# Researchers invent novel ingestible capsule X-ray dosimeter for real-time radiotherapy monitoring

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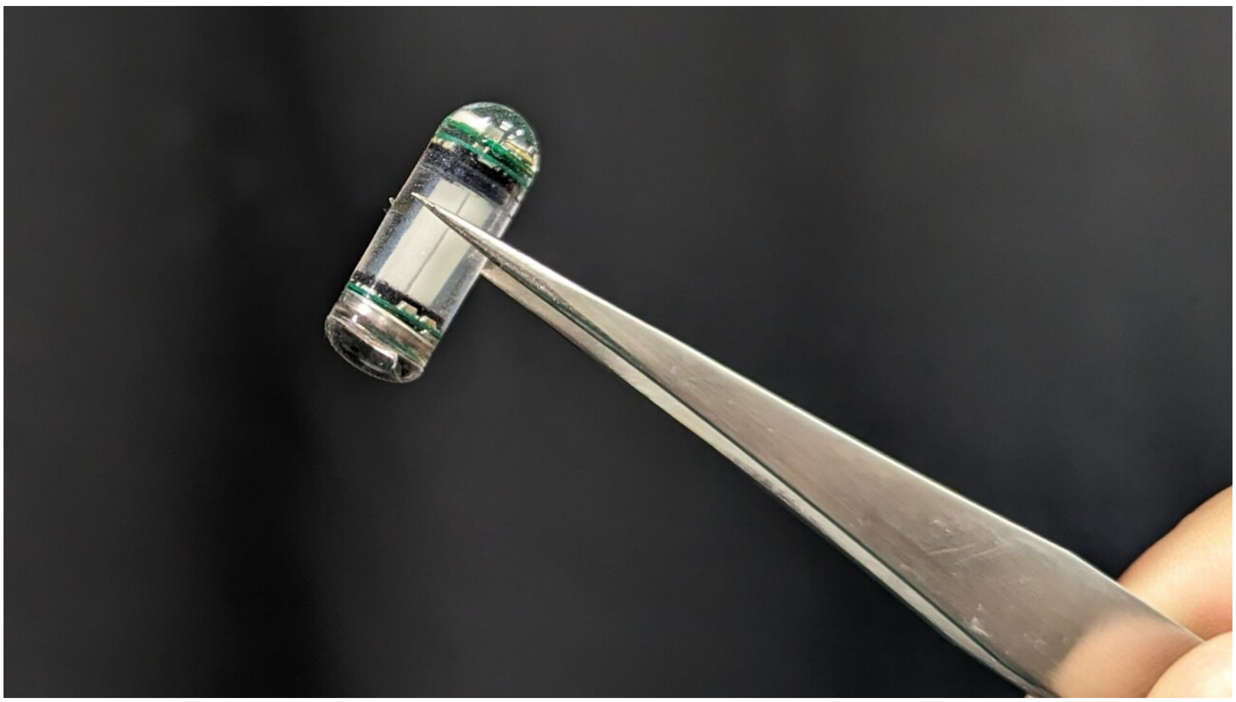


The components of the dosimeter fit into an 18mm by 7mm capsule, a common size for many supplements and medicines. Credit: National University of Singapore

Gastric cancer is one of the most common cancers worldwide. A new invention by researchers from the National University of Singapore

(NUS) could help improve the treatment of this cancer by enhancing the precision of radiotherapy, which is commonly used in combination with treatment options such as surgery, chemotherapy or immunotherapy.

