Better health through your cell phone

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In many Third World and developing countries, the distance between people in need of health care and the facilities capable of providing it constitutes a major obstacle to improving health. One solution involves creating medical diagnostic applications small enough to fit into objects already in common use, such as cell phones — in effect, bringing the hospital to the patient.

UCLA researchers have advanced a novel lens-free, high-throughput imaging technique for potential use in such medical diagnostics, which promise to improve global disease monitoring, especially in resource-limited settings such as in Africa. The research, which will be published in the quarterly journal *Cellular and Molecular Bioengineering* (CMBE) and is currently available online, outlines improvements to a technique known as LUCAS, or Lensless Ultra-wide-field Cell monitoring Array platform based on Shadow imaging.

First published in the Royal Society of Chemistry's journal *Lab Chip* in 2007, the LUCAS technique, developed by UCLA researchers, demonstrated a lens-free method for quickly and accurately counting targeted cell types in a homogenous cell solution. Removing the lens from the imaging process allows LUCAS to be scaled down to the point that it can eventually be integrated into a regular wireless cell phone. Samples could be loaded into a specially equipped phone using a disposable microfluidic chip.

The UCLA researchers have now improved the LUCAS technique to the point that it can classify a significantly larger sample volume than previously shown — up to 5 milliliters, from an earlier volume of less than 0.1 ml — representing a major step toward portable medical diagnostic applications.

The research team, led by Aydogan Ozcan, assistant professor of electrical engineering at the UCLA Henry Samueli School of Engineering and Applied Science and a member of the California NanoSystems Institute (CNSI), includes postdoctoral scholar Sungkyu Seo, doctoral student Ting-Wei Su, master's student Derek Tseng and undergraduate Anthony Erlinger.

Ozcan envisions people one day being able to draw a blood sample into a chip the size of a quarter, which could then be inserted into a LUCAS-equipped cell phone that would quickly identify and count the cells within the sample. The read-out could be sent wirelessly to a hospital for further analysis.

"This on-chip imaging platform may have a significant impact, especially for medical diagnostic applications related to global health problems such as HIV or malaria monitoring," Ozcan said.

LUCAS functions as an imaging scheme in which the shadow of each cell in an entire sample volume is detected in less than a second. The acquired shadow image is then digitally processed using a custom-developed "decision algorithm" to enable both the identification of the cell/bacteria location in 3-D and the classification of each microparticle type within the sample volume.

Various cell types — such as red blood cells, fibroblasts and hepatocytes — or other microparticles, such as bacteria, all exhibit uniquely different shadow patterns and therefore can be rapidly identified using the decision algorithm.

The new study demonstrates that the use of narrowband, short-wavelength illumination significantly improves the detection of cell shadow images. Furthermore, by varying the wavelength, the two-dimensional pattern of the recorded cell signatures can be tuned to enable automated identification and counting of a target cell type within a mixed cell solution.

"This is the first demonstration of automated, lens-free counting and characterization of a mixed, or heterogeneous, cell solution on a chip and holds significant promise for telemedicine applications," Ozcan said.

Another improvement detailed in the UCLA research is the creation of a hybrid imaging scheme that combines two different wavelengths to further improve the digital quality of shadow images. This new cell classification scheme has been termed "multicolor LUCAS." As the team illustrated, further improvement in image quality can also be achieved through the use of adaptive digital filtering. As result of these upgrades, the volume of the sample solution that can be imaged has been increased, as mentioned, from less than 0.1 ml to 5 ml.

"This is a significant advance in the quest to bring advanced medical care to all reaches of the planet," said Leonard H. Rome, interim director of the CNSI and senior associate dean for research at the David Geffen School of Medicine at UCLA. "The implications for medical diagnostic applications are in keeping with CNSI initiatives for new advances toward improving global health."

Ozcan has already received accolades for this research, including the prestigious 2008 Okawa Foundation Research Award, which he will receive at a ceremony in San Francisco on Oct. 8. The award honors top young researchers working in the fields of information and telecommunications. The CMBE paper has also been selected for the Outstanding Paper award at the upcoming annual meeting of the

Biomedical Engineering Society this fall.

The CMBE journal paper is available at www.springerlink.com/content/h526u7t0429q0121/ .

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