Available online at www.sciencedirect.com

ScienceDirect

EJSO 40 (2014) 270–276

EJSO the Journal of Cancer Surgery

www.ejso.com

Review

Current techniques for lymphatic imaging: State of the art and future perspectives

L. Xiong [a], H. Engel [a], E. Gazyakan [a], M. Rahimi [a], M. Hünerbein [b], J. Sun [c], U. Kneser [a], C. Hirche [a,*]

[a] Department of Hand, Plastic and Reconstructive Surgery, Burn Care Unit, BG-Trauma Centre Ludwigshafen, University of Heidelberg, Ludwig Guttmann Str. 13, 67071 Ludwigshafen, Germany
[b] Department of General and Oncological Surgery, Helios Hospital Berlin-Buch, Berlin, Germany
[c] Department of Plastic and Reconstructive Surgery, Union Hospital, Huazhong University of Science and Technology, Wuhan, PR China

Accepted 29 November 2013
Available online 14 December 2013

Abstract

Techniques for lymphatic imaging are aiming at accurate, simple and minimal-invasive approaches with less side-effects and repetitive application. Limitations are emerging in conventional techniques, and new techniques have shown their advantages in high resolution and sensitivity as well as transcutaneous imaging. In the present review, these techniques and their applications are reviewed and elucidated, aiming at a better understanding of recent advancements and current trends of lymphatic imaging as well as promising techniques for future research.

Keywords: Lymphatic imaging; Near-infrared; MRI; Lymphography; Radiocolloid; Blue-dye

Introduction

The lymphatic system reflects a complex network of lymphatic vessels (LVs), lymph nodes (LNs) and lymphatic organs involved in the transportation of lymph via lymphangions and valves as the basic units of lymphatic vessels. Diagnostic and therapeutic approaches to the lymphatic network are required for both benign and malignant diseases. Currently, there are still limitations in understanding basic mechanisms and concrete structures. These limitations subsequently impact exploration of lymphatic functions, diagnosis of lymphatic diseases and controlling of cancer metastasis negatively.[1] Lack of effective and intuitive methods for imaging in vivo lead to these limitations.

To assess the lymphatic system clinically, imaging techniques are frequently applied. Previously, techniques such as lymphangiography, lymphography with a dye, lymphoscintigraphy, computed tomography (CT), and ultrasound (US) have been employed, but none is able to fully satisfy clinical requirements.[2] Recently, new techniques such as magnetic resonance imaging (MRI), ^{18}fluorodeoxyglucose-positron emission tomography (^{18}FDG-PET)/CT, single-photon emission computed tomography (SPECT)/CT, contrast-enhanced ultrasound (CEUS) and near-infrared (NIR) imaging using Indocyanine green (ICG) have been reported to provide more accurate and detailed information on the lymphatic system.[3]

In order to critically review this emerging field for diagnostic and therapeutic approaches, this article analyzes advantages and disadvantages of current lymphatic imaging techniques and their fields of application. Finally, the requirements for future modalities and the need for further studies are discussed.

Techniques of lymphatic imaging

Direct techniques

Lymphangiography

In lymphangiography, the iodinated contrast agent (ICA) is directly injected into lymphatic vessels, which is the major difference compared to indirect lymphatic imaging

* Corresponding author. Tel.: +49 0621 6810 0; fax: +49 621 6810 211.
E-mail address: Christoph.hirche@bgu-ludwigshafen.de (C. Hirche).

0748-7983/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejso.2013.11.027

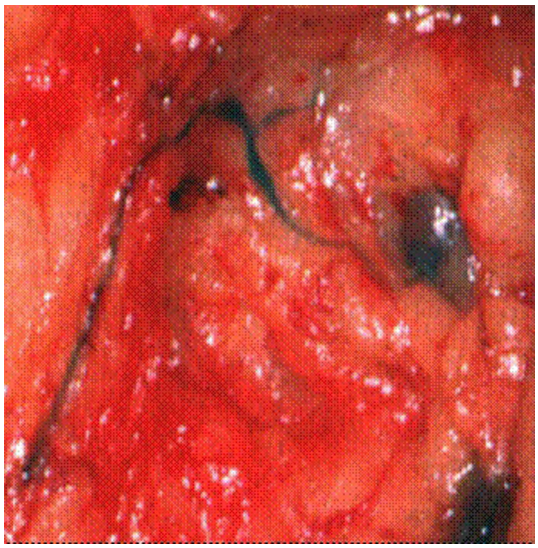

Figure 1. Indirect lymphography guided by a blue dye.

