Interstitial Transpedal MR-Lymphangiography of Central Lymphatics Using a Standard MR Contrast Agent: Feasibility and Initial Results in Patients with Chylous Effusions

Interstitielle transpedale MR-Lymphangiografie zentraler Lymphbahnen mit einem Standard-MRT-Kontrastmittel: Machbarkeit und erste Ergebnisse bei Patienten mit chylösen Ergüssen

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ZUSAMMENFASSUNG

Ziel Beschreibung einer neuen Technik der transpedalen Magnetresonanzlymphangiografie (tMRL) mittels interstitieller Injektion eines gadoliniumhaltigen Standardkontrastmittels zur Visualisierung des zentralen Lymphsystems bei Patienten mit chylösen Ergüssen.

Material und Methoden Erste Erfahrungen mit der tMRL bei sieben aufeinanderfolgenden Patienten mit chylösen Ergüssen wurden retrospektiv ausgewertet. Es wurde eine hochaufgelöste dreidimensionale Multiecho (mDIXON) Sequenz verwendet, um den gesamten Torso der Patienten vor und nach interstitieller pedaler Injektion eines regulären extrazellulären gadoliniumhaltigen Kontrastmittels abzuzeichnen. Die MRT-Untersuchungen wurden von zwei Radiologen qualitativ hinsichtlich Darstellung der zentralen (abdominellen und thorakalen) Lymphbahnen, deren Anatomie sowie hinsichtlich einer lymphatischen Pathologie (chylolymphatische Leckage oder Reflux) analysiert.

Ergebnisse Die tMRL war in 6/7 Patienten technisch erfolgreich und zeigte eine chylolymphatische Leckage in 3/7 Fällen, eine lymphatische Malformation in 1/7 Fällen, einen chylolymphatischen Reflux in 1/7 Fällen sowie regelrechten chylolymphatischen Fluss in den zentralen Lymphbahnen in 1/7 Fällen. Bei einem Patienten wurde weder eine Kontrastierung zentraler Lymphbahnen, noch eine Leckage beobachtet. Die Ergebnisse der tMRL waren prospektiv in allen technisch erfolgreichen Fällen hilfreich zur Planung der weiteren Therapie und beeinflussten diese in vier Fällen erheblich. Alle Untersuchungen wurden von den Patienten gut toleriert ohne Auftreten von Komplikationen. Eine Allgemeinanästhesie oder Sedierung war nicht erforderlich.

Schlussfolgerung Die transpedale MR-Lymphangiografie mit interstitieller Injektion eines regulären extrazellulären gadoliniumhaltigen Kontrastmittels ist ohne Allgemeinanästhesie in der klinischen Routine durchführbar und erlaubt die Beurteilung von Pathologien des zentralen Lymphsystems.

Kernaussagen
- Eine transpedale Kontrastierung zentraler Lymphbahnen in der MRT ist technisch machbar.
- Hierzu kann reguläres extrazelluläres gadoliniumhaltiges Kontrastmittel verwendet werden.
- Anatomie und pathologische Veränderungen zentraler Lymphbahnen können mittels MR-Lymphangiografie evaluiert werden.
- Die transpedale MR-Lymphangiografie ist hilfreich zur Therapieplanung von chylösen Ergüssen.

ABSTRACT

Purpose To describe a novel technique for transpedal magnetic resonance lymphangiography (tMRL) with interstitial injection of a standard gadolinium-based contrast agent, and to assess its ability to visualize the central lymphatic system (CLS) in patients with chylous effusions.
Introduction

Intractable chylous effusions are associated with considerable morbidity and mortality [1, 2]. One of the main problems, especially in minimally invasive treatment of lymphatic pathologies [2–5] is the lack of simple imaging techniques for the visualization of the central lymphatic system (CLS; i.e., cisterna chyli (CCh), thoracic duct (TD) and direct tributaries) [6].

There are certain disadvantages associated with existing CLS imaging approaches. Conventional X-ray lymphangiography is technically challenging, invasive and time-consuming [7]. Lymphoscintigraphy has insufficient anatomical resolution for CLS evaluation [7]. On non-contrast MR-lymphangiography, central lymphatics can be evaluated, but it can be difficult to distinguish lymphatics from surrounding tissue [7, 8]. Dynamic contrast-enhanced MR-lymphangiography is a promising new approach [9, 10]. However, it is time-consuming due to necessary sonographically guided lymph node puncture outside the scanner room, and usually requires general anesthesia or at least sedation.

