphography.

Results

ICG lymphography was conducted on 10 healthy controls and 16 individuals who had undergone neck dissection for head and neck cancer treatment. (unilateral dissection: n = 5, bilateral dissection: n = 11). Fourteen out of 16 head and neck cancer survivors received radiation treatment during their cancer treatment. No adverse effects were observed during or after the ICG lymphography.

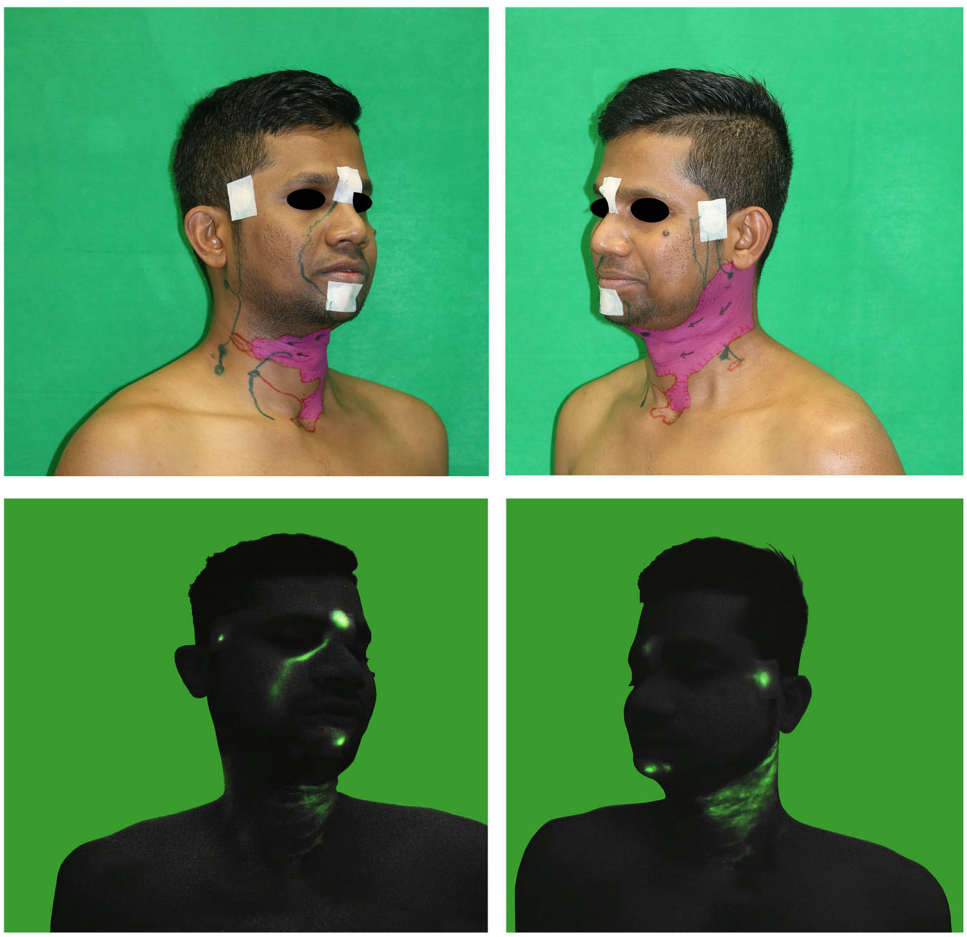

Figure 4. ICG image of an individual with unilateral neck dissection and radiation treatment. Photos with lymphatic mapping (top) and ICG images (bottom).

In the healthy control group, linear lymphatic vessels were identified from each injection site. Dermal backflow was not present in any of the healthy controls. Lymphatic vessels were visualized running vertically down from the temporal injection site to the upper cervical lymph nodes, while 2 curved vessels ran from each side of the mentum injection site to the submental lymph nodes. The lymphatic vessels ran parallel to the nasolabial fold bilaterally to the submandibular lymph nodes from the glabellar injection site (**Figure 2** and Supplemental Video S1, available online). The efferent lymphatic vessels from each sentinel node group demonstrated 3 lymphatic pathways bilaterally in the neck: accessory, internal jugular, and anterior jugular pathways (**Figure 3**).

In all individuals who had undergone neck dissection for head and neck cancer, the presence of dermal backflow was observed. The extent of dermal backflow related to the levels of lymph node dissection rather than the location of surgical scars. In cases following unilateral neck dissection, dermal backflow was generally identified only on the operated side but in some cases, the dermal backflow on the operated side extended to the unoperated side demonstrating collateralization (**Figure 4** and Supplemental Video S2, available online). In cases following bilateral neck dissection, dermal backflow was observed bilaterally. Dermal backflow was observed to cross surgical scars, and the presence of scar did not interrupt lymphatic drainage.

In addition to the 3 lymphatic drainage pathways described in the healthy controls, 2 compensatory drainage pathways were identified in individuals postneck dissection. Dermal backflow extended posteriorly to the paraspinal region and it crossed the clavicle draining to ipsilateral axillary nodes (**Figure 5** and Supplemental Video S3, available online).

Discussion

This study proposes a prospective protocol for using ICG lymphography for assessment of anatomical changes in the superficial lymphatics postneck dissection for head and neck cancer. The study found that ICG lymphography revealed the presence of dermal backflow only in posttreatment neck dissection patients. Imaging studies in extremity lymphedema suggest that dermal backflow can bridge between non-patent and patent lymphatic drainage pathways.[5] Similar patterns were observed in the head and neck region.

Head and neck cancer has been reported to metastasize to the axillary lymph nodes,[6] our study results suggest that the axillary lymph node metastasis may result from direct lymphatic spread, following the development of a collateral lymphatic drainage pathway to the axillary nodes, rather than through hematogenous seeding. ICG lymphography in head and neck cancer survivors may provide

Figure 5. ICG image of an individual with bilateral neck dissection and radiation treatment. Photos with lymphatic mapping (top) and ICG images (bottom).

personalized information about potential metastatic spread for surveillance.

Medical management of lymphedema and fibrosis-related symptoms and functional deficits has been largely reactive with treatment only initiated at the time symptoms manifest.[2] Identifying lymphatic drainage pathways can help modify the conservative management of head and neck lymphedema including the manual lymphatic drainage (MLD) performed by lymphedema therapists as well as identifying patients for potential lymphvenous anastomosis (LVA). In this study, dermal backflow was observed to drain through the skin incision scars. This challenges traditional therapy approaches which may intentionally avoid directing MLD over the incision scar.

Conclusions

ICG lymphography demonstrates value in diagnosing superficial head and neck lymphedema, particularly by the identification of the location of dermal backflow. The identification of lymphatic drainage pathways offers potential for personalizing lymphedema and oncologic management.

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Author Contributions

Hiroo Suami, design, collecting the data, analysing the data, presenting the research, editing the manuscript; **Katrina Gaitatzis**, design, collecting the data, analysing the data, presenting the research, editing the manuscript; **Helen Mackie**, collecting the data, analysing the data, editing the manuscript; **Belinda Thompson**, analyzing the data, editing the manuscript; **Fiona Tisdall Blake**, collecting the data, analysing the data, editing the manuscript; **Dion Forstner**, collecting the data, analysing the data, editing the manuscript; **Puma Sundaresan**, collecting the data, analysing the data, editing the manuscript; **Roman Skoracki**, design, analysing the data, editing the manuscript; **Louise Koelmeyer**, analysing the data, editing the manuscript.

Disclosures

Competing interests: None.

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Supplemental Material

Additional supporting information is available in the online version of the article.

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