Potential new tool for cervical cancer detection and diagnosis

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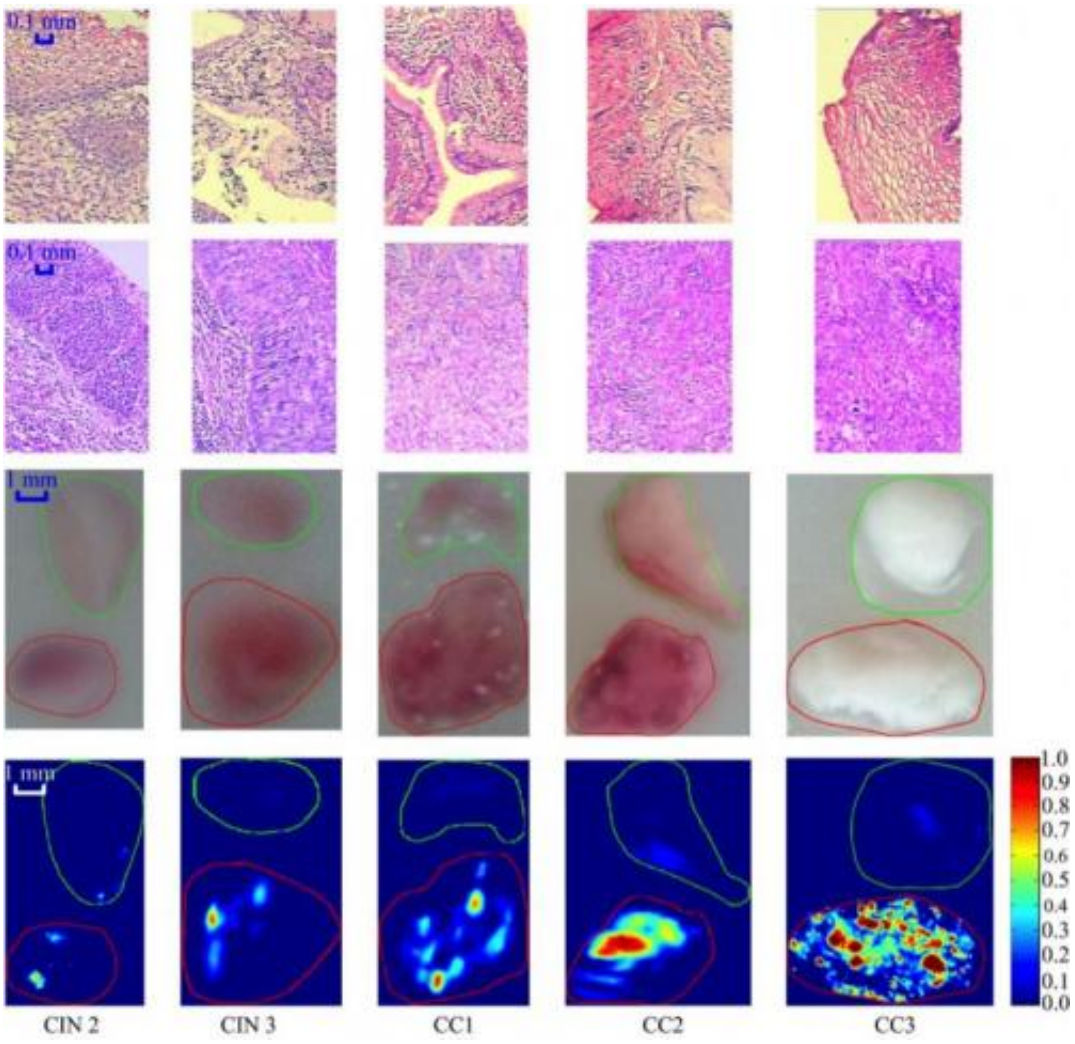

This shows a comparison between the normal cervical tissue and tissue lesion for different stages. From top to bottom are the pathological images for the normal cervical tissue (first row) and tissue lesion (second row), the photo image (third row) and corresponding DMAP images (fourth row) of representative experiments respectively. Margins of the normal tissue (green) and cervical

lesion (red) are indicated in the photo and DAMP images. The scale bar for the histological images represents 0.1 mm, and that for the photo and DMAP images is 1 mm. Credit: *Biomedical Optics Express*

Cervical cancer is, in many ways, a shining example of how successful the war on cancer can be. Thanks largely to the advent of Pap smear screening, U.S. cervical cancer deaths decreased dramatically, by more than 60 percent, between 1955 and 1992. In the last two decades, better treatment outcomes and more powerful imaging techniques have steadily pushed 5-year survival rates ever higher. The latest weapons in modern medicine's arsenal are two new vaccines that were recently approved by the U.S. Food and Drug Administration for preventing this type of cancer altogether.

As rosy a picture as that paints, cervical cancer continues to claim far too many lives. Thousands of American women still die from the disease every year, and hundreds of thousands of other women around the world suffer the same fate—sad, stark statistics that showcase the continued need for more advanced screening methods to catch more cases of the disease early, when it is most treatable.

Now a team of researchers from Central South University in China have demonstrated that a technique known as photoacoustic imaging, which is already under investigation for detecting skin or breast cancers and for monitoring therapy, also has the potential to be a new, faster, cheaper and non-invasive method to detect, diagnose and stage cervical cancer with high accuracy. Their work appears in a new paper in The Optical Society journal *Biomedical Optics Express*.

