Letter to the Editor

Application of novel dynamic optical imaging for evaluation of peripheral tissue perfusion ☆

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Abstract

Measurement of functional tissue perfusion should be needed for preventive measures, early diagnosis, and adequate treatment especially in the patients with peripheral vascular diseases (PVD). Significant attention has also been given to *in vivo* near-infrared (NIR) fluorescence imaging because of deep tissue penetration due to low absorbance and scattering. In this study, a new method, indocyanine green (ICG) perfusion imaging to evaluate the peripheral tissue perfusion that employs the intravenous injection of ICG dye, planar imaging with a CCD digital imaging system, and analysis of spatiotemporal dynamics have been applied to diagnose perfusion rate of human lower extremities from a normal and a PVD case. The feet tissue perfusions of the PVD patient were measured as 25% to 50% compared with those of normal feet tissue. The diagnostic result indicates that ICG perfusion imaging method is sensitive enough to diagnose PVD and take noninvasive monitoring treatment effects of peripheral vascular diseases in clinical setting.
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Keywords: Peripheral vascular disease; Diagnostic tool; Tissue perfusion; Imaging

Optical imaging, especially indocyanine green (ICG) fluorescence imaging, has been the focus of research due to its convenience and effectiveness in imaging vasculature and allowing estimation of tissue perfusion [1,2]. Because local concentrations of ICG are dependent mainly on regional tissue perfusion, time-series analysis of ICG pharmacokinetics can provide functional information about local tissue perfusion [1]. We have recently developed a novel optical imaging-based technology for translating ICG time-series images into quantitative perfusion maps [3]. An ICG fluorescence imaging system (Fig. 1) has been developed by Vieworks (Seongnam, Gyeonggi-do, Korea) to validate the clinical feasibility of this novel technique in diagnosing peripheral vascular diseases (PVDs). In total, 120 images (748 × 518 pixels) of both feet were taken at 5-s intervals for 10 min immediately after an intravenous bolus injection of ICG (0.16 mg/kg) for time-series analysis of ICG fluorescence and then translated into the perfusion rate of the pixel. The perfusion rate (%/min) was defined as the fraction of blood exchanged per min in the vascular volume. The perfusion rate of each pixel was represented in a perfusion map as a color-coded picture and the distributions of the pixel perfusion rates in each foot were expressed as a histogram. To evaluate the time-series ICG fluorescence imaging as a reliable tool for diagnosis of PVD, we performed also Computed tomography (CT)-angiography and ankle brachial index (ABI) to compare results. This study was approved by the institutional review board of Mokdong Medical Center (Ewha Womans University).

A 76-year-old man with no previous medical history was admitted with claudication in the left calf which gradually
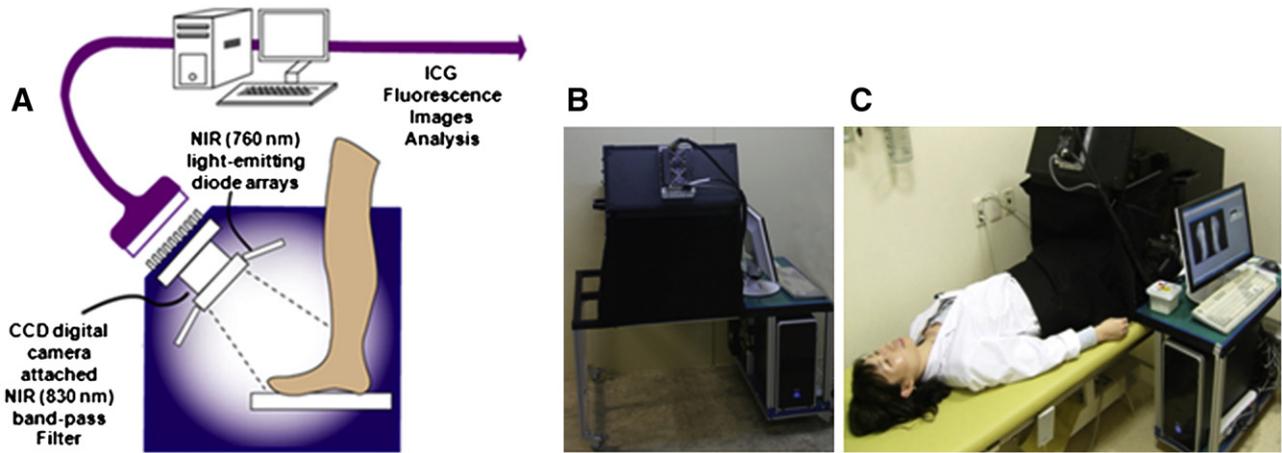
Fig. 1. NIR fluorescence imaging system. (A) Diagram of the imaging system. The imaging system is composed of a CCD digital camera (RXD-500; Vieworks Co., Seongnam, Korea) with an 830-nm long-pass filter (RG830; Edmund Optics, Barrington, NJ, USA) that uses 760-nm light-emitting diode arrays (SMC760; Marubeni America Co., Sunnyvale, CA, USA). (B) Outside view of the system. (C) Capturing an ICG perfusion image.

