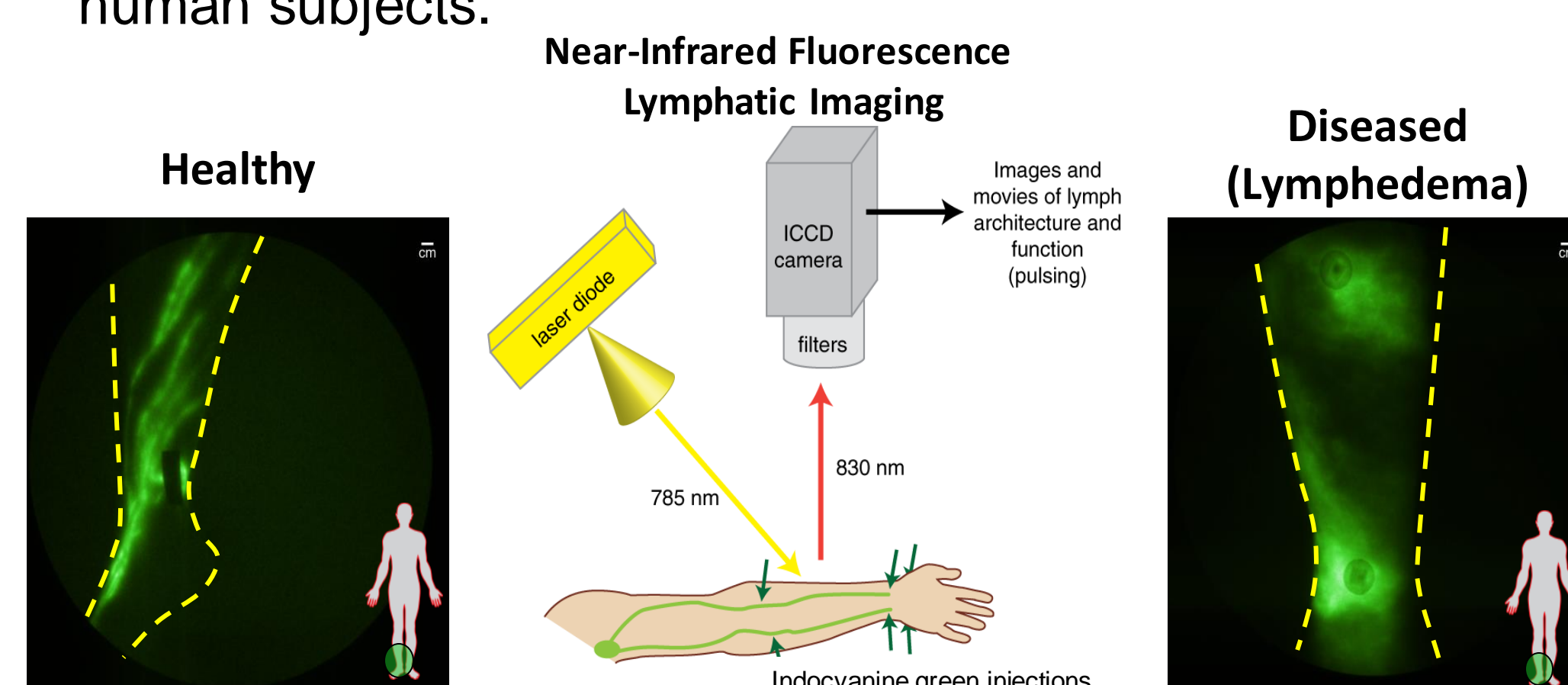


## INTRODUCTION

- The lymphatic system is a unidirectional circulatory system that plays a vital role in maintaining cardiovascular health and facilitating immune surveillance.
- Historically, the lymphatics have largely been clinically neglected, in part due to the difficulty in visualizing them owing to their small size and the lack of endogenous contrast.
- The lymphatics provide a primary pathway for metastasis and are frequently targeted for the surveillance and treatment of cancer.
- Treatment for cancer can result in cancer-related lymphedema (LE) for survivors, marked by increased tissue volumes, presenting notable management difficulties given its incurable nature.
- Cancer-related LE in the limbs is clinically diagnosed based on a 5-10% increase in the relative limb volume compared to the contralateral limb. [1]
