Spectral Cytopathology (SCP): A summary

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SCP, the infrared spectroscopic diagnosis of exfoliated human cells, has been a major research topic at the authors' laboratory, the Laboratory of Spectral Diagnosis (LSpD) in Boston. In collaboration with the Department of Pathology at Tufts Medical Center (TMC) in Boston, exfoliated cervical cells from normal subjects, exfoliated cells from patients diagnosed with cervical disease (dysplasia) and exfoliated cells from the nasopharyngeal and oral cavities from patients diagnosed with dysplasia and cancer have been obtained. In addition, oral samples from student participants of an oral disease study at Northeastern University (under a local Institutional Review Board permit) have been collected. The total number of participants in both the cervical and oral studies is about 300. For the oral study, samples were collected from the tongue, the mouth floor (under the tongue) and from the inside of the cheeks. Since 2009, more than 1.2 million cell spectra have been collected.

The sample collection and cell fixation procedures have been standardized and the effect of fixation times and fixation procedures has been evaluated [1]. Data collection has been accelerated by more than an order of magnitude since the early studies [2] by an imaging approach that has been reported [3], without sacrificing data quality. This is achieved by using areas not occupied by cells to construct a measurement-specific noise matrix, and performing noise adjusted principal component analysis (PCA) [4] to reconstruct spectra. Finally, cellular spectra have been corrected for dispersive band shape by a phase correction procedure. These studies have revealed a number of important results:

1. Hormonal effects influence the maturation of cervical cells, which can be monitored spectroscopically. The observed spectral changes are manifested not only by variations in glycogen content, but also by changes in the protein spectral region.
2. Cells from the oral cavity exhibit slightly different spectral characteristics depending on their area of origin. Thus, cells from the tongue, from under the tongue and from the inside of the cheeks can be distinguished. Furthermore, drug metabolites and effects of smoking can be detected.
3. Spectra of cancerous, dysplastic and normal cells can be readily distinguished by PCA.
4. Disease affects the majority of cells from a given collection site. Thus, morphologically normal cells collected from the vicinity of a cancerous lesion show abnormal spectra. The spectral abnormality may persist even after cancer treatment.
5. At least some spectral changes of cells appear to be caused by viral infection from *herpes simplex*, or *human papillomavirus* (HPV). The viral load in cultured cells has been detected both by infrared and Raman spectral studies.

These results indicate that SCP offers some promising advantages over classical cytological methods in that the number of diagnostic cells is vastly larger, that one measurement may be able to diagnose both dysplasia and viral infection, and that it is an instrument-based method that can be implemented to be objective, fast and inexpensive.

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