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Tissue Modulated in vivo Raman Spectroscopy: Noninvasive Blood Analysis

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We have presented results earlier relating to the use of "tissue modulation", i.e. mechanical pressure, thermal gradients and chemical loading to differentiate tissue types for in vivo Raman spectroscopic analysis [1-5]. Although we expect this technique to have some general applicability, we are presently interested in obtaining Raman spectra of human capillary blood suitable for quantitative analysis of glucose and possibly other analytes.

The approach we describe uses an external cavity diode laser to excite Raman spectra containing molecule specific information relating to the probed tissues in vivo. The fluorescence that occurs simultaneously is used as a measure of the probed volume of tissue. This tissue volume is important in that it allows us to compare concentration measurements on different tissues to each other as well as concentration measurements on the same tissues at different times. The sources of the fluorescence, the factors affecting the variability of the fluorescence and the relationship between the fluorescence and the concentrations of various analytes of potential interest will be discussed. In addition to the porphyrin-based emission from various sources, e.g. cytochrome, hemoglobin, we believe that amino acids and proteins and metal ions are important.

Tissue modulated Raman spectra of human capillary beds in vivo can be associated with the most mobile tissues in the probed volume. In the present study, tissue modulated spectra obtained as the difference between spectra obtained with and without mechanical pressure applied on the capillary bed using a metal plate with a small hole. The stress field obtained using this geometry produces about a 10-15% modulation in Raman and wavelength shifted fluorescence. We associate the difference spectra with blood, with the spectral features weighted more heavily with contributions from plasma and serum constituents. These constituents are more mobile than those normally associated with hematocrit and so the tissue modulation approach enhances their contributions to the spectra.

Previous clinical results established that certain Raman spectral features can be associated with glucose and that the modulated fluorescence is an accurate and precise measure of modulated blood volume. Recent clinical results will be presented which suggest that this approach is quite robust and that tissue modulated Raman spectroscopy can monitor blood glucose noninvasively in vivo with accuracy and precision equal to or better than that demonstrated by any portable fingerstick technology or device. In a broader sense, these results suggest that near infrared fluorescence can be the basis for quantitation of in vivo Raman spectra spanning a wide range of spatial scales.

[1] J. Chaiken et al., Proc SPIE, vol. 3918, pp. 134-145(2000) and references therein

[2] J. Chaiken et al., Proc SPIE, vol. 3918, pp. 135-143(2000) and references therein
[3] J. Chaiken et al., Proc SPIE, vol. 4254, pp. 216-127(2001) and references therein
[4] J. Chaiken et al., Proc SPIE, vol. 4254, pp. 106-118(2001) and references therein
[5] J. Chaiken et al., Proc SPIE, vol. 4368, pp. 134-145(2001) and references therein

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