- Diagnosis of head and neck cancer-related LE remains challenging due to the lack of contralateral comparison.
- Recent advancements indicate that the presence of dermal backflow (DBF) in lymphatics is predictive of LE.
- DBF refers to the retrograde flow of lymphatic fluid from collecting lymphatic vessels into the lymphatic capillaries and not only affects fluid dynamics but also induces irreversible tissue changes, including tissue swelling, subcutaneous adipose tissue deposition, and, ultimately, fibrosis.
- Using near-infrared fluorescence lymphatic imaging (NIRF-LI) techniques with indocyanine green (ICG) as a contrast agent, we are able to image and characterize lymphatic architecture (Figure 1) and pumping function in human subjects.



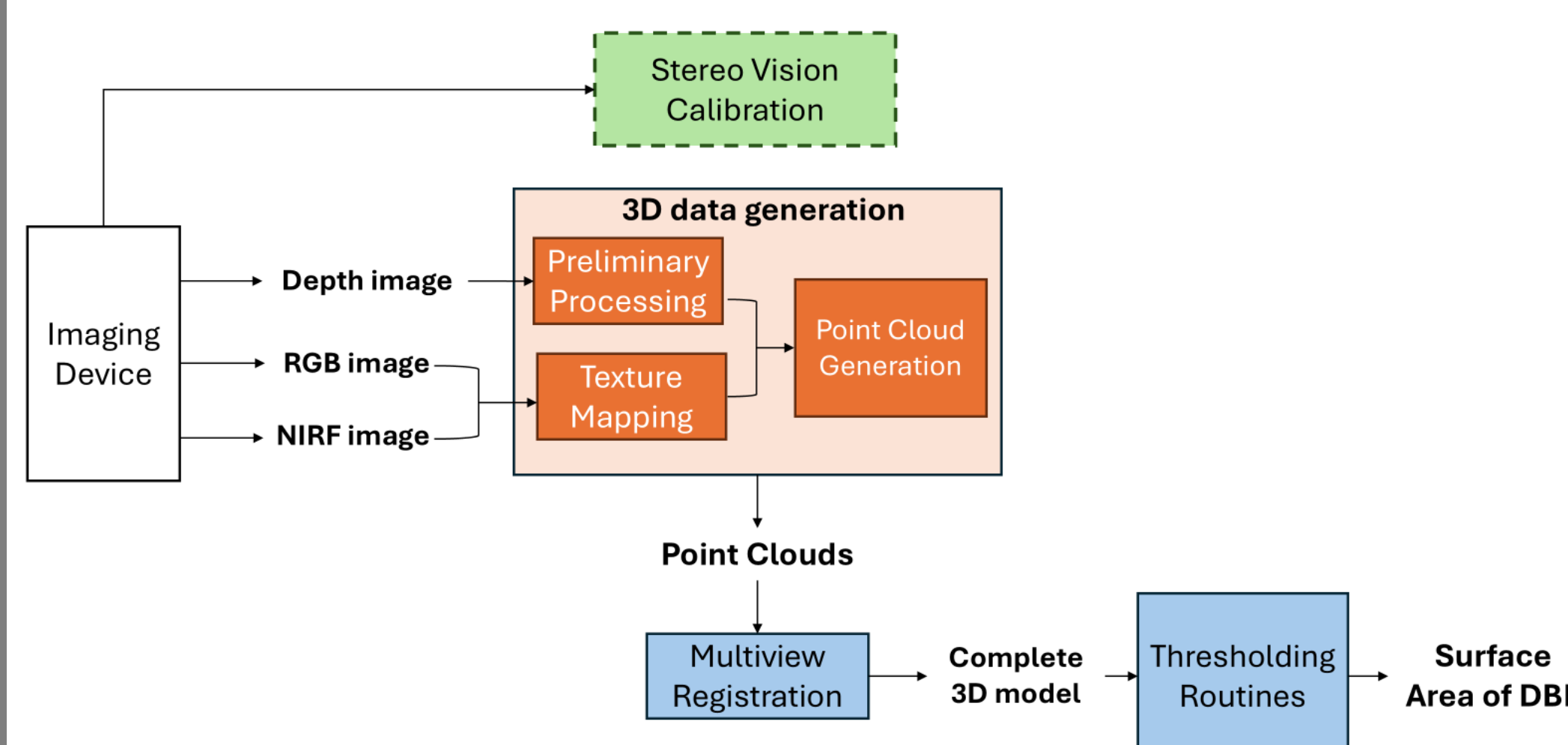
**Figure 1.** Schematic of the NIRF lymphatic imaging system (center) and example images [2] of healthy lymphatics (left) and diseased lymphatics (right).

