It has long been established that the lymphatic vasculature plays an important role in cardiovascular health, but there have been few methods to diagnose lymphatic dysfunction. To aid real-time, point-of-care monitoring of the lymphatic system, Dr Eva M Sevick has devised a breakthrough investigational technique based on laser diode technology used by Dr Matthew Greives to diagnose vascular abnormalities in the paediatric population.

The non-invasive nature of the NIRF technique is a great improvement, especially for paediatric patients where excessive levels of stress need to be kept to a minimum.
vasculature. The fluorescence that is emitted from the tissue surface is then collected using the near-vision technology coupled to a detection system that registers images within ten to 100s of milliseconds. The images can be compiled into movies showing the active “pumping” through the lymphatic vasculature in real-time.

As Dr Sevick highlights: “It’s amazing how just two injection sights, essentially 10 to 15 micrometers of ICG, will fill up the entire lymphatics, and once the contrast agent flows back into the blood vasculature via the subclavian vein, the trace dose of ICG is diluted and cleared to such an extent it’s essentially gone. So essentially, we visualise only the lymphatics, and because the detection is so sensitive, we can actually see a real-time movie of lymph flow.”

Historically, with established imaging modalities, such as lymphoscintigraphy or CT or MRI lymphangiography, contrast agents are required for static imaging. In addition, lymphangiography techniques require lymphatic vessel cannulation or ultrasound guided injection into lymph nodes to introduce large amounts of contrast agents into the lymphatics. These techniques require the sedation of infants and children for both contrast administration and the comparatively long image acquisition times. The non-invasive and non-radioactive nature of trace contrast administration and rapid imaging provided by the NIRF technique is a great improvement, especially for paediatric patients where sedation can add complication to the diagnostic procedure. Recently, Drs. Greives and Sevick demonstrated the utility of the technology on a 21 month old subject diagnosed with congenital lymphoedema (Greives, et al., Pediatrics, 2017).

Paediatric lymphoedema is thought to be caused by developmental malformations which, if left untreated, results in interstitial protein accumulation, tissue fibrosis and disfigurement, and reduced immune response. Early treatment is especially paramount for children who are at risk of a lifetime of sequelae arising from lymphatic impairment. Yet management of paediatric lymphoedema is typically based upon adult treatment, which lacks evidence for effective use in paediatric populations. The main impediment to understanding, diagnosing, and treating paediatric lymphoedema is the lack of an imaging modality that is safe, inexpensive, and effective. In their recently published work, the Greives and Sevick team used near-infrared fluorescence imaging to show intact, apparently normal lymphatic anatomy in an infant with lymphoedema in the right arm, but with decreased lymphatic pumping function relative to the contralateral and lower extremities. Their work showed that the lack of pumping function rather than anatomical malformation was the source of irreversible arm swelling and that physiotherapies that stimulated lymphatic function could be effective therapies.

**How long has current research into the technique been carried out?**

The investigational technique has been deployed on the Texas Medical Center in Houston since 1994 and used safely in over 350 adults, children and infants.

**Can you see NIRF imaging being used in other areas of medicine?**

We use NIRF imaging for imaging the lymphatic system in more common chronic conditions, such as inherited forms of lymphoedema (Agollih, et al., Plos One, 2014; Gonzalez- Garay, Vascular Cell, 2016). The team has also pointed out the importance of near-infrared imaging in the treatment of paediatric patients where early treatment is critical for survival (Tan, et al., Pediatric Cardiol. 2014). Because the near-infrared imaging technique can also be delivered without sedation and in a bedside environment or on the lap of a parent or caregiver, it is especially suited to applications in the paediatric population.

**FUTURE AVAILABILITY**

Owing to the high degree of ICG safety, its trace dose in this application, and the lack of radiation or radioactivity, the technique of near-infrared fluorescence lymphatic imaging has significant potential for point-of-care application in community-based health care practices. Future expansion into the medical community is predicted, with the technology to be rolled out in the not too distant future.

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**RESEARCH OBJECTIVES**

Dr Eva Sevick, PhD has pioneered the development of near-infrared fluorescence optical imaging and together with Dr Matthew Greives, MD, Director of the UTHealth Vascular Anomalies Clinic, is using the technology to understand the lymphatic contribution to vascular disorders in children.

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**BIO**

Dr Sevick is Kinder Distinguished Chair of Cardiovascular Research, University of Texas Health Science Center at the Texas Medical Center, where she and her team developed from the bench and translated to the clinic, near-infrared lymphatic imaging in infants, children, lymphoedema patients, and animal models of human lymphatic diseases.

Dr Matthew Greives is Director of the Vascular Anomalies Clinic at UTHealth where he deploys the investigational lymphatic imaging technique in paediatric populations.

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