developed, and he had abnormal ABI values, 0.73 on the right and 0.24 on the left side. CT-angiography of lower extremity revealed occlusion at left external iliac artery, proximal and mid-portion of superficial femoral artery and left distal posterior tibial artery (Fig. 2A). The patient's ICG dynamics showed delayed filling with ICG (60–65 s), a notably delayed time to peak (160–180 s), and significantly delayed washout kinetics (Fig. 2B) compared to the normal control, 74-year old woman who had an asymptomatic occlusion of both anterior tibial arteries with normal ABI values (Fig. 3B).
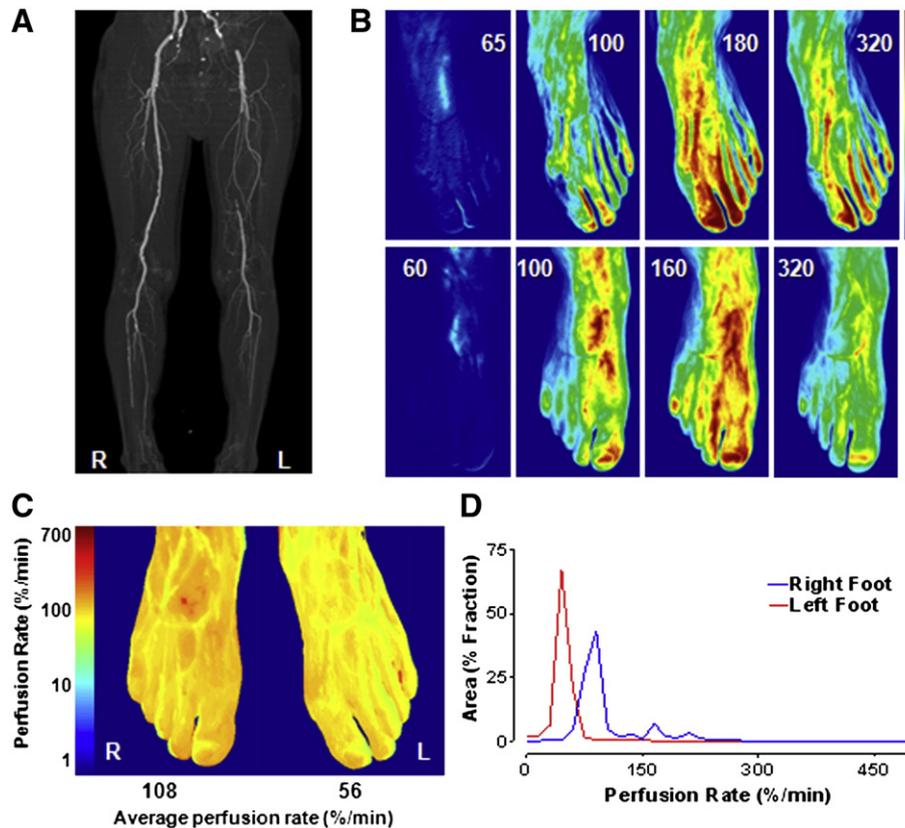

