Novel imaging platform for early and precise cancer diagnosis

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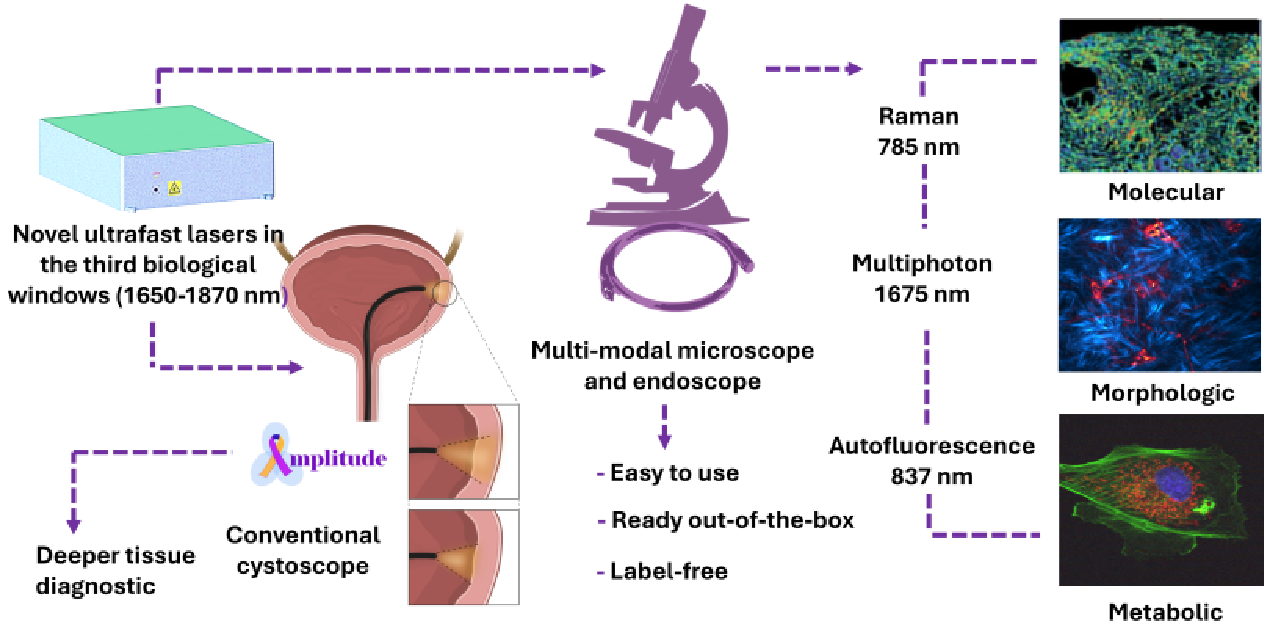
11 March 2025



Regina Gumenyuk, Adjunct Professor at Tampere University, is exploring a novel imaging platform for early and precise cancer diagnosis. Read more about this exciting innovation here

New cancer diagnostic techniques are essential for increasing survival rate

Cancer is the second leading killer in the world, behind cardiovascular diseases. Survival rates are highly dependent on early detection, the accuracy of lesion stage diagnosis, and state-of-the-art treatment methods. Despite tremendous worldwide efforts to improve the diagnosis and treatment of cancer, current approaches are unable to shift the negative paradigm in terms of mortality rate. One of the main reasons is cancer's cunning and unpredictability.

Cancerous tumours are heterogeneous, meaning the cancer cells are different within and between tumours. They progress differently; they grow differently and affect neighbouring tissue differently. A possible resolution to this situation lies in developing powerful and robust techniques for detecting tumours with high accuracy in the differentiation of cancer cells. The AMPLITUDE consortium tackled this challenge and developed novel photonics-based tools harnessing the power of laser light to improve the diagnosis and treatment of cancer.

Optical imaging through thick tissue

Light is a part of electromagnetic radiation, with the photon as the smallest wave packet. When generated by a laser, light features a high degree of coherence; in other words, it can interfere at different points, forming maxima and minima of the field. When the light travels through tissue, it experiences scattering and absorption.

However, some light propagates in straight lines, experiencing less scatting and retaining coherence properties. This light is used to form an optical image of the tissue structure. Therefore, the deeper the light can penetrate tissue, the more information about its structure below the surface can be obtained.

