

ADVANCED IMAGING TECHNOLOGIES FOR MAPPING CADAVERIC LYMPHATIC ANATOMY: MAGNETIC RESONANCE AND COMPUTED TOMOGRAPHY LYMPHANGIOGRAPHY

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ABSTRACT

Lymphatic anatomy has become increasingly clinically important as surgical techniques evolve for investigating and treating cancer metastases. However, due to limited anatomical techniques available, research in this field has been insufficient. The techniques of computed tomography (CT) and magnetic resonance (MR) lymphangiography have not been described previously in the imaging of cadaveric lymphatic anatomy. This preliminary work describes the feasibility of these advanced imaging technologies for imaging lymphatic anatomy. A single, fresh cadaveric lower limb underwent lymphatic dissection and cannulation utilizing microsurgical techniques. Contrast materials for both CT and MR studies were chosen based on their suitability for subsequent clinical use, and imaging was undertaken with a view to mapping lymphatic anatomy. Microdissection studies were compared with imaging findings in each case. Both MR-based and CT-based contrast media in current clinical use were found to be suitable for demonstrating cadaveric lymphatic anatomy upon direct intralymphatic injection. MR lymphangiography and CT lymphangiography are feasible modalities for cadaveric anatomical research for lymphatic anatomy. Future studies including refinements in scanning techniques may offer these technologies to the clinical setting.

Keywords: lymphatic anatomy, computed tomography, magnetic resonance imaging, cadaver, lymphangiography

Unlike the arterial and venous systems, lymphatic anatomy still remains an inadequately understood vascular area largely due to a paucity of anatomic techniques available for research in this field. Early techniques comprised injection of readily visible substances into lymphatics, such as mercury, plaster, milk or ink, followed by dissection (1,2). These techniques were largely used prior to the advent of radiography which next produced lymphangiography with plain radiology.

Lymphangiography uses microsurgical techniques to cannulate lymphatics and inject contrast media suitable for radiography (3,4). This technique enabled lymphatic mapping of high accuracy and reproducibility and provided the source of recent advances in cadaveric lymphatic anatomical research.

The techniques of computed tomography (CT) and magnetic resonance (MR) lymphangiography have not been described previously in the imaging of cadaveric lymphatic anatomy, tools which could significantly improve our understanding of the lymphatic system. We present our preliminary work in this field, describing herein the feasibility of advanced imaging technologies in the imaging of the lymphatic



Fig. 1. Concordant findings between microdissection of the lower limb lymphatics (left; black arrows) when compared with magnetic resonance (MR) lymphangiography (right; white arrows).

system, with the use of microsurgical techniques for lymphatic contrast injection and subsequent lymphangiography.

METHODS

A single, fresh cadaveric lower limb was utilized in the study. The cadaver was an 80 year old male, with no lymphedema or known malignancy. Utilizing microsurgical techniques, a single lymphatic network was dissected free and cannulated with a 30 gauge needle. Contrast materials for both CT and MR studies were chosen based on their suitability for subsequent clinical use.

MR studies were completed first. Iron oxide magnetic nanoparticles have been widely investigated as MR contrast agents and have shown promise as contrast agents, with early clinical results reported (5-7). Modifications have been sought as improvements, with highly crystalline magnetic nanoparticles synthesized by modifying the benzyl

alcohol component as originally proposed by Niederberger (8). These nanoparticles, 15 nm in diameter on average, were coated with a protective polyethylene glycol polymeric layer (Ian Wark Research Institute, Adelaide, Australia). A 1.5ml slow injection of the nanoparticulate MR contrast agent was injected into the cannulated lymphatic, and MR scanning was subsequently undertaken using a matrix coil plated over the entire specimen in a 3 Tesla magnet (Magnetron Trio, Siemens). Optional images (0.8 mm) were obtained using TIM (Total Imaging Matrix Technology) with an in-plane resolution of 0.9 mm x 0.8 mm x 0.8 mm.

The feasibility of CT lymphangiography was next assessed by lymphangiography utilizing intralymphatic injection with Iohexol 350mg/ml (Omnipaque 350; Amersham Health), an iodinated, non-ionic radiographic contrast medium in clinical use as a CT contrast medium. Prior to injection, the Iohexol was mixed with Patent Blue V (Sigma-

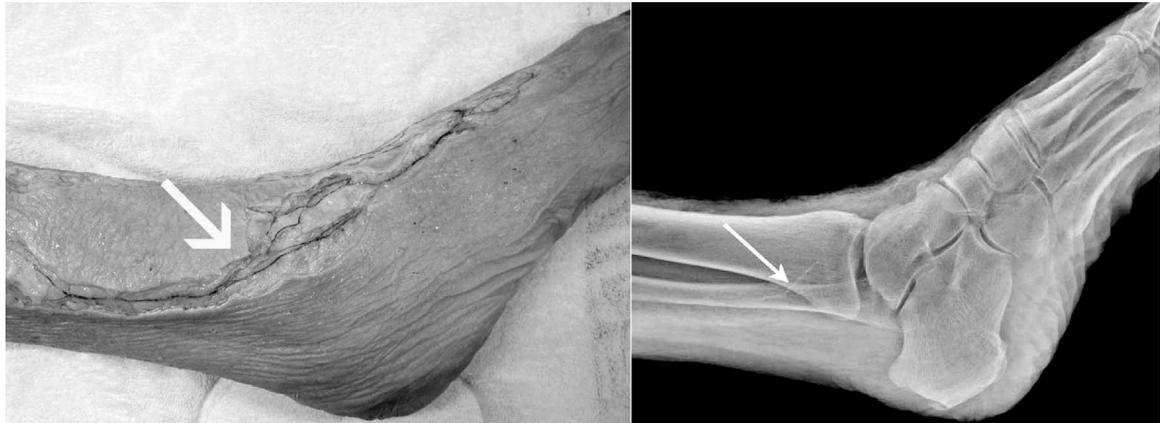


Fig. 2. Concordant findings between microdissection of the lower limb lymphatics (left; arrow) when compared with lymphangiography using the radiographic contrast medium suitable for computed-tomography (CT) lymphangiography (right; arrow).