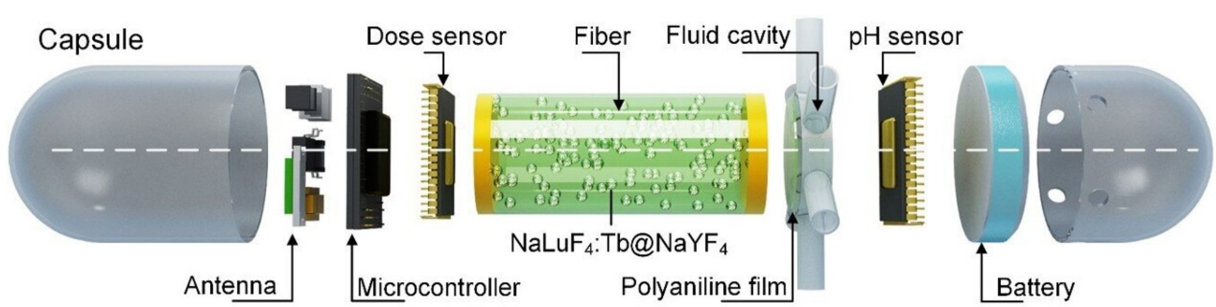
In the field of modern radiotherapy, precision in targeting tumor tissue while minimizing damage to healthy tissue is crucial. However, low efficacy and variable outcomes remain a challenge due to patient diversity, treatment uncertainty, and differences in delivery types. Monitoring the dose of radiation delivered and absorbed in real-time, particularly in the gastrointestinal tract, could enhance the precision of radiotherapy to improve its effectiveness, but it is difficult to achieve. Additionally, existing methods used for monitoring biochemical indicators such as pH and temperature are inadequate for comprehensive evaluation of radiotherapy.

To address this challenge, a research team led by Professor Liu Xiaogang from the Department of Chemistry under the NUS Faculty of Science, in collaboration with researchers from NUS Yong Loo Lin School of Medicine, Tsinghua University and Shenzhen Institute of Advanced Technology, has developed an ingestible X-ray dosimeter that detects radiation dose in real time. Combining their novel capsule design and a neural-network based regression model which calculates radiation dose from the information captured by the capsule, the team found that they could provide approximately five times more accurate monitoring of the dose delivered than current standard methods.

This technological breakthrough was published in the journal *Nature Biomedical Engineering* on April 13, 2023.

Clinical dosimeters such as metal-oxide-semiconductor field-effect transistors, thermoluminescence sensors, and optically excited films are commonly placed directly on or near the patient's skin to estimate the radiation dose absorbed in the target area. While such dosimetry with electronic portal imaging devices has been explored for treatment verification, these devices can be expensive and, furthermore, they absorb radiation and decrease the intended dose of radiation for the patient. Ingestible sensors are limited to pH and pressure monitoring, and there is a need for an inexpensive swallowable sensor that can simultaneously track biochemical indicators and X-ray dose absorption during gastrointestinal radiotherapy.

To address these limitations, Prof Liu and his team developed a novel ingestible X-ray dosimeter capsule capable of measuring the dose of radiation, and physiological changes in pH and temperature in real time during gastrointestinal radiotherapy. Key components of the capsule include a flexible optical fiber encapsulated with nanoscintillators that illuminate in the presence of radiation, a pH-responsive film, a fluidic module with multiple inlets for dynamic gastric fluid sampling, two sensors for dose and pH measurements, a microcontroller circuit board that processes photoelectric signals to be transmitted to a mobile application, and a button-sized silver oxide battery powering the capsule.



