PRESS RELEASE

NUS Biomedical Engineering team pioneers world's first real time in-vivo molecular diagnostic system that diagnoses even pre-cancerous tissues during endoscopy

In-Vivo Molecular Diagnostic System developed by NUS team makes objective, real time cancer diagnosis during endoscopic examination a reality

Singapore, 10 February 2014 – A National University of Singapore (NUS) team led by Associate Professor Huang Zhiwei, Department of Biomedical Engineering, has developed an In-Vivo Molecular Diagnostic System that could change the way cancer diagnosis is made.

Their diagnostic system is the only one in the world, so far, clinically proven to be used in human patients for diagnosing even pre-cancerous tissue in gastrointestinal tract during endoscopic examination in real time. Unlike conventional endoscopic techniques that relies on doctors' eyeball interpretation of the images followed by pathologists' analysis of the biopsy specimen several days later, their diagnostic system utilises computer analysis of biomolecular information and therefore can provide objective diagnosis of cancer in real time. It is a paradigm shift in how a complex process of cancer diagnosis can be made simply, objectively, and rapidly.

The In-Vivo Molecular Diagnostic System, based on Confocal Raman spectroscopy, includes a proprietary confocal fibre-optic probe and customised online software control system designed by the NUS team. The fibre-optic probe enables the collection of biomolecular fingerprint of tissues in less than one second -- while the online software enables the biomolecular information collected to be extracted and analysed with diagnostic result that is presented in real time during endoscopic examination.

The In-Vivo Molecular Diagnostic system has been used in more than 500 patients in Singapore across diverse cancer types like stomach, oesophagus, colon, rectum, head and neck, and cervix. The researchers have also published more than 40 peer-reviewed publications -- their most recent publication being "Fiberoptic Confocal Raman Spectroscopy for Real Time In-Vivo Diagnosis of Dysplasia in Barret's Esophagus" (January 2014) in *Gastroenterology*, the most

prominent publication in the field of gastroenterology. They have also filed two U.S. and two U.K. patents for their invention.

"We are delighted to not only overcome the technical challenges of weak Raman signal, high fiber background noise, and lack of depth perception by using our specially designed probe, but also to enable real time diagnostic results to be displayed during endoscopy with our customised software," said Assoc Prof Huang.

For the clinical testing, the NUS Engineering team has been collaborating with researchers from the NUS Yong Loo Lin School of Medicine led by the School's Dean, Associate Professor Yeoh Khay Guan; Professor Ho Khek Yu, Head, Department of Medicine; and Associate Professor Teh Ming, Head, Department of Pathology.

"It has been a long tedious journey of more than 10 years. The journey could be longer if not for the excellent cross-disciplinary teamwork at NUS. The contribution of the NUS clinical team is invaluable in demonstrating the clinical benefits of the system," added Assoc Prof Huang.

Assoc Prof Yeoh commented, "This remarkable new system is the first such diagnostic probe that can be used real time, inside the human body, providing almost instantaneous information on cellular changes including cancer and pre-cancer. This is a first in the world development, pioneered here in Singapore. It has the potential to make enormous clinical impact to how cancer is diagnosed and managed. The immediate point-of-care diagnosis during live endoscopic examinations will provide benefits in time and cost-savings, and will improve our patients' prognosis as a result of early diagnosis."

Moving forward, Assoc Prof Huang said they will be conducting clinical trials on a larger scale to further validate the clinical utility of their novel system especially in gastrointestinal cancers.

Real time and early diagnosis can reduce gastrointestinal cancer deaths

Gastrointestinal cancer as a class is very prevalent in Asia with stomach and colorectal cancer being the most common cancer types. It is also a very treatable cancer class when diagnosed early. Unfortunately mortality within gastrointestinal cancer is disproportionately high; gastrointestinal cancer is currently the second highest contributor to cancer deaths.

"We look forward to improving the prognosis of patients with gastrointestinal cancer by facilitating early cancer diagnosis with our In-Vivo Molecular Diagnostic System," he said.

This research is supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship programme and is administered by the Singapore Ministry of Health's National Medical Research Council.

Please refer to the Annex for background information on Raman spectroscopy and gastrointestinal cancer, as well as photographs of the research team and the In-Vivo Molecular Diagnostic System.

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About National University of Singapore (NUS)

A leading global university centred in Asia, the National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education and research, with a focus on Asian perspectives and expertise.

NUS has 16 faculties and schools across three campuses. Its transformative education includes a broad-based curriculum underscored by multi-disciplinary courses and cross-faculty enrichment. Over 37,000 students from 100 countries enrich the community with their diverse social and cultural perspectives.

NUS has three Research Centres of Excellence (RCE) and 23 university-level research institutes and centres. It is also a partner in Singapore's fifth RCE. NUS shares a close affiliation with 16 national-level research institutes and centres. Research activities are strategic and robust, and NUS is well-known for its research strengths in engineering, life sciences and biomedicine, social sciences and natural sciences. It also strives to create a supportive and innovative environment to promote creative enterprise within its community.

For more information, please visit www.nus.edu.sg

ANNEX

Background Information on Raman Spectroscopy

Raman spectroscopy is a vibrational spectroscopy technique used to collect a unique chemical fingerprint of molecules. As each molecule has a different set of vibrational energy levels, they have unique wavelength shifts. Raman spectroscopy's ability to detect variance related to DNA/RNA, proteins, and lipids have made it an excellent tool for quantifying changes on the cellular level, as well as differentiating between various cell and tissue types.