To overcome these disadvantages, we sought to develop an MR imaging technique that can provide information on CLS anatomy, without time-consuming intranodal contrast application or general anesthesia. The aim of this study is to describe this new technique for transpedal MR-lymphangiography (tMRL) with interstitial injection of a standard gadolinium-based contrast agent and to assess its ability to visualize the CLS in patients with chylous effusions.

Materials and Methods

Experiences with tMRL were retrospectively reviewed in seven patients with chylous effusions. High-resolution three-dimensional multi-echo (mDIXON) images of the entire torso were obtained before and after interstitial injection of an extracellular gadolinium-based contrast agent. MR examinations were assessed qualitatively by two radiologists with respect to visualization of central lymphatics, delineation of their anatomy and presence of a lymphatic pathology (chylolymphatic leakage or reflux).

Results

Examination was technically successful in 6/7 patients. tMRL confirmed the location of chylolymphatic leakage in 3/7, demonstrated a lymphatic malformation in 1/7, chylolymphatic reflux in 1/7, and confirmed normal chylolymphatic flow in the central lymphatics in 1/7 patients. In one patient neither CLS enhancement nor leakage were detectable. tMRL findings were considered helpful in all technically successful cases, and considerably influenced further treatment in four patients. All examinations were well tolerated without complications. No general anesthesia or conscious sedation was necessary.

Conclusion

Transpedal MR-lymphangiography with interstitial injection of a standard extracellular gadolinium-based contrast agent is feasible in clinical routine without general anesthesia and allows for assessment of pathologic conditions of central lymphatics.

Key Points

- Transpedal MR-lymphangiography of central lymphatics is technically feasible.
- A standard extracellular gadolinium-based contrast agent can be used for tMRL.
- tMRL allows for evaluation of anatomy and pathologies of central lymphatics.
- tMRL is a useful tool for treatment planning in chylous effusions.

Citation Format

Repetition time | Shortest
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Echo time | 1.8 ms and 4 ms
Flip angle | 15°
k-space acquisition | Cartesian
Field of view | 300 × 400 mm
Acquired voxel size | $1 \times 1.2 \times 2.5$ mm³
Reconstructed voxel size | $1 \times 1 \times 1$ mm³
Parallel imaging factor | 1.65
Acquisition time per stack | 10 seconds

Table 1 Imaging parameters.

Results

Case studies

Patient 1

A 24-year-old patient presented with left-sided non-traumatic chylothorax. Thoracoscopic surgery and parenteral nutrition had been unsuccessful with persisting leakage of 1000 ml/day. On tMRL the pelvic and retroperitoneal lymphatics, CCh and the lower two-thirds of the TD appeared normal with segmental TD duplication in the lower thorax. Abnormally dilated lymphatic ducts surrounded the left-sided termination of the TD (Fig. 1). Chylolymphatic leakage or reflux was not observed. A diagnosis of localized lymphatic malformation as the cause of the chylothorax was established and confirmed by conventional lymphangiography during the subsequent lymphatic intervention. After transabdominal embolization of the malformation, drainage via the chest tube ceased immediately.

Patient 2

A 54-year-old patient suffering from necrotizing pancreatitis with left subclavian vein thrombosis developed bilateral chylothorax, chylopericardium and chylous ascites that were refractory to conservative treatment. TD ligation, pleurectomy and irradiation of the TD had been unsuccessful. Lymphoscintigraphy was reported to show normal tracer flow without depiction of pathology.

On tMRL contrast medium flow was unobstructed. The CLS appeared normal with segmental duplications of the TD in the mid and upper thorax. There was extensive chylolymphatic reflux from the cervical part of the TD into dilated mediastinal, pericardial and bronchial lymphatics (Fig. 2). Leakage was not identified. Reflux was confirmed by intranodal lymphangiography. After TD embolization, drainage via bilateral chest tubes and an ascites drain ceased within three days. The chylopericardium also decreased on follow-up imaging.