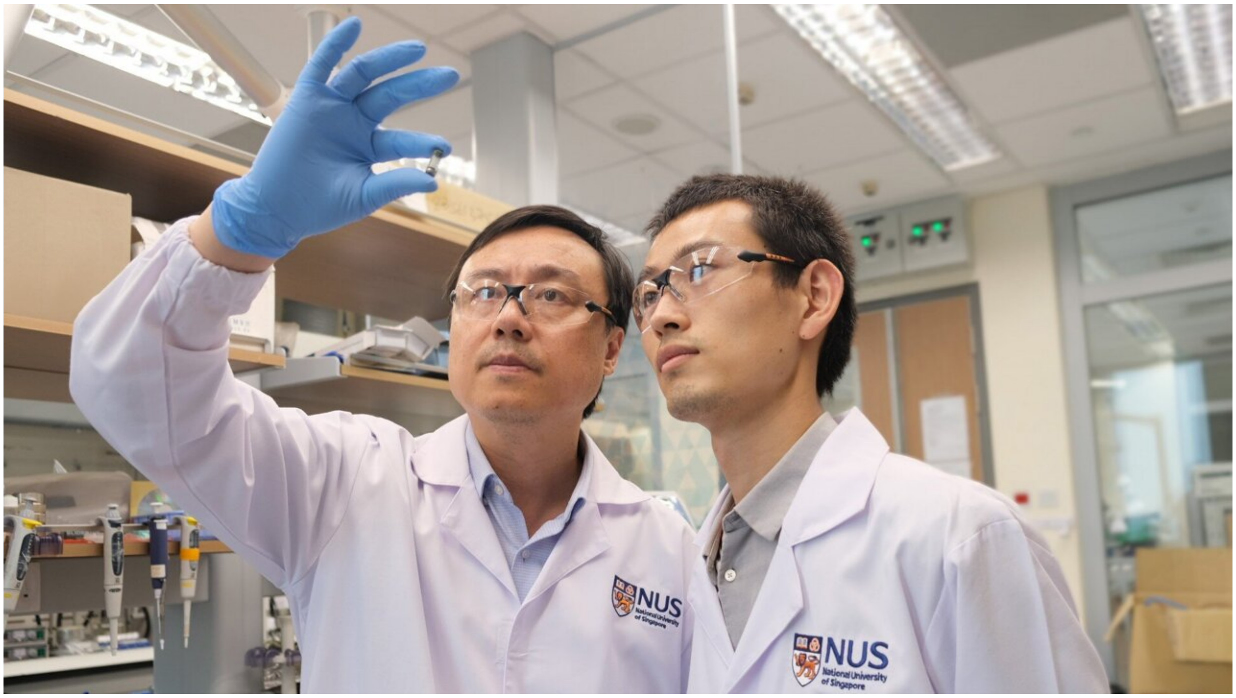

The components of the dosimeter fit into an 18mm by 7mm capsule, a common size for many supplements and medicines. Credit: National University of Singapore

When the capsule is ingested and reaches the gastrointestinal tract, the nanoscintillators will exhibit heightened luminescence in the presence of increased X-ray radiation. A sensor within the capsule measures the glow from the nanoscintillators to determine the radiation delivered to the targeted area.

At the same time, the fluidic module allows gastric fluid to be collected for pH detection by a film which changes color according to pH. This change in color is captured by a second sensor within the capsule. In addition, the two sensors are able to detect temperature which could give an indication of any negative reactions to radiotherapy treatment, such as allergies.

The photoelectric signals from the two sensors are processed by a microcontroller circuit board which sends information via Bluetooth technology and an antenna to a mobile phone app. Using a neural network-based regression model, the mobile app processes the raw data to display information such as the radiotherapy dose as well as the temperature and pH of the tissues undergoing radiotherapy.

"Our novel capsule is a game-changer in providing affordable and effective monitoring of the effectiveness of radiotherapy treatment. It has the potential to provide quality assurance that the right dose of radiation will reach patients," said Prof Liu.




Prof Liu Xiaogang (left) and Dr Hou Bo from the NUS Department of Chemistry were key members of the team that developed the novel capsule dosimeter. Credit: National University of Singapore

The capsule dosimeter measures 18mm in length and 7mm in width, a common size used for supplements and medicines, and costs S$50 to produce. Currently designed to monitor radiotherapy dose for gastric cancer, it could also be used to monitor treatment in different malignancies with further customizations to the capsule's size. For example, making the capsule smaller could allow it to be placed in the rectum for prostate cancer brachytherapy or in the upper nasal cavity for real-time measurement of the absorbed dose in nasopharyngeal or brain tumors, minimizing radiation damage to surrounding structures.

The research team is working to bring their innovation to clinical application. Further research includes identifying the capsule's position and posture after ingestion, developing a robust positioning system to anchor the capsule at the intended target site, and further calibrating the accuracy of the ingestible dosimeters for safe and effective clinical use.

**More information:** Bo Hou et al, A swallowable X-ray dosimeter for the real-time monitoring of radiotherapy, *Nature Biomedical Engineering* (2023). DOI: 10.1038/s41551-023-01024-2

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