Need for early, minimally-invasive cancer diagnosis

Maria Paraskevaidi[a,1], Pierre L. Martin-Hirsch[b] and Francis L. Martin[a,c]

[a]School of Pharmacy and Biomedical Sciences, University of Central Lancashire, Preston PR1 2HE, UK; [b]Department of Obstetrics and Gynaecology, Lancashire Teaching Hospitals NHS Foundation, Preston PR2 9HT, UK; [c]Biocel Ltd, Hull, Yorkshire, UK

[1]To whom correspondence should be addressed. Email: mparaskevaidi@uclan.ac.uk

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.

References

1. Mittal S*, et al.* (2018) Simultaneous cancer and tumor microenvironment subtyping using confocal infrared microscopy for all-digital molecular histopathology. *Proc Natl Acad Sci USA*:201719551.
2. Richards M (2009) The national awareness and early diagnosis initiative in England: assembling the evidence. *Br J Cancer* 101(S2):S1.
3. Hiom S (2015) Diagnosing cancer earlier: reviewing the evidence for improving cancer survival. (Nature Publishing Group).
4. Mohs AM*, et al.* (2010) Hand-held spectroscopic device for in vivo and intraoperative tumor detection: contrast enhancement, detection sensitivity, and tissue penetration. *Anal Chem* 82(21):9058-9065.
5. Wang W, Zhao J, Short M, & Zeng H (2015) Real-time in vivo cancer diagnosis using raman spectroscopy. *J Biophotonics* 8(7):527-545.
6. Mackanos MA & Contag CH (2010) Fiber-optic probes enable cancer detection with FTIR spectroscopy. *Trends Biotechnol* 28(6):317-323.
7. Baker MJ*, et al.* (2016) Developing and understanding biofluid vibrational spectroscopy: a critical review. *Chem Soc Rev* 45(7):1803-1818.
8. Shaw RA & Mantsch HH (2000) Infrared spectroscopy in clinical and diagnostic analysis. *Encyclopedia Anal Chem* 1:83-102.
9. Gajjar K*, et al.* (2013) Fourier-transform infrared spectroscopy coupled with a classification machine for the analysis of blood plasma or serum: a novel diagnostic approach for ovarian cancer. *Analyst* 138(14):3917-3926.
10. Goodacre R. (2003) Explanatory analysis of spectroscopic data using machine learning of simple, interpretable rules. *Vibr Spectrosc* 32(1):33-45.