- Similarly, DBF can be visualized following intradermal administration of ICG. [3]
- Studies indicate that early intervention, before tissue swelling occurs, could improve LE outcomes. However, the limited diagnostic tools available for monitoring lymph flow and identifying early lymphatic dysfunction pose a challenge in preventing LE onset.
- In fact, reliably quantifying the extent or area of dermal backflow over time remains clinically challenging owing to the limitations of planar, fluorescence lymphatic imaging devices and changing fields of view.

- New methods for accurate, 3-dimensional (3D) quantification of dermal backflow are needed before lymphatic dysfunction can be a clinically useful measurement of progressive disease and treatment response.

## METHODS

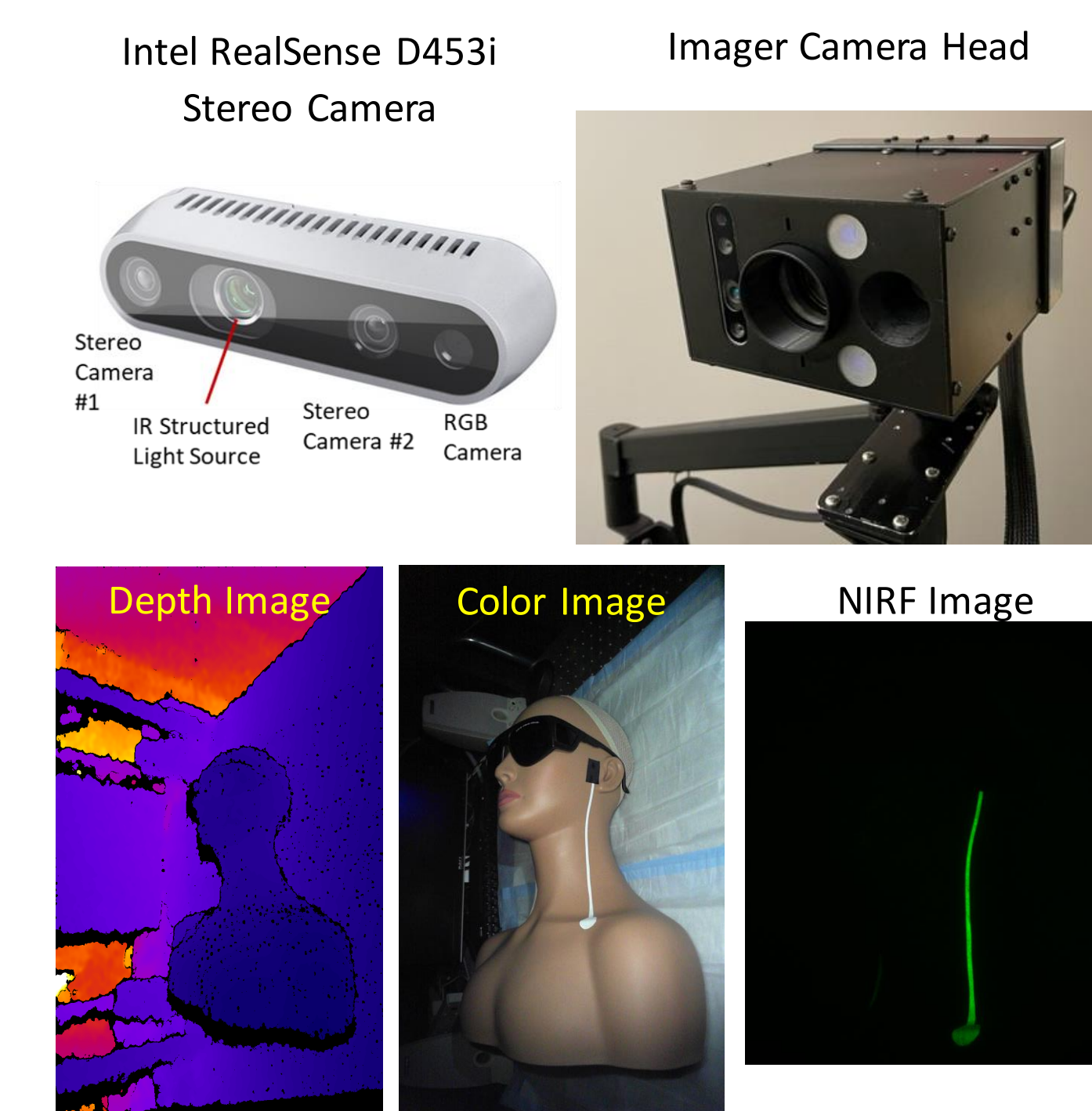
- We propose a framework to visualize and quantify the lymphatics' activity in the head or arm using data from an imaging device integrating NIRF-LI and the Intel RealSense RGB-D cameras. [4]
- Figure 2 provides an overview of the proposed framework. Initially, we save a set of fluorescent images from the NIRF camera stream capturing lymph flow in the arm following ICG injections, and color and depth images from the RGB-D streams for 3D rendering.
- Stereo-camera calibration is used to find the relative pose of the RGB to the depth camera and that of the NIRF to the RGB camera. RGB-D cameras are pre-calibrated with metadata including their intrinsic/extrinsic matrices.
- A custom checkerboard is used to estimate the transformation of the NIRF camera to the RGB camera and calibration quality is evaluated using the mean reprojection error.
- Preliminary processing is performed to enhance depth quality through an edge-preserving temporal filter.
- The 3D point cloud (PC) is computed using the depth image and the depth camera intrinsic matrix, and color texture is added to this PC from the RGB and NIRF images using their intrinsic/extrinsic matrices.
- During multiview registration, distinct poses are captured from various angles, and a PC is created for each pose. These PCs are fused using fiducial markings and Iterative Closest Point (ICP) algorithm [5] to create a complete PC.
- The ball pivoting algorithm [6] is applied on the resulting PC to generate a mesh representation.
- Finally, adaptive thresholding is used to segment fluorescence in the mesh and the surface area of relevant segmented components is computed.
- Image acquisition modules were developed in LabVIEW and the software modules intended for stereo vision calibration, 3D rendering, registration, and segmentation were developed using Python 3.8.



