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Cancer Diagnosis and Detection via Infrared Microspectroscopy of Cells and Thin Tissue Sections. What Have we Learned?

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"Infrared spectroscopy and/or microspectroscopy can detect cancer in cells and thin tissue sections". This statement has been debated for over ten years, spurred by the promise that IR techniques might serve as sensitive and specific probes of disease at the molecular level. It is accepted as a self-evident truth that morphological changes in tissue/cellular structure must be accompanied by characteristic changes in the (bio)chemistry of the affected tissue/cells. The question that has provoked much debate in the IR spectroscopy community is whether these changes are pronounced enough to be observed spectroscopically.

We present here a perspective gained through three relevant studies, one employing IR microspectroscopy to characterize lung tumors in a mouse model, a second using the same technique to grade brain cancers (astrocytoma/glioblastoma), and a third study assessing new approaches to the study of cervical cells:

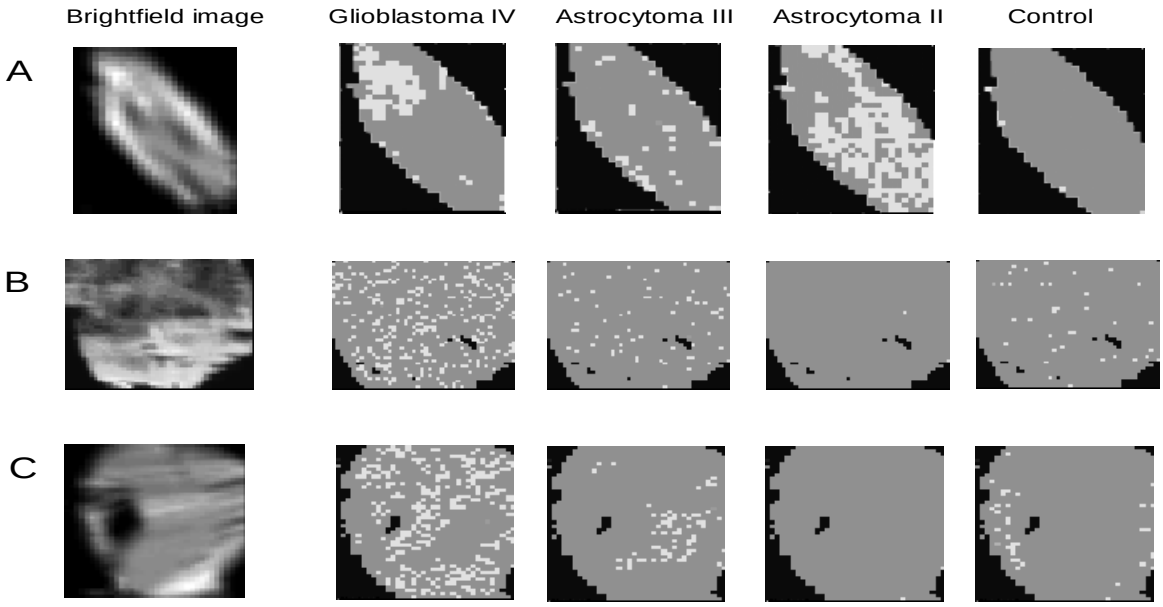
Microspectroscopic characterization of lung tumours

Methods based on infrared microspectroscopy were explored as a means to distinguish normal from neoplastic lung tissue. Mice were exposed to urethane, a known environmental carcinogen. After 3-8 months, lungs were removed, snap-frozen, sectioned and analyzed by standard histological methods and by infrared microspectroscopy. Neoplasms were readily observed in mice treated with urethane. Ultra-structurally, the neoplasms were composed entirely of type II alveolar cells displaying intracellular lamellar bodies. A fusion of two spectral preprocessing techniques, optimal region selection and linear discriminant analysis, was used to search for infrared spectral signatures distinguishing normal from neoplastic tissue. These techniques showed clear and reproducible differences between the complex spectra of these tissue types, suggesting that infrared microspectroscopy in conjunction with spectral processing technology may be useful to reveal subtle spectral differences occurring following induction of neoplastic changes and to interpret their biochemical origins.

Detection and grading of brain tumours

An approach was developed to distinguish cancerous brain tissue from normal brain tissue on the basis of Fourier transform infrared (FTIR) spectroscopy and a genetic classification algorithm. FTIR microspectroscopy was used to map various thin-section tumour samples with different malignancy grades (grades II-VI) and non-tumour samples

obtained from various patients by surgical removal. Spectral analysis revealed features characteristic of tumors with increasing malignancy. A genetic region selection algorithm combined with linear discriminant analysis was used to derive classifiers distinguishing among spectra of control tissue, astrocytoma grade II, astrocytoma grade III and glioblastoma grade IV. A classification success rate of ~ 85 % was obtained. These results demonstrate the potential of the combination of FTIR spectroscopy and pattern recognition routines in providing a more objective method for brain tumour grading and diagnosis.



Highlighted pixels delineate regions within each of three tissue sections (A, B, and C) that are identified as glioblastoma (grade IV), astrocytoma (grade III), astrocytoma (grade II), and control tissue via non-subjective automated classification of the corresponding IR (microspectroscopy) spectra. These results suggest that microspectroscopy may provide spatial resolution of different histological classes that is difficult or impossible to achieve via conventional histopathology.

Heterogeneity in cervical cell preparations

One of the most attractive aims of current biomedical spectroscopy is to develop a spectroscopy-based method for the routine screening of cervical cells (the “infrared Pap smear”). Having tried the direct approach previously – accumulating many spectra of bulk samples and seeking correlation with the cytological diagnoses – we are now revisiting the problem with the aim of developing more mature experimental and interpretational methods. One of the areas we are re-examining is how best to sample the cells that are available. Is a bulk measurement the best possible reflection of the properties of interest, or is there a better way? While the answer is not yet clear, a number of relevant insights have been gained via microspectroscopy of cellular films prepared from bulk specimens – i.e. the same films that were characterized previously by conventional ‘macro’ transmission spectroscopy. In particular, the spectral heterogeneity suggests that a set of microspectroscopy measurements might provide a better basis from which to seek diagnostic information than a single measurement of the bulk sample can provide.

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