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SYMPOSIUM

Impact of Tissue Heterogeneity on Noninvasive Near-Infrared Glucose Measurements in Interstitial Fluid of Rat Skin

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Abstract

Background:

Movement of the optical interface used to collect noninvasive near-infrared spectra is known to dramatically increase prediction errors for glucose concentration measurements within the interstitial fluid of living rat skin. Prediction errors increase by more than 2.5-fold when the interface is moved before each non-invasive measurement compared to measurements where the interface position is constant throughout. Chemical heterogeneity of the skin matrix is examined as a possible mechanism for the strong sensitivity to the interface placement during noninvasive measurements conducted from transmission near-infrared absorption spectroscopy.

Method:

Microspectroscopy was performed over a region of the near-infrared spectrum (4000–5000 cm^{-1}) to map the concentrations of water, collagen protein, fat, and keratin protein within the skin tissue matrix through which noninvasive spectra are collected. Maps were created for multiple samples of skin excised from male and female animals. Sets of near-infrared spectra were constructed to simulate noninvasive spectra in accord with the basic tissue composition found from the microspectroscopic maps with added information corresponding to a span of glucose concentrations ranging from 5 to 35 mM and Gaussian-distributed noise.

Results:

Microspectroscopic maps of rat skin reveal similar patterns of heterogeneity for major chemical components of skin samples excised from both male and female animals. These maps demonstrate concentration domains with dimensions similar to the size of the fiber interface used to collect noninvasive spectra. Partial least squares calibration models generated from sets of simulated spectra demonstrate increases in prediction errors for glucose when the spectral matrix is changed in accord with the degree of chemical heterogeneity displayed in the skin maps. Prediction errors typically increase between 100 and 1000% when comparing errors generated from spectra that represent a single tissue composition versus spectra that represent a varied skin composition in accord with the distribution displayed in the skin maps.

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Abbreviations: (μAU) micro absorbance units, (FTIR) Fourier transform infrared, (ISF) interstitial fluid, (PLS) partial least squares, (RMS) root mean square, (SD) standard deviation, (SEC) standard error of calibration, (SEP) standard error of prediction, (SNR) signal-to-noise ratio

Keywords: interstitial fluid, microspectroscopic mapping, near-infrared spectroscopy, noninvasive glucose sensing, partial least squares regression, skin heterogeneity

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Abstract cont.

Conclusions:

The distribution of the major components of skin is not uniform, but establishes domains within the skin matrix that strongly impact prediction errors for the noninvasive spectroscopic measurement of glucose within the interstitial fluid of rat dermis tissue. The observed increase in prediction error (>2.5-fold) determined from actual noninvasive measurements is within the lower range of prediction error increases demonstrated by this simulation study. These findings implicate that chemical heterogeneity within the tissue matrix is a major factor in the sensitivity of the location of the fiber interface used to collect noninvasive spectral data.

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