However, it has thus far been used mainly for in-vitro analysis as the signals obtained through Raman spectroscopy are extremely low which means that it would need a long time for the system to collect data. As such, this would not be suitable for in-vivo analysis as the patient would need to be monitored for a long time before any signals could be gathered and transformed into readable data.

In-Vivo Molecular Diagnostic system developed by the research team from the National University of Singapore (NUS) uses a specially designed confocal probe that could overcome the technical challenge of weak Raman signal, lack of depth perception and high reflectance noise generated by the probe. The system also enables real time diagnostic results during endoscopy with a customised software.

Background information on Gastrointestinal Cancer (GC)

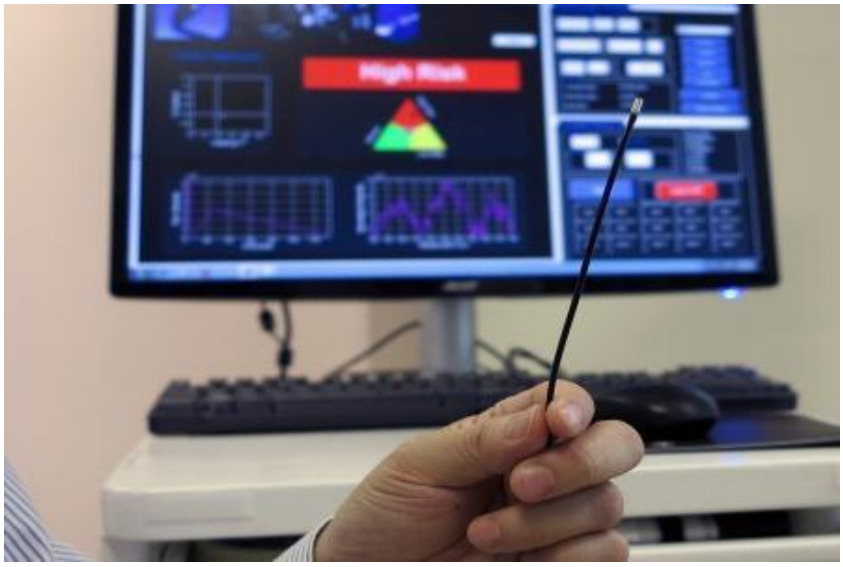
Cancer is a leading cause of disease and second leading cause of death worldwide. The latest cancer statistics released in GLOBOCAN 2012 shows that the global burden of cancer increased in 2012 to 14.1 million new cases and 8·2 million deaths, compared with 12.7 million and 7.6 million in 2008. GLOBOCAN 2012 predicts that there will be 19.3 million new cancer cases per year by 2025. It is estimated that of the worldwide 12.7 million new cancer cases and 7.6 million death in 2008, gastrointestinal cancers which include all cancers of the gastrointestinal tract, comprising malignancies of the oesophagus, stomach, colon, rectum and anus, account for more than 27 per cent of total new cases and a disproportionately higher 32 per cent of total deaths respectively.

Amongst the 29 million people diagnosed with cancer within the five years previously and still alive in 2008, most (40 per cent) were breast, colorectal and prostate cancer patients. One common trait linking these cancers with better five years survival prevalence and lower mortality, compared to the incidence, is the availability of better diagnostic tools for earlier detection and efficacious treatment options.

According to an interim annual registry report on "Trends in Cancer Incidence in Singapore 2008-2012" by the Singapore Cancer Registry, lung cancer and breast cancer had the highest mortality rates in males and females respectively. Colo-rectum cancer, stomach cancer and oesophagus cancer were ranked 2nd (14.4 per cent), 4th (6.9 per cent) and 9th (2.8 per cent) respectively in males, and 3rd (15 per cent) and 5th (6.2 per cent) respectively in females.

Within gastrointestinal cancer as a cancer class, prognosis is dependent on the type of cancer and the anatomical location in the gastrointestinal tract of the lesion. Good prognosis can be achieved with complete surgical removal and peri-operative or adjuvant chemotherapy when diagnosed and treated at an early stage as reflected by the significantly improved survival outcome for colorectal cancer; Endoscopic imaging is in part responsible for this drop and also for detecting pre-cancerous and non-cancerous conditions and allowing them to be treated effectively. However, gastrointestinal cancer as a class continues to be a contributing cause of cancer mortality with stomach cancer as the second leading cause of cancer death, behind lung cancer, accounting for 9.7 per cent of total cancer deaths. The death rate from gastrointestinal cancer like stomach and oesophagus cancer can be attributed to late diagnosis; in Western countries 80 to 90 per cent of patients are diagnosed at an advanced stage, when the tumour is inoperable or recurrence within five years after surgery was initially performed.

For the clinical testing, the NUS Engineering team led by Assoc Prof Huang Zhiwei (on left), Dept of Biomedical Engineering, has been collaborating with researchers from the NUS Yong Loo Lin School of Medicine led by the School's Dean, Assoc Prof Yeoh Khay Guan (right); Prof Ho Khek Yu, Head, Dept of Medicine (centre); and Assoc Prof Teh Ming, Head, Dept of Pathology.



A close-up view of the proprietary confocal fibre-optic probe which enables the collection of biomolecular fingerprint of tissues in less than 1 second.