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Title	Need for early, minimally invasive cancer diagnosis
Type	Article
URL	https://clok.uclan.ac.uk/id/eprint/26416/
DOI	https://doi.org/10.1073/pnas.1817551116
Date	2019
Citation	Paraskevaidi, Maria, Martin-Hirsch, Pierre L and Martin, Francis L (2019) Need for early, minimally invasive cancer diagnosis. Proceedings of the National Academy of Sciences of the United States of America. ISSN 0027- 8424
Creators	Paraskevaidi, Maria, Martin-Hirsch, Pierre L and Martin, Francis L

It is advisable to refer to the publisher's version if you intend to cite from the work. https://doi.org/10.1073/pnas.1817551116

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Need for early, minimally-invasive cancer diagnosis

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Dear Editor,

We have read the article by Mittal et *al.* (1) and we would like to congratulate the authors for an excellent piece of work demonstrating spectroscopy's capability for accurately subtyping epithelial cells and the tumor-associated microenvironment. Herein we would like to add some insights and comment on how this work could take the field forward.

In this recent paper, a high-definition Fourier-transform infrared imaging method using a quantum cascade laser (QCL) source has been employed for the characterization of 100-case breast tissue samples. This advancement has the potential to facilitate label-free molecular histopathology and bring spectroscopy one step closer to the clinic: undoubtedly, this study would be of great benefit with regards to expediting the diagnostic workflow as well as in terms of saving the pathologist's and / or surgeon's precious time and caseloads - not to mention providing high-quality data. Having said that, the most critical point with regards to patient benefit still remains unanswered:

"Could this technique be used for improving cancer patients' prognosis and survival?" "Could this method allow for an earlier, non-invasive diagnosis while there is still room for timely intervention and favorable outcomes (2, 3)?"

For instance, the technological development of hand-held spectroscopic devices and fiber optics has previously shown tremendous promise when it comes to characterization of cancer and could be used for *in-vivo* diagnostics without the need for tissue resection (4-6). Recent studies have also shown the promise of biological fluids for a minimally-invasive and pre-symptomatic cancer detection (7-9). Different types of machine learning algorithms have been developed to interpret spectroscopic data (10) with the aim of detecting cancer. A major field will be the development of predictive algorithms in order to identify pre-symptomatic cases that are destined to develop the disease; this would allow earlier intervention.

The results presented in this carefully-conducted work are undeniably a progressive step towards an accurate and differential diagnosis; however, we also propose that further spectroscopic / clinical research should focus on the development of screening tools for an earlier and minimally invasive detection of cancer.

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