Patient 3

A 78-year-old patient developed chylous ascites refractory to conservative treatment after surgical abdominal aortic aneurysm repair. tMRL demonstrated normal pelvic lymphatics. At the bifurcation of the aortic graft, contrast medium leaked into a small retroaortic recess which communicated with the peritoneal cavity. Intranodal oily lymphangiography was performed with continuation of parenteral nutrition. After one week the leakage resolved and did not recur during follow-up of 15 months under full oral nutrition.

Patient 4

A 62-year-old patient developed a left-sided chylothorax after surgery for recurrent pleural mesothelioma. Parenteral nutrition with somatostatin application and several attempts of TD ligation and pleurodesis were unsuccessful. tMRL demonstrated unobstructed lymph flow without reflux. Several tortuous lymphatic channels in the middle and upper thorax coalesced into a single TD before its termination. Retrocardially the tortuous lymphatic channels showed contrast leakage into the left pleural cavity (Fig. 3). Intranodal lymphangiography confirmed the diagnosis of post-operative leakage of three lymphatic channels. Leakage ceased immediately after successful TD embolization.

Patient 5

A 58-year-old patient suffered from a right-sided chylothorax after esophagectomy with gastric interposition for esophageal cancer. Chest tube drainage did not drop below 1000 ml per day under total parenteral nutrition. tMRL was performed to assess lymphatic anatomy which can be altered after gastric interposition surgery. The retroperitoneal lymphatics, the CCh and the lower part of the TD appeared normal. Contrast medium extravasation from a side branch of the TD was visible retrocardially (Fig. 4). Importantly tMRL demonstrated an additional retroaortic lymphatic channel receiving lymph flow from the retroperitoneal lymphatics not draining into the CCh. This channel drained into the TD immediately below the leakage. During embolization special care was taken to occlude this channel and the leakage site...
itself to prevent further chylolymphatic flow towards the leak. Leakage ceased immediately after intervention.

![Fig. 1](image1.png)

- **Fig. 1** Case study 1. **a-c** Axial tMRL images in a patient with extensive left-sided chylothorax with mediastinal shift to the right. Examination showed normal thoracic lymphatic anatomy with duplication of the thoracic duct in the lower thorax (inset magnification in c) and dilated left-sided lymphatics surrounding the termination of the TD (arrows). Due to the employed imaging technique, the thyroid gland appears hyperintense in a. This does not reflect contrast enhancement. **d** Posterior-anterior intra-interventional image after transabdominal embolization showing the left periclavicular lymphatic malformation (arrows). The duplication of the TD in the lower thorax is partially obscured by mild contrast medium leakage from the puncture site.
Patient 6

A 54-year-old patient presented with chylous ascites refractory to conservative treatment after radical peritonectomy and hyperthermic intraperitoneal chemotherapy for peritoneal metastases of colorectal cancer (1500 ml per day). tMRL showed prompt contrast enhancement of the pelvic lymphatics while the retroperitoneal lymphatics showed only minimal enhancement. The CLS and a leakage site could not be identified. Intranodal oily lymphangiography initially demonstrated venous drainage of contrast medium due to inguinal lymphovenous anastomoses. After additional pelvic lymph node punctures, contrast agent ascended into the retroperitoneal lymphatics demonstrating diffuse leakage into the peritoneal cavity. As in tMRI the CLS did not show any enhancement. Leakage ultimately resolved under parenteral nutrition two weeks after lymphangiography.

Patient 7

A 72-year-old female patient with a history of lymphoma currently in partial remission after radiochemotherapy presented with a right-sided chylothorax unresponsive to conservative treatment. tMRL demonstrated unobstructed lymph flow without reflux. The CLS appeared normal without leakage. There was residual lymphoma in the upper retroperitoneum surrounding the CCh not showing contrast enhancement. Based on these findings, a lymphatic intervention was not indicated. Continuation of conservative treatment ultimately was successful without recurrence of the chylothorax.

Overall imaging results

Interstitial tMRL was technically successful in 6/7 patients with visualization of the CLS rated as excellent in 5/7 and good in 1/7 patients. tMRL confirmed the location of leakage in 3/7, demonstrated a lymphatic malformation in 1/7, reflux in 1/7 and confirmed normal chylolymphatic flow in the central lymphatics in 1/7 patients. In patient 6 neither CLS enhancement nor leakage was detectable.

