Feasibility of laser marking in Barrett's esophagus with volumetric laser endomicroscopy: first-in-man pilot study

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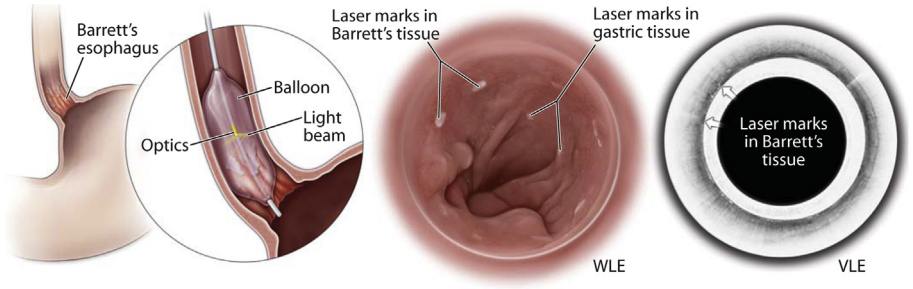
GRAPHICAL ABSTRACT



Background and Aim: Volumetric laser endomicroscopy (VLE) provides a circumferential scan of the esophageal wall layers and has potential to improve detection of neoplasia in Barrett's esophagus (BE). The novel VLE laser marking system enables direct in vivo marking of suspicious areas as identified on VLE. These laser marked areas can subsequently be targeted for biopsies. The aim was to evaluate the visibility and positional accuracy of laser marks (LMs) in different esophageal tissue types on white light endoscopy (WLE) and VLE.

Methods: Patients with BE with or without neoplasia underwent imaging with VLE. Protocol refinements were practiced in a learning phase. In the second phase, visibility of LMs was assessed by random marking in squamous, BE, and gastric tissue. In phase 3, positional accuracy of the LMs was tested by identifying and laser marking surrogate targets (endoscopically placed cautery marks). In the final phase, the most suspicious areas for neoplasia were identified in each patient using VLE, targeted by LMs, and biopsy samples subsequently obtained.

Results: Sixteen patients with BE were included (14 men; median age, 68 years), 1 of whom was included twice in different study phases. Worst histologic diagnoses were 9 non-dysplastic Barrett's esophagus (NDBE), 3 low-grade dysplasia (LGD), 4 high-grade dysplasia (HGD), and 1 early adenocarcinoma (EAC). In total, 222 LMs were placed, of which 97% was visible on WLE. All LMs were visible on VLE directly after marking, and 86% could be confirmed during post hoc analysis. LM targeting was successful with positional accuracy in 85% of cautery marks. Inaccurate targeting was caused by system errors or difficult cautery mark visualization on VLE. In the final phase (5 patients), 18 areas suspicious on VLE were identified, which were all successfully targeted by LMs (3 EAC, 3 HGD, 1 LGD, and 11 NDBE). Mean VLE procedure time was 22 minutes (±6 minutes standard deviation); mean endoscopy time was 56 minutes (±17 minutes). No adverse events were reported.

Conclusions: This first-in-human study of VLE-guided laser marking was found to be feasible and safe in 17 procedures. Most LMs were visible on WLE and VLE. Targeting VLE areas of interest proved to be highly successful. VLE-guided laser marking may improve the detection and delineation of Barrett's neoplasia in the future. (Gastrointest Endosc 2017;86:464-72.)

(footnotes appear on last page of article)

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INTRODUCTION

Volumetric laser endomicroscopy (VLE) is an advanced imaging system incorporating second-generation optical coherence tomography (OCT) technology. OCT uses light waves to create cross-sectional images of tissue, based on differences in optical scattering of tissue structures. VLE is a through-the-scope, balloon-based system, and provides a circumferential scan of the entire distal esophagus up to 3 mm in depth. Barrett's esophagus (BE) is a known precursor lesion for early esophageal adenocarcinoma (EAC). Patients with BE therefore undergo regular endoscopic surveillance for early detection of neoplasia. Early neoplasia in BE can be treated endoscopically with an excellent prognosis. However, the current BE surveillance protocol is not optimal as early lesions are often missed because of their subtle appearance on endoscopy and sampling error of random biopsies. VLE creates a 3-dimensional scan visualizing the subsurface esophageal wall layers of the BE segment in near-microscopic resolution. Therefore, VLE has the potential to increase the detection rate of early neoplasia and improve current surveillance protocols.

Recently, a VLE laser marking system has become available that is capable of applying VLE-guided superficial cautery marks on the esophageal mucosa. These temporary marks enable the endoscopist to place a reference location directly onto the tissue, in an area that has just been imaged with VLE, without the need to exchange devices through the endoscope. Thereafter, the marked area can be located accurately on the esophageal surface using white light endoscopy (WLE), allowing the endoscopist to obtain direct histologic samples. With VLE imaging and laser marking, random biopsies could potentially become obsolete, causing a paradigm shift from random biopsies to VLE-targeted biopsies. Furthermore, laser marking could facilitate and improve endoscopic treatment by aiding in lesion delineation. Feasibility studies in swine and in human participants have been performed using a comparable imaging and laser marking system.[1,2] These first exploratory studies, using a custom-made prototype system, showed that imaging-guided laser marking was safe and provided reliable endoscopically visible marks on the esophageal mucosa. Our study provides systematic examination of the functionalities of the commercial VLE laser marking system.

The key feature of the VLE laser marking system is that it allows correlation between in vivo VLE findings and its corresponding histology. The aim of this first-in-man feasibility study was to assess the visibility and positional accuracy of VLE laser marks (LMs) on WLE and VLE.

METHODS

Setting

This feasibility study was conducted at the Department of Gastroenterology and Hepatology of the Academic Medical Center in Amsterdam, a tertiary referral center for patients with BE and Barrett's neoplasia. This study was approved by the local medical ethical committee (NTR5567, registered at http://www.trialregister.nl).

Design

This prospective study consisted of 4 phases. First, a learning phase was performed to assess and optimize the procedural workflow. In the second phase, visibility of randomly positioned LMs was assessed on WLE and VLE. In the third phase, the positional accuracy of the LMs was assessed. The fourth phase was designed to simulate clinical practice in which the most suspicious areas on VLE were targeted with the laser marking system and biopsy samples were subsequently taken to obtain histologic correlates.

Outcome measurements

Primary outcome measurements

- Visibility of LMs on WLE
- Positional accuracy of LMs

Secondary outcome measurements:

- Visibility of LMs on VLE
- Feasibility of targeting areas suspicious for neoplasia with LMs
- Time of VLE and endoscopic procedures
- Adverse events

Patients

Patients undergoing endoscopy for the evaluation and/or treatment of BE with or without dysplasia or neoplasia (low-grade dysplasia [LGD], high-grade dysplasia [HGD], EAC) were eligible for this study. Patients with characteristics precluding full distension of the balloon (eg, an esophageal mass, stricture or tears), were excluded.

NvisionVLE imaging and laser marking system

The VLE system (NvisionVLE Imaging System; NinePoint Medical, Bedford, Mass) incorporates second-generation OCT technology, termed optical frequency domain imaging (OFDI).[3,4] Backscattered light from different layers of tissue is measured and mathematical improvements in the OFDI technology enable high-speed image acquisition. In 90 seconds, the VLE system performs a circumferential scan of the esophagus over a length of 6 cm, to a depth of 3 mm and with an axial and lateral resolution of 7 μm and 40 μm, respectively. The console generates near-infrared light and transmits