The ability of light to penetrate deep tissue depends on the tissue composition. Different wavelengths of light offer different levels of transparency concerning biological matter, forming so-called "biological windows" with minimum water absorption. Within these windows, three distinctive wavelength regions have been identified. The first biological window spans the wavelength range from 700 nm to 950 nm, the second biological window spans the region from 1000 to 1350 nm, and the third biological window covers 1550 to 1870 nm.

Biological windows one and two have been extensively investigated using widely available light sources for many years. However, the third biological window wavelength range is relatively unexplored but has the potential to unlock several advantages for optical imaging in thick tissue. Firstly, the longer wavelength decreases the scattering in tissue, resulting in improved image contrast. Secondly, the nonlinear effect causes the elevated absorption for diffused (scattered) light compared to the signal (ballistic) light, further contributing to the improved image contrast.

Multimodal approach

The benefits of the third biological window can be fully exploited using multiphoton imaging techniques that rely on tissue interaction with two or more photons. Multiphoton imaging is a non-invasive technique used for examining tissue morphology. It is based on nonlinear effects, for which efficiency depends on intrinsic material properties and light intensity. When incorporated with tight focusing and longer wavelength, the technique exhibits a decrease in the photobleaching area, leading to the reduction of phototoxicity. Using multiphoton imaging with light emitting in the third biological window, therefore, enables the examination of tissue structure in the deeper layers.

However, despite being a precise and powerful approach, multiphoton imaging cannot on its own discover all the hidden secrets of cancer tumours. For an accurate diagnosis, it is also essential to determine the heterogeneous distribution of cells within tumours by identifying metabolomic markers and molecular signatures. This can be realised by implementing a multimodal approach, where multiphoton imaging is augmented by autofluorescence imaging and Raman spectroscopy.

AMPLITUDE innovative imaging diagnostic platform

The AMPLITUDE diagnostic imaging platform is based on a non-invasive multi-modality approach incorporating three technologies for early and precise cancer diagnosis at a cellular level. The platform incorporates three-photon imaging, autofluorescence imaging and Raman spectroscopy. The three-photon imaging is realised by innovative compact and high peak power fibre laser operating at 1675 nm and generating 100 fs pulses. This laser is used for deep tissue penetration to identify cancer invasiveness into the muscle layer and its pathological stage. Owing to long wavelengths and high light intensity, this modality offers label-free operation, avoiding photodamage of the tissue.

The second harmonic of the laser signal at 837 nm is used for autofluorescence imaging of endogenous metabolic biomarkers, which are the essential presence in tumours at multiple steps of metabolic pathways and antioxidant defence. As the wavelength of the second harmonic signal is relatively long, it also falls into the first biological window, therefore guaranteeing deep penetration into the tissue. Autofluorescence imaging is also based on the label-free principle of minimising possible phototoxicity of the tissue.

Finally, Raman scattering spectroscopy at a wavelength of 785 nm, from a separate continuous laser source, enables analysis of the chemical composition of biological systems by probing the vibrational energy levels of molecules, providing highly specific information on tissue molecular composition. This is possible as Raman is an optical technique based on an inelastic scattering process in which non-resonant photons lose part of their energy colliding with a molecule; the measurement of the energy lost in the event, gives a spectrum, which is characteristic of the molecular vibrational energy structure.

All three modalities are integrated into the state-of-the-art imaging platform, enabling the capture of high-resolution images at depths greater than those of existing clinical diagnostic tools. The potential of the AMPLITUDE diagnostic platform to improve the speed and accuracy of the detection of cancer is currently under investigation in a proof-of-concept study. Clinical assessment of the platform will be carried out with the aim of demonstrating that the images produced by AMPLITUDE technology can enhance the ability of doctors to diagnose, treat and monitor bladder cancer patients.

This project has received funding from the European Union's HORIZON 2020 Research and Innovation programme under the Grant Agreement no. 871277

Contributor Details

- Article Categories
- Health

- Article Tags

- Cancer Research
- Horizon 2020

- Publication Tags
- OAG 046 – April 2025

- Stakeholder Tags
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