In technically successful cases, contrast medium was detectable in the central lymphatics on initial images acquired after contrast injection. Image acquisition was performed for at least 20 min after contrast injection (at least 5 repetitions of the 3D T1w-sequence). The median time a patient was in the scanner was 59.5 minutes.
for contrast-enhanced MRL (including preparation, pre-injection T1-images, contrast injection and post-contrast T1-images) was 48 min (range 37–61 min). Contrast medium washout was observed within 15 to 25 minutes after initial post-contrast images. Although contrast medium was also already present within the renal pelvis on initial images, relevant venous contamination was not observed.

tMRL findings were considered helpful in all technically successful cases, and considerably influenced further treatment in four patients. In patient 2 suffering from chylothorax, chylopericardium and chylous ascites, the decision to perform TD embolization despite the presence of ascites was supported by tMRL findings of chylolymphatic reflux as the primary pathology. In patient 3 intranodal lymphangiography was performed with con-

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**Fig. 3** Case study 4. Multiplanar reconstruction a and axial slices b – d of tMRL demonstrates several tortuous lymphatic channels in the middle to upper thorax (arrow) with postoperative chylous leakage (arrow heads) with left-sided chylothorax. Singular thoracic duct before its termination (short arrows).

**Abb. 3** Fallstudie 4. Multiplanare Rekonstruktion a und axiale Bilder b – d einer tMRL mit mehreren geschlängelt verlaufenden Lymphbahnen im mittleren und oberen Thoraxdrittel (Pfeile) und postoperativer chylöser Leckage (Pfeilspitzen) mit linksseitigem Chylothorax. Singulärer Ductus thoracicus vor seiner Mündung im linken Venenwinkel (kurze Pfeile).
Pieper CC et al. Interstitial Transpedal MR-Lymphangiography

Discussing the importance of contrast enhancement in lymphatic pathways, Pieper et al. highlight the significance of T2-weighted images in depicting lymphatic structures. They emphasize the need for adequate timing of image acquisition to evaluate the passage of contrast agents. The authors underscore that interstitial application is an off-label use and note the potential for local complications.

In a case study, the authors present a patient with a retroaortic lymph channel leading to an altered extent of lymphatic flow, successfully treated with lymph vessel embolization. This demonstrates the utility of T2-weighted images, particularly in visualizing lymphatic pathways.

Moreover, the study discusses the limitations of DCE-MRL and Dynamic contrast-enhanced MR-lymphangiography, suggesting that contrast enhancement of the central lymphatics after interstitial contrast injection has only been reported in one case of an infant with chylothorax [16]. In contrast, contrast enhancement of the pelvic lymphatics [10, 15] has been observed. However, the authors caution against the overuse of contrast agents due to the risk of local complications.

The study also addresses the importance of appropriate anesthesia and sedation, particularly in adults, with neither general anesthesia nor conscious sedation being necessary. Time-consuming sonographically guided puncture is feasible inside the scanner room, avoiding the need for general anesthesia or sedation. Similarly, dynamic information can be obtained without general anesthesia or sedation.

The authors conclude by emphasizing the potential of T2-weighted images in depicting lymphatic structures and the importance of adequate timing of image acquisition for evaluating the passage of contrast agents. They also caution against the overuse of contrast agents to avoid local complications.

Overall, Pieper et al. provide a comprehensive overview of the utility and limitations of T2-weighted images in lymphatic imaging, emphasizing the importance of appropriate imaging techniques and anesthesia/sedation protocols.
In conclusion, this study demonstrates the feasibility of contrast-enhanced MR imaging of the CLS by interstitial pedal injection of a standard extracellular contrast agent. tMRL is a new imaging technique that allows for assessment of pathologic conditions of central lymphatics that can be performed in clinical routine without general anesthesia.

Implications for patient care
- Interstitial transpedal MR-lymphangiography allows for minimally invasive assessment of central lymphatic anatomy and pathology in patients suffering from chylous effusions.
- tMRL can be performed in clinical routine without general anesthesia or sedation.
- It can be employed in the pre-interventional workup of lymphatic interventions, possibly influencing the therapeutic strategy.

Conflict of Interest

The authors declare that they have no conflict of interest.

References