Aldrich), a dye used to aid visualization during dissection, in a ratio of 20ml:10drops (0.7ml). Direct intra-lymphatic injection of the Iohexol mixture into the same lower limb lymphatic used for MR analysis was performed, with segmental injections performed with a total of 1ml of the contrast mixture used. Lymphangiography was subsequently undertaken with plain radiography.

RESULTS

Microdissection studies were compared with imaging findings. Both MR-based and CT-based contrast media in current clinical use were found to be suitable for demonstrating cadaveric lymphatic anatomy upon direct intralymphatic injection.

MR lymphangiography was able to demonstrate the injected lymphatics, with demonstration of the size, location and course of the lymphatics. These imaging findings were concordant with dissection findings (*Fig. 1*).

Lymphangiography with iodinated contrast was able to demonstrate the injected lymphatics, again with demonstration of the size, location and course of the lymphatics. These imaging findings were concordant with dissection findings (*Fig. 2*).

Both contrast media were able to flow lengthy distances along the lymphatic vessels. Single injections traversed distances up to 10cm, with multiple injections able to traverse up to 2/3 the length of the entire leg. The distances were only limited by two factors: volume of injectant and lymphatic obstruction by valves or lymph nodes.

DISCUSSION

Lymphatic anatomy has become increasingly clinically important. The understanding of lymphatic metastases in cancer spread has contributed to the development of techniques for treating lymphatic metastases. Similarly in lymphedema, the understanding of lymphatic obstruction has led to surgical techniques for treatment that are based on lymphatic anatomy. As such, research into lymphatic anatomy has become increasingly required, with the imaging of lymphatic anatomy of paramount importance.

Early cadaveric techniques lacked radiographic and photographic reproducibility. Sappey (1874) produced groundbreaking drawings of lymphatic anatomy based on his studies with mercury (2). Although mercury had been previously widely used, it is now known to be toxic and thus these

studies cannot be reproduced today (9,10). Furthermore, radiography had not been invented, and thus Sappey's work lacked radiographic analysis. Gerota (1896) used Prussian Blue dye combined with turpentine and was able to locate fine lymphatics in the tissues surrounding the injection point (11). This resulted in studies of limited value, with poor reproducibility and lack of radiography. Rouviere (1938) used ink injections as a replacement for mercury, producing valuable results but this permitted only drawings of his findings, again without radiographic analysis (12). Castenholtz (1984) evaluated the finer structure of lymphatics using electron microscopy, which, although providing important ultrastructural information, was not an appropriate tool for lymphatic mapping (13,14). Cadaveric imaging with plain radiography has become a source of anatomical information, with Foldi, Foldi and Kubik demonstrating their dissections, drawings and indeed radiographs, but lacking in depth descriptions of their methodology (15,16).

The use of microsurgical techniques to cannulate lymphatics and inject contrast media into both initial and collecting lymphatics has revolutionized lymphatic research by allowing widespread mapping of lymphatics with high accuracy and reproducibility (3,4). This technique, using direct lymphangiography with plain radiography, has since provided the source of recent advances in cadaveric lymphatic anatomical research.

The development of the clinical technique of lymphoscintigraphy was a substantial advance using uptake by lymphatics of a radiotracer to enable lymphatic mapping with nuclear scintigraphy. While this technique is functionally accurate and useful for the clinic, it is limited by the diffusion of a medium into the lymphatics, and direct injection has been the technique of choice for anatomical research into arterial, venous, and lymphatic anatomy.

The use of advanced imaging technologies has contributed to this field, with CT

lymphangiography and MR lymphangiography initiated clinically, and functional uptake of contrast media into lymphatics and subsequent imaging demonstrated (17-20). However, limitations exist with in vivo lymphatic flow, especially in the setting of lymphatic obstruction where contrast is not taken up by the affected lymphatics. As such, anatomical information is significantly lacking from these methods.

The current paper demonstrates the feasibility of advanced imaging technologies in the imaging of the lymphatic system for cadaveric, anatomical research. With the use of microsurgical techniques for lymphatic contrast injection and subsequent lymphangiography, we have utilized both MR and CT contrast media, and demonstrated the accuracy of these media for identifying lymphatics. With ongoing studies, we expect to improve the quality of contrast media and the image resolution of scanning techniques and implement these advances for both clinical and research use.

CONCLUSION

MR lymphangiography and CT lymphangiography are new modalities for cadaveric anatomical research into lymphatic anatomy. Further research utilizing these modalities should improve our understanding of the lymphatic system in both the normal state and in disease. As the contrast media for current clinical usage are suitable for cadaveric research, anatomical findings may have direct translational implications for treatment.

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