Fig. 2. A 76-year-old patient with PVD. (A) CT-angiography. (B) Time-series ICG fluorescence images. The upper panel is from the right foot, and the lower panel shows the left foot. A pseudocolor intensity scale bar is indicated on the right-hand side of the upper panel. The numbers in the figures indicates the time (seconds) after ICG injection. (C) A perfusion map with a pseudocolor intensity scale. The perfusion rate is defined as the fraction of blood exchanged per minute in the vascular volume, and the mathematical model was utilized for the translation from time-series ICG fluorescence images into functional perfusion maps. (D) Histogram of the perfusion rate.
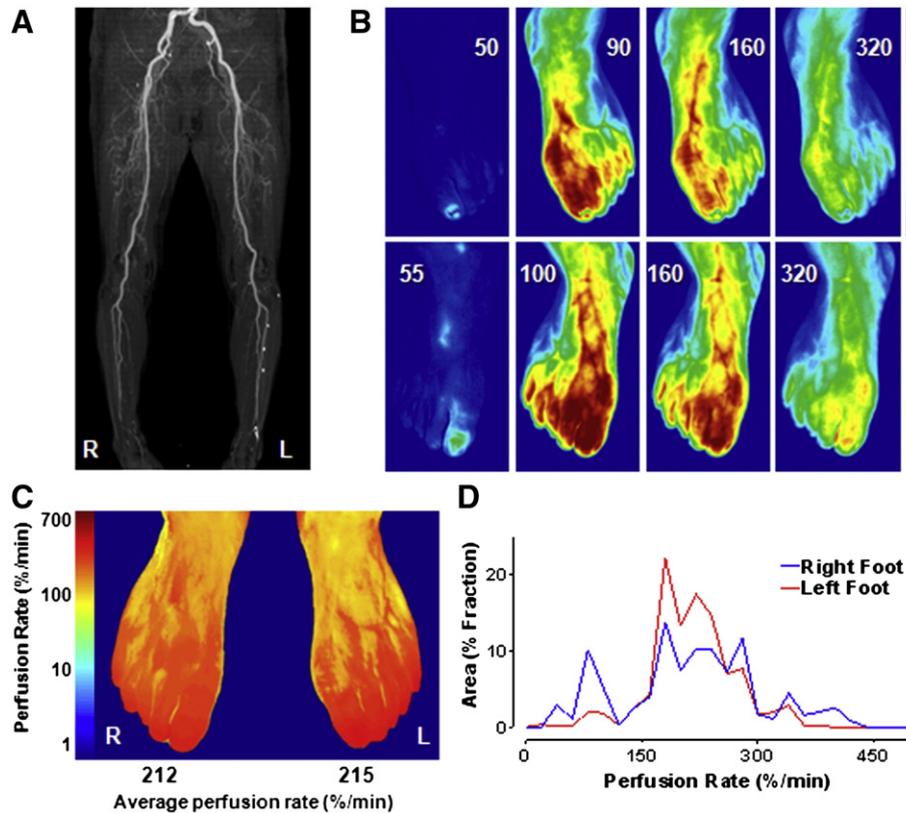
Fig. 3. A 74-year-old healthy control. (A) CT-angiography. (B) Time-series ICG fluorescence images. (C) Perfusion map. (D) Histogram of the perfusion rate.

Consistent with the abnormal findings in CT-angiography and the ABI test, the ICG perfusion map demonstrated that the perfusion rate was estimated to be lower than 150%/min in most regions of both feet (Fig. 2C and D), whereas the perfusion rate was calculated to be over 150%/min in most regions in the normal control (Fig. 3C and D).

These case studies clearly indicate that the novel ICG dynamic perfusion imaging technique can be effectively applied in clinical settings for the diagnosis of PVDs.

Even though CT angiography is widely used, it severely underestimated the extent of atherosclerosis in PVD patients with symptoms of intermittent claudication [4] and can offer only structural information but not functional information of blood flow. The other limitations of CT-angiography are the high cost, low availability, and limiting their application for screening or early diagnosis of PVD. ICG perfusion imaging can be a cost- and time-efficient tool for diagnosis of patients with peripheral vascular insufficiencies. Although NIR imaging is restricted to analysis of tissues at depths of less than several centimeters, the measurement of perfusion rate through macrovessels such as the dorsalis pedis and the microvasculature might provide sufficient information to diagnose PVD. Since ICG perfusion imaging can measure the functional blood flow of peripheral tissues with long term follow up, drug treatment can be improved by feedback on measured perfusion rate after drug treatments, and personal response of medical treatment can be studied. Our method has several potential limitations as well. First, the patient

with chronic occlusive disease such as progressive artheromatous stenosis and gradual collateralization, may be measured as normal tissue perfusion even with severe arterial occlusions. Second, presence of open wounds or inflammations on instep can change perfusion rate, which can affect to overestimate the actual perfusion rate. If above points are considered, the multiple advantages of this novel method necessitate the performance of large-scale clinical studies to validate its efficacy for the diagnosis of PVDs and other related vascular disorders.

Acknowledgments

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