**Figure 2.** Overview of the proposed framework for the 3D rendering and quantification of lymph flow.

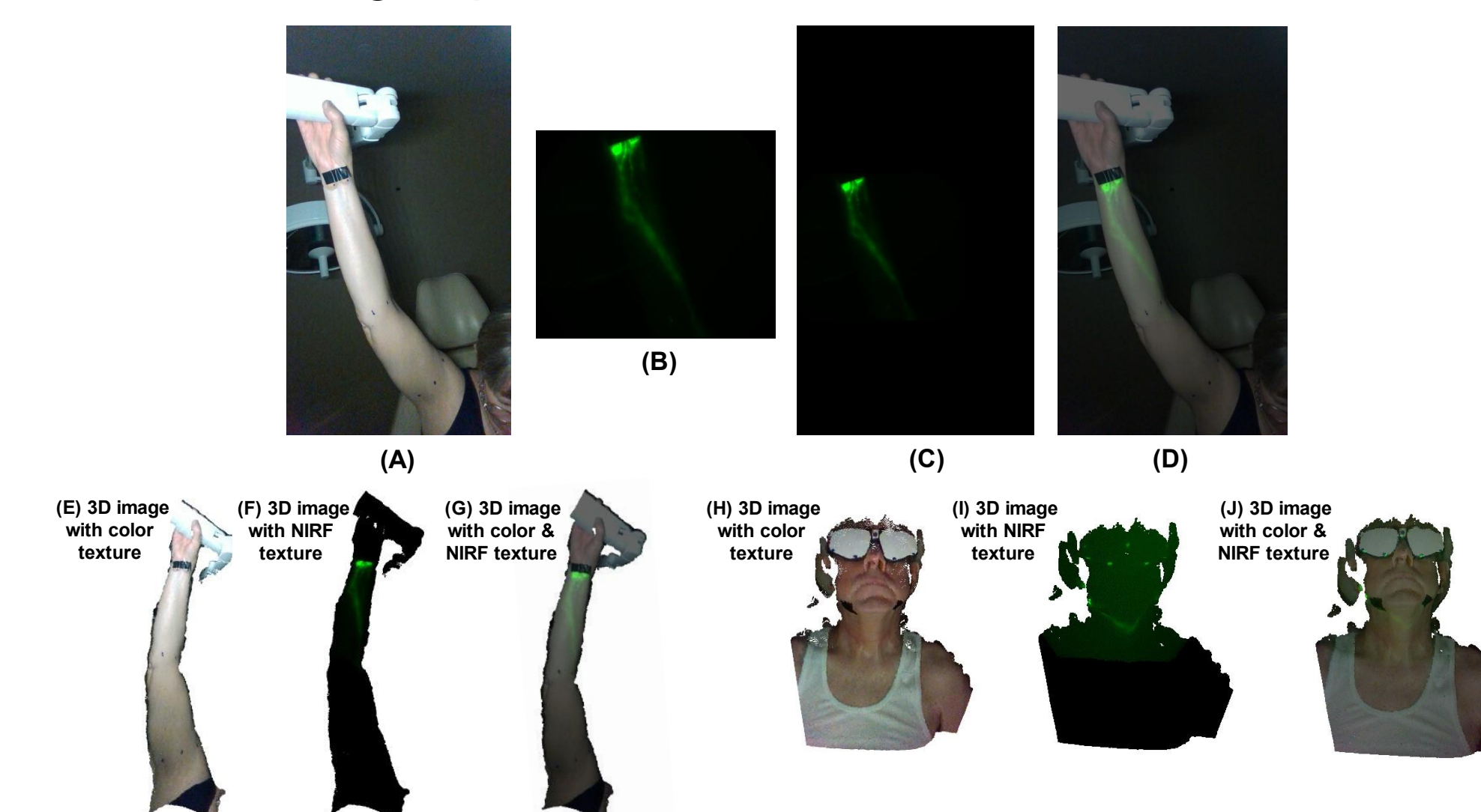
## RESULTS

- By integrating the depth module into the NIRF lymphatic imaging system, fluorescence, color, and depth images, with fixed frames of reference can be acquired (Figure 3).



