

## Label free, real time tumour detection offers the promise of enhancing intraoperative decision-making

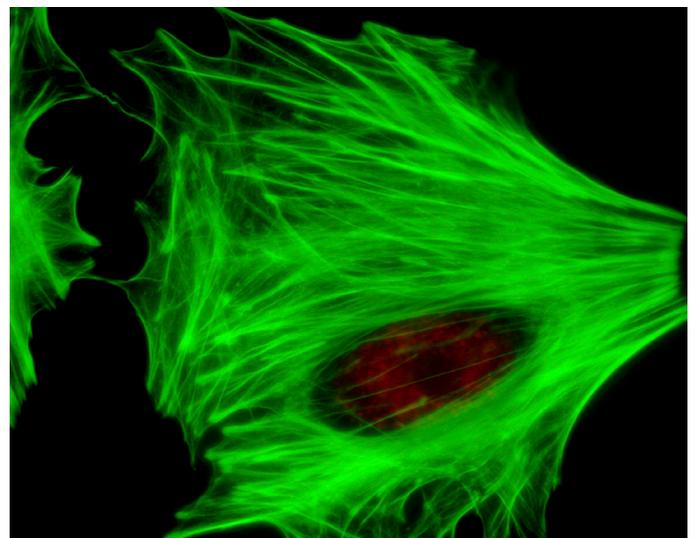
Clinical practice continues to benefit from developments in smart surgery: that is improved surgical decision making enabled by real time intraoperative information. Of the many examples, the most widespread is the intraoperative detection and imaging of tumour tissue. As more of these developments are brought to market, competing approaches will emerge for each specific tumour type, and users will select their preferred approach based on factors such as sensitivity, specificity, patient safety and workflow efficiency. Techniques which allow label free tumour tissue detection offer a number of advantages for both the user and the developer.

Molecular imaging methodologies have allowed tumour tissue to be visualised with a high level of specificity and sensitivity. For example fluorescence imaging agents are clinically available for imaging bladder cancer and brain tumours. In each case, however, a specific imaging agent must be developed through the necessary preclinical and clinical trials required to demonstrate safety and efficacy.

In contrast, label free detection methods offer the potential for more widespread application with faster development timescales. By removing the need to administer a pharmaceutical agent to the patient, label free methods also offer patient safety and workflow efficiency advantages.

[Label free detection methods offer the potential for more widespread application with faster development timescales](#)

Raman scattering forms the basis of a number of label free tumour detection techniques currently in preclinical and clinical development. Raman spectroscopy is used to distinguish between the molecular fingerprints of cancerous tissue compared to normal tissue. Researchers at McGill University and Polytechnique Montréal are developing a hand held Raman spectroscopy probe for in situ detection of brain cancer cells during surgery. Verisante Technology Inc is developing an endoscopic Raman probe for lung, cervical and colon cancer. The development follows an earlier trial of Raman spectroscopy, in combination with white light and autofluorescence bronchoscopy, in lung cancer diagnosis at Vancouver General Hospital <sup>1</sup>. A study is also being initiated at Charing Cross Hospital, London, to evaluate the Verisante Core technology for intraoperative brain tumour mapping.



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Raman spectroscopy is being combined with autofluorescence imaging in breast cancer surgery by workers at The University of Nottingham <sup>2</sup>. In this example, the autofluorescence method is used to locate the suspected tumour tissue, allowing the more specific but more time consuming Raman method to be applied to biopsies in the operating room. Stimulated Raman scattering, which offers enhanced faster spectral acquisition compared to conventional Raman scattering, is being used at the University of Michigan for in situ microscopic imaging of brain tumours <sup>3</sup>. The specificity and sensitivity of each of these Raman methods will need to be demonstrated during clinical trials but the potential for label free, real time tumour tissue detection is an exciting prospect for the enhancement of surgical decision making in the operating room.

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<sup>1</sup>Using laser Raman spectroscopy to reduce false positives of autofluorescence bronchoscopies, M. A. Short et al, Journal of Thoracic Oncology, 6, 1206-1214 (2011)

<sup>2</sup>Towards intra-operative diagnosis of tumours during breast conserving surgery by selective sampling Raman micro-spectroscopy, K. Kong et al; Physics in Medicine & Biology, 59, 6141-6152 (2014)

<sup>3</sup> Rapid, label-free detection of brain tumors with stimulated Raman scattering microscopy, M. Ji et al, Science Translational Medicine, 5, 201ra199 (2013)