(Mar. 27, 2012) The novel H1N1 flu pandemic in 2009 underscored weaknesses in methods widely used to diagnose the flu, from frequent false negatives to long wait times for results. Now a four-year, National Institutes of Health-funded study of 146 patients with flu-like symptoms spearheaded by Associate Professor Catherine Klapperich (BME, MSE) has validated a prototype rapid, low-cost, accurate, point-of-care device that promises a better standard of care. Once optimized and deployed in the clinic, the new device could provide clinicians with an effective tool to quickly diagnose both seasonal and pandemic strains of influenza, and thus limit the spread of infection.

The study's research team -- Klapperich, Qingqing Cao(ME PhD'11), Madhumita Mahalanabis(BME postdoctoral fellow), Jessie Chang (BME MS'10), Brendan Carey (BME'11), Christopher Hsieh (BME'11) and Ahjegannie Stanley (summer intern) from the College of Engineering; medical personnel from the Boston University Medical Center (BUMC) Emergency Department; and an infectious disease physician from Beth Israel Deaconess Medical Center (BIDMC)/ Harvard Medical School -- published its findings in the March 22 online edition of *PLo S ONE*
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To produce a faster, cheaper, highly accurate flu diagnostic test that could be run at the point of care, the researchers miniaturized an expensive, three-hour, lab-scale diagnostic test -- known as RT-PCR and now considered the gold standard in flu detection -- into a single-use microfluidic chip. About the size of a standard microscope slide, the integrated chip consists of a column at the top that extracts RNA from signature proteins in the sample associated with the influenza A virus; a middle chamber that converts the RNA into DNA; and a climate-controlled lower channel used to replicate the DNA in sufficient quantities so it can be detected by an external reader.

Working with two types of nasal specimens, the researchers used the chip to produce results that matched the high accuracy and relatively fast turn-around time of the lab-scale method.

"We wanted to show that our technique was feasible on real-world samples prepared on the chip," said Klapperich. "Making each chip single-use decreases the possibility of cross-contamination between specimens, and the chip's small size makes it a good candidate for true point-of-care testing."

The microfluidic chip also proved far more effective than other commonly used flu diagnostic tests including viral culture, a lab procedure requiring up to a week to produce results; rapid immunoassays, which work like pregnancy tests but were only 40 percent reliable in detecting the presence of a flu virus in this study; and direct fluorescent antigen testing (DFA), a more accurate but labor-intensive process in which medical personnel prepare and interpret samples stained with fluorescent antibodies.

"The new test represents a major improvement over viral culture in terms of turn-around time, over rapid immunoassay tests in terms of sensitivity (ability to detect the virus from minimal sample material) and over DFA and RT-PCR in terms of ease of use and portability," Klapperich observed.

Ultimately seeking to enable clinicians to use their microfluidic chips for frontline flu virus detection, the researchers next plan to optimize their method so that it can produce results in a third less time (an hour) with chips that cost half as much to make (five dollars). In addition, they are exploring ways to develop a lower cost external reader that's no bigger than a clinical digital thermometer.

Story Source:

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Journal Reference:

1. Qingqing Cao, Madhumita Mahalanabis, Jessie Chang, Brendan Carey, Christopher Hsieh, Ahjegannie Stanley, Christine A. Odell, Patricia Mitchell, James Feldman, Nira R. Pollock, Catherine M. Klapperich. **Microfluidic Chip for Molecular Amplification of Influenza A RNA in Human Respiratory Specimens** . *PLoS ONE* , 2012; 7 (3): e33176 DOI: 10.1371/journal.pone.0033176

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