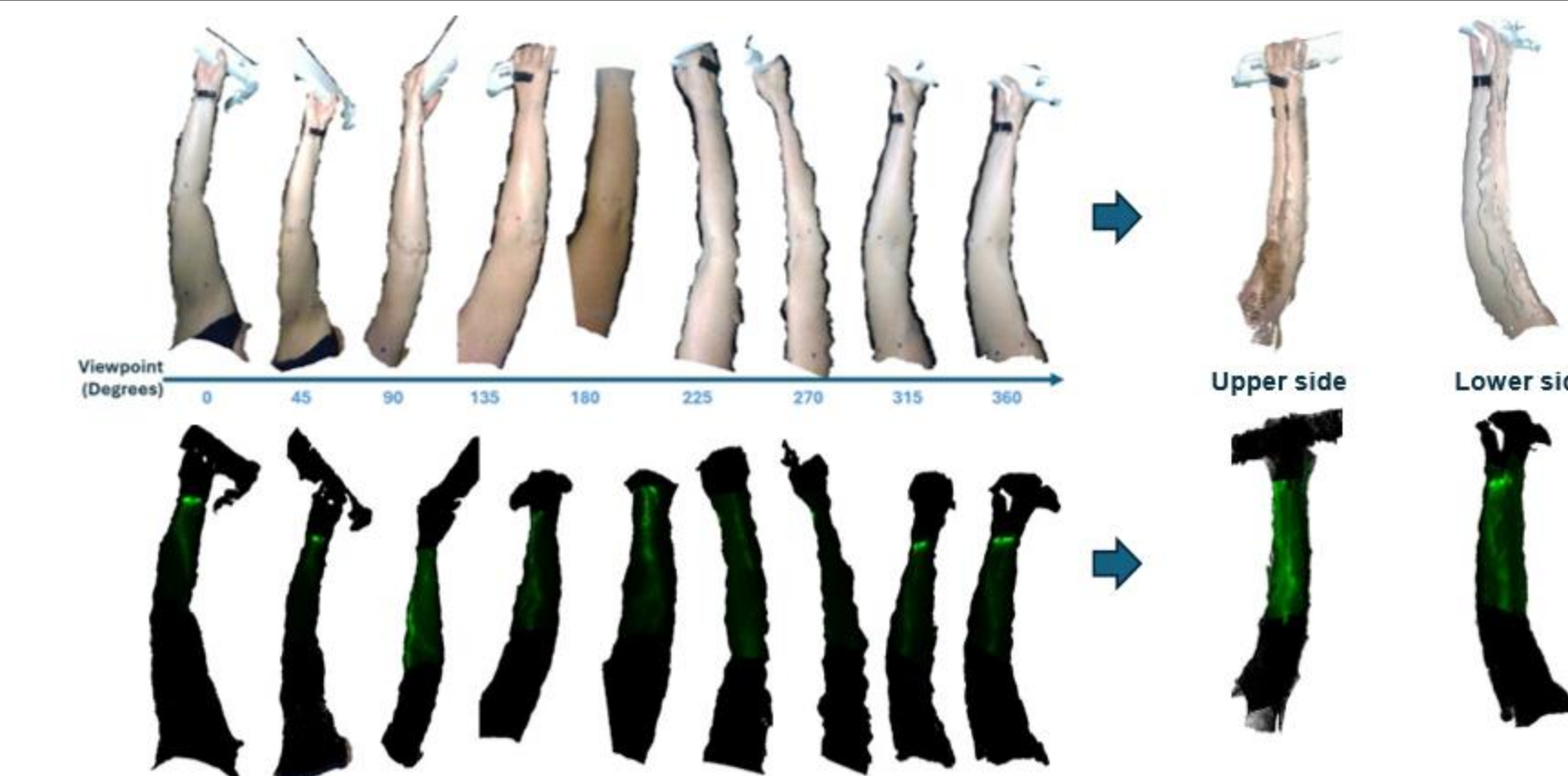
**Figure 3.** The depth sensor module integrated into the NIRF lymphatic imaging system enables the near simultaneous acquisition of depth, color, and NIRF images.

