Low-Cost, *In Vivo* Optical Microscopy Methods for Examining Cellular Details at the Point of Care

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In vivo microscopy is an optical imaging approach that can directly visualize cellular details of the human tissue without removing the tissue from the patient. Reflectance confocal microscopy (RCM) is one such *in vivo* microscopy method. RCM has been shown promising in diagnosing various human diseases, including skin cancers and corneal ulcers. The use of RCM in low-resource settings could be potentially impactful, because low-resource settings (e.g., low- and middle- income countries, rural clinics in the US) often lack the facility, equipment, and trained personnel needed for microscopic examination of excised tissues. However, RCM has not been widely adopted in low-resource settings yet, partially due to the high device cost. In this paper, we present the development of low-cost, *in vivo* microscopy devices.

Portable confocal microscopy (PCM) is an approach for reducing the cost and complexity of RCM devices. In PCM, an inexpensive LED, slit apertures, and gratings are used to generate spectrally-dispersed line illumination on the tissue [1]. Each line on the tissue is encoded with a distinctive wavelength, making it possible to examine two-dimensional imaging area without having to use mechanical beam scanning devices as used in conventional RCM devices. Light reflected back from the tissue and filtered by the detection slit is dispersed by another grating to generate a two-dimensional confocal image on an image plane. The confocal image is then acquired by a low-cost, two-dimensional imaging sensor.

The first PCM prototype was built by using a visible-spectrum LED (center wavelength = 590 nm) and a smartphone camera. The smartphone-based PCM device was built with a low material cost, ~$4,200, and achieved the lateral resolution of 2 μm and axial resolution of 4 μm, comparable to the values for the conventional RCM devices. The smartphone-based PCM device was demonstrated to visualize characteristic cellular features of skin non-invasively. While promising, the smartphone-based PCM device had two main challenges, shallow imaging depth (limited to epidermis) and slow imaging speed (4 fps).

The second PCM prototype was built with a near-infrared LED (center wavelength = 820 nm) and a low-cost monochromatic CMOS sensor [2]. The second PCM prototype was also built with a low material cost, ~$5,000, and was able to reveal previously-validated diagnostic cellular features of benign and malignant skin conditions with an improved imaging depth (superficial dermis) and imaging speed (20 fps) [3].

Another benefit of the PCM approach is that the imaging speed can be high because no mechanical beam scanners are used for confocal imaging. We have demonstrated the imaging speed of 203 fps by using a spatially-coherent light source, a superluminescent diode [4]. We also demonstrated speckle-free, high-speed imaging of human skin at the speed of 180 fps, by using an LED as the light source and employing a deep learning-based noise reduction method [5].

In summary, we have developed low-cost, *in vivo* microscopy devices and demonstrated the feasibility of visualizing cellular details of human tissue non-invasively. In the future, we will further improve the low-cost, *in vivo* microscopy devices and evaluate them for various clinical and research applications.

References:

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[6] The University of Arizona has a technology-licensing agreement with ArgosMD on the portable confocal microscopy technology. DK has the rights to receive royalties as a result of this licensing agreement. DK serves as a scientific advisor to ArgosMD. Conflicts of interest resulting from this interest are being managed by The University of Arizona in accordance with its policies.