techniques. Lymphatic structures and functions can be observed until the amount of ICA is insufficient.[4] ICA may stay in the body for months to years, which allows long-time follow-up but makes repetitive injections impossible. Due to the invasive and technically difficult cannulation as well as several rare but life-threatening complications, such as contrast-induced nephropathy,[5] lymphangiography has been eliminated in most areas.

Indirect techniques

Lymphography

The indirect lymphography refers to a contrast agent or dye which drains to the lymphatic vessels after being injected interstitially (Fig. 1). The various indirect lymphography techniques are characterized by different modalities which are applied for detection and visualization. While some modalities allow transcutaneous imaging, others require incision and navigation during tissue dissection. Further measures are real-time imaging with or without the application of X-rays. Indirect lymphography allows easier and less time-consuming image generation without further procedures. Furthermore, it avoids side effects of the ICA. Various measures are displayed in Table 1.

Lymphoscintigraphy and single-photon emission computed tomography/computed tomography (SPECT/CT)

Lymphoscintigraphy is the most commonly used indirect lymphatic imaging technique (Fig. 2). Its principle refers to introduction of radioactive tracers and detection with external radiation detectors. The most frequently used tracer is ^{99m}-technetium (^{99m}-Tc) which has a relatively short half-life (6 h) and emits low-energy photons (98.6% at 140.5 KeV, 1.4% at 142.6 KeV).[6] Scintillation cameras are used to form two-dimensional (2D) projection images of radioactive tracer distribution in order to observe lymphatic structures and function. Compared to lymphangiography, the absorption of radioactive tracers is more physiological in lymphoscintigraphy. There is no direct damage to lymphatic vessels, it is easy to repeat, and its sensitivity is much higher.[7] However, its resolution is very poor and the accurate location of lymphatic vessels and nodes cannot be identified because of blurry 2D images. Detailed in vivo navigation to the LN is usually performed by a hand-held probe. There is also an exposure to radiation which requires special radiation protection measures and special waste policies. All together, the technique has limitations with reference to the current requirements for lymphatic imaging in modern clinical practice.

Conventional SPECT is the three-dimensional (3D) reconstruction of multiple-angle projections of radioactive tracers. Although it offers more information than lymphoscintigraphy, its spatial resolution is not satisfactory (1–2 cm).[8] It cannot provide anatomic details, leading to considerable uncertainties in localizing radioactive tracers as well as making correct diagnoses and proper therapy plans.[9] In SPECT/CT, in contrast to the functional SPECT, the relatively precise anatomical location is visualized by CT, and the attenuation can be corrected automatically. A combined 3D reconstruction of SPECT and CT can provide a 360° view of the whole area of interest, which is important in the clinical mapping of LNs.

Table 1
Techniques of lymphatic imaging and their characteristics.

Techniques	Lymph vessels location	Lymph nodes location	Real-time generation	Transcutaneous	Radioactive	Relatively complex equipment	Hand-held
Lymphangiography	+	+	−	+	+	+	−
Blue dye Lymphography	+	+	−	−	−	−	+
Lymphoscintigraphy	−	+	−	+	+	+	+
SPECT/CT	+	+	−	+	+	+	−
^{18}FDG-PET/CT(MRI)	−	+	−	+	+	+	−
MRL	+	+	−	+	−	+	−
CEUS	−	+	−	+	−	−	+
NIR technique	+	+	+	+	−	−	+

SPECT: single-photon emission computed tomography; CT: computed tomography; ^{18}FDG-PET/CT: ^{18}fluorodeoxyglucose-positron emission tomography; MRI: magnetic resonance imaging; MRL: magnetic resonance lymphography; CEUS: contrast-enhanced ultrasound; NIR: near-infrared.