- We generate a 3D point cloud with color texture using the depth image, color image, intrinsic, and extrinsic calibration acquired from the intel RealSense RGB-D camera and the metadata provided by the manufacturer as shown in Figures 4E and 4H.
- Using the inferred transformation between the color and NIRF cameras in the stereo calibration step, we estimate the correspondences between the pixels of images of the same scene captured by both cameras.
- We use these correspondences to provide the 3D PC with a second texture from the NIRF camera (Figures 4F and 4I).
- Prior to generating the PC, we apply edge-preserving filtering to the depth maps using temporal smoothing filters. This allows for the creation of PCs with smoother surfaces without losing important details.



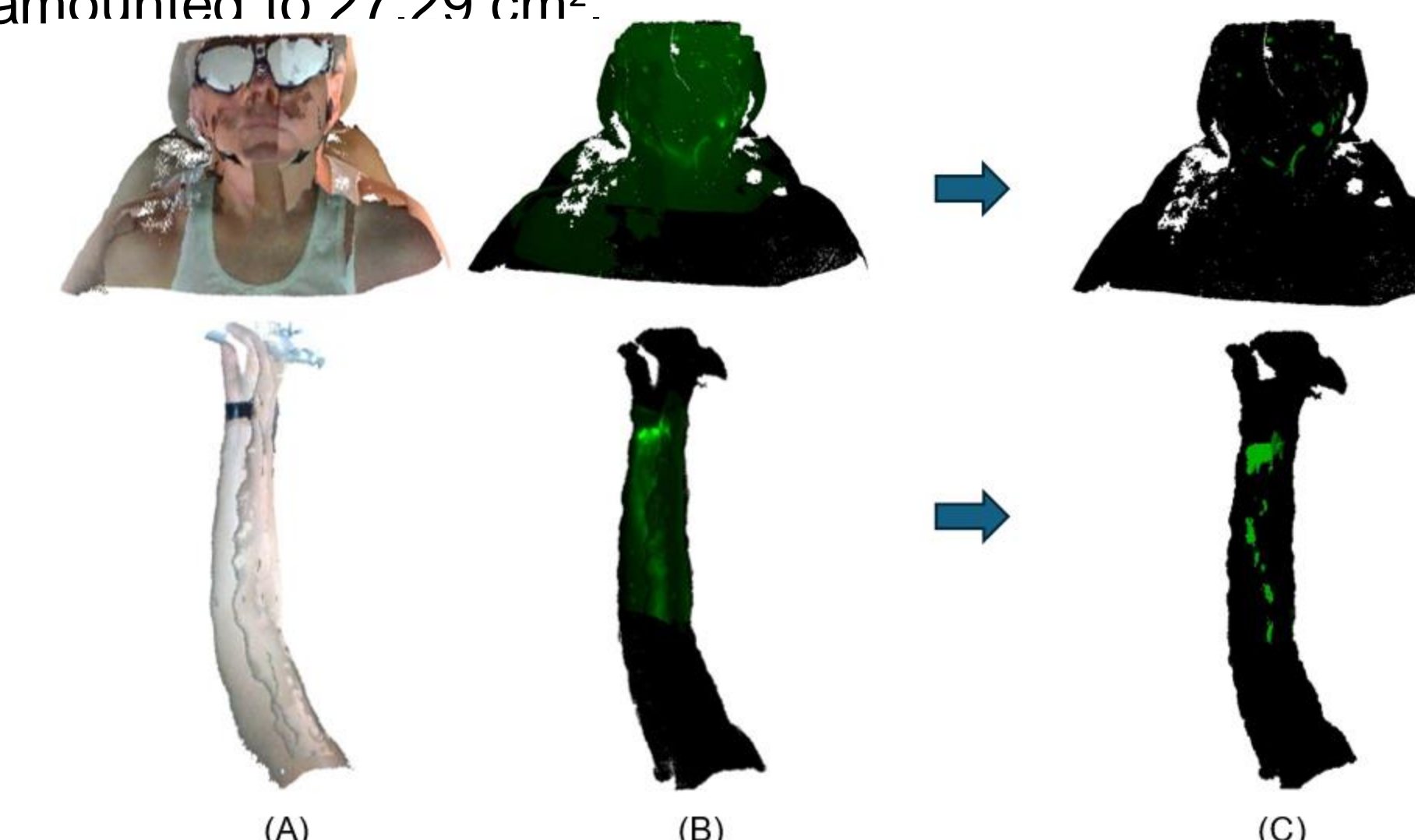
**Figure 4.** Visualization of blended NIRF and color images in 3D following calibration & transformation. (A) Color image from RGB-D camera. (B) Image from NIRF camera. (C) NIRF image after calibration. (D) Overlay of color and NIRF image. (E-G) and (H-J) highlight the 3D point cloud generation results using the arm images and a subject's head & neck, respectively.