In this paper, the researchers describe how they examined 30 cervical tissue samples with photoacoustic imaging. Some were taken from

healthy women and some of the samples contained the cancerous cells of a cervical tumor. They found that photoacoustic imaging could distinguish the cancerous from the normal tissue and had the potential to evaluate the stage of the cancer.

"Our results show that the photoacoustic imaging may have great potential in the clinical diagnosis of cervical cancer," said Jiaying Xiao, an assistant professor of biomedical engineering at Central South University, who led the research. "The technique is non-invasive and can detect the lesions in the cervical canal, an area conventional methods fail to observe. The photoacoustic imaging can also evaluate the invasion depth of cervical lesions more effectively."

A Common Cancer Among Women

According to the National Institutes of Health (NIH), cervical cancer is the third most common cancer among women worldwide and the second most frequent cause of cancer-related death worldwide, claiming nearly 300,000 lives every year around the globe. In the United States, cervical cancer is also one of the most common cancers affecting women, and the NIH estimates that in 2014 more than 12,000 women will be diagnosed with the disease and more than 4,000 will die from it. Cancer screening and routine tests are critical for preventing cancer deaths because cases caught early are often more treatable.

According to Xiao, one of the conventional screening methods is colposcopy, a technique in which doctors to use a special magnifying device to examine the vulva, vagina and cervix and identify suspicious lesions, which are then biopsied.

Although colposcopy is effective in detecting lesions around the external cervical orifice, and cervical biopsy is considered the gold standard for diagnosing cancer in the cervix, these conventional methods are both

time- and labor-intensive and expensive. Moreover, colposcopy may miss some cancer lesions.

For example, Xiao explained, a considerable number of the cervical cancer cases start from lesions in the cervical canal, but the interior of cervical canal cannot be directly observed with colposcopy. Because of that, these lesions may not be detected until the cancer has advanced and spread to other tissues.

"Thus, there is still a need to develop new diagnostic technologies with higher accuracy, deeper penetration, larger scanning regions, and lower cost for the routine tests of cervical cancer," Xiao said.

A New Cancer Detection Tool: Photoacoustic Imaging

According to Xiao, photoacoustic imaging (PAI) is a hybrid optical imaging technique that combines the high optical contrast of pure optical imaging with the high spatial resolution and the deep imaging depth of ultrasound.

In photoacoustic imaging, short laser pulses are employed to irradiate biological tissues. Some of the laser energy is absorbed by the tissues and converted into heat, leading to rapid thermal expansion inside the tissues that produces ultrasonic waves. The generated waves are then detected by an ultrasonic sensor to form photoacoustic images of the tissues.

To date, photoacoustic imaging has been employed for the diagnosis of various cancers with different scanning configurations, Xiao said. Their goal is to explore the feasibility of photoacoustic imaging for the diagnosis of cervical cancer, he added.

By using hemoglobin as the contrast agent or indicator, photoacoustic imaging is highly sensitive to abnormal angiogenesis, the abnormal

formation of new blood vessels, which is a hallmark of the cancer tumors.

"Due to the higher hemoglobin concentration, abnormal angiogenesis has higher optical absorptions in certain wavelengths than normal tissues," Xiao explained. If you irradiate a tissue with a short laser pulse, the part with abnormal angiogenesis will absorb more laser energy than the surrounding tissues and produce a different acoustical signature. Using ultrasound detectors, researchers can map these photoacoustic signals and identify the locations of lesions.

In their new paper, Xiao and his colleagues conducted 30 in vitro experiments with tissue samples representing different cancer stages.

In each experiment, researchers embedded one piece of normal cervical tissue and one piece of cervical lesion from the same person in a cylindrical phantom for simultaneous photoacoustic imaging. Part of each sample was also sent to histological evaluation for cross-photoacoustic imaging.

By processing all of the photoacoustic imaging data with computer programs, scientists obtain a 2-D en-face photoacoustic image called a depth maximum amplitude projection (DMAP) image, which shows the optical absorption distribution or photoacoustic contrast of the sample. The image can help scientists identify the lesion location and evaluate different cancer stages of cervical cancer.

"Stronger absorption from the cervical lesions is observed compared to that of normal tissue," Xiao said. Statistical results also show that the mean optical absorption (MOA) of the cervical lesions is closely related to the severity of cervical cancer.

Compared with other cervical screening methods, Xiao added,

photoacoustic imaging also has a much higher penetration depth by using ultrasound as the localizing signal, which is less scattered than light. Therefore, the optical absorption distribution can be obtained deep in the biological tissue.

While the work is preliminary, it provides solid experimental basis for future studies, showing for the first time that photoacoustic imaging has the potential to make better diagnoses and help save lives, Xiao said. The next step, he added, is to prove the applicability of photoacoustic imaging in tumor models and ultimately in patients.

"Our ultimate goal is to develop an endoscopic photoacoustic imaging probe scanning the cervical canal, which would be a quicker, cheaper and non-invasive method for the diagnosis of cervical cancer," Xiao said.

More information: "Detection of cervical cancer based on photoacoustic imaging—the in-vitro results," J. Xiao et al., Biomedical Optics Express, Vol. 6 Issue 1, pp. 135-143 (2015). The paper is available at www.opticsinfobase.org/boe/abs … .cfm?uri=boe-6-1-135

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