- Figure 5 highlights the registration of multiple 3D views to produce a more complete surface rendering of the arm.
- A full mesh is created by applying the ball pivoting algorithm to the resulting PC. A color correction algorithm is in development to address the texture disparities in the full mesh.



**Figure 5.** Multiview alignment results (Left) from 3D surface scans of a healthy arm from 9 viewpoints (Right). The top row depicts viewpoints of the arm point cloud with color texture. The bottom row shows corresponding viewpoints with NIRF texture.

- After applying thresholding routines on the rendered complete mesh with NIRF texture, lymph flow can be segmented as shown in Figure 6 and its corresponding surface area is computed.
- The surface area of the segmented lymph flow in the head and neck was 24.32 cm<sup>2</sup>, while the surface area in the arm amounted to 27.29 cm<sup>2</sup>.



**Figure 6.** Results of thresholding on the head and neck (Top) and arm (Bottom) of two subjects. (A) 3D mesh with color texture from Intel RealSense camera. (B) 3D mesh with NIRF texture, the captured fluorescence is highlighted in green. (C) 3D mesh after thresholding the 3D mesh with NIRF texture, the fluorescence from the lymph flow is colored in green.

## CONCLUSIONS AND DISCUSSIONS

- Our preliminary results demonstrate the reconstruction of head and arm 3D models with NIRF texture overlay using data from our NIRF and RGB-D stereo-camera device.
- Moreover, we demonstrate the feasibility of quantification of lymph fluid on clinically relevant 3D surfaces.
- This framework can provide a clinically useful measurement for monitoring lymphatics to identify dysfunction and assess early physiotherapy impact on the progression of LE in cancer survivors.

## References

- Armer, J. M. The problem of post-breast cancer lymphedema: Impact and measurement issues. *Cancer Invest* 23, 76–83 (2005).
- O'Donnell, *et al.*, *J. Vasc. Surg. Venous. Lymphat. Disord.* 5(2):261-271, 2017 (PMID: 28214496).
- Aldrich, M. B. *et al.* Prediction of breast cancer-related lymphedema by dermal backflow detected with near-infrared fluorescence lymphatic imaging. *Breast Cancer Res Treat* 195, 33–41 (2022).
- Bouhali, S., Merchant, F., Karni, R. J., Gutierrez, C. & Rasmussen, J. C. 3D rendering and analysis of dermal backflow as an early indicator of cancer-acquired lymphedema using RGB-D and near-infrared fluorescence lymphatic imaging. in *Medical Imaging 2024: Clinical and Biomedical Imaging* (eds. Gimi, B. S. & Krol, A.) vol. 12930 1293008 (SPIE, 2024).
- Segal, A., Haehnel, D. & Thrun, S. Generalized-icp. in *Robotics: science and systems vol. 2* 435 (Seattle, WA, 2009).
- Bernardini, F., Mittleman, J., Rushmeier, H., Silva, C. & Taubin, G. The ball-pivoting algorithm for surface reconstruction. *IEEE Trans Vis Comput Graph* 5, 349–359 (1999).