Intracellular glucose concentration in skeletal muscle of awake rats was determined under conditions of hyperglycemic (10.2 +/- 0.6 mM) hyperinsulinemia (approximately 1,200 pM) and hyperglycemic (20.8 +/- 1.5 mM) hypoinsulinemia (< 12 pM) by use of 13C nuclear magnetic resonance (NMR) spectroscopy during a prime-constant infusion of [1-13C]glucose and [1-13C]mannitol with either insulin (10 mU.kg-1.min-1) or somatostatin (1.0 microgram.kg-1.min-1). Intracellular glucose was calculated as the difference between the concentrations of total tissue glucose (calculated from the in vivo 13C NMR spectrum with mannitol as an internal concentration standard) and extracellular glucose, corrected by the ratio of intra- and extracellular water space. Extracellular concentration was corrected for an interstitial fluid-to-plasma glucose concentration gradient of 0.83 +/- 0.07, determined by open-flow microperfusion. The mean ratio of intra- to extracellular glucose space, determined from the relative NMR signal intensities and concentrations of mannitol and total creatine, was 9.2 +/- 1.1 (hyperglycemic hyperinsulinemia, n = 10), and 9.0 +/- 1.7 (hyperglycemic hypoinsulinemia, n = 7). Mean muscle intracellular glucose concentration was < 0.07 mM under hyperglycemic-hyperinsulinemic conditions (n = 10) and 0.32 +/- 0.06 mM under hyperglycemic-hypoinsulinemic conditions (n = 7). This method is noninvasive and should prove useful for resolving the question of whether glucose transport or phosphorylation is responsible for the reduced rate of muscle glycogen synthesis observed in diabetic subjects.

HIT TERMS: GLUCOSE?; SPECTROSCOP?.

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4. Phantoms for noninvasive blood glucose sensing with near infrared transmission spectroscopy. - MED 98-06 98138252 NDN- 176-0121-2654-3

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In vivo spectra from human subjects can be simulated with a phantom composed of different layers of water, fat and muscle tissue. All three components are necessary to simulate in vivo spectra collected over the combination spectral region (5000-4000 cm-1). Muscle tissue is not required, however, to accurately simulate overtone spectra (6600-5400 cm-1). The near-IR spectral characteristics of fat and muscle tissue from several animal sources are essentially identical to those found for human tissue, hence, the animal source for these phantom components is not critical. Thickness of each tissue layer can be determined by a regression analysis where the in vivo spectrum of interest is regressed against standard absorbance spectra of the necessary model components (water, fat and muscle). In general, in vivo overtone spectra collected across human webbing tissue with a thickness of 6.7 mm can be simulated with water layer thicknesses ranging from 5.0 to 6.4 mm combined with fat layer thicknesses from 1.4 to 4.2 mm.

HIT TERMS: GLUCOSE?; SPECTROSCOP?.

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remained as still as possible. The intensity is plotted versus detector distance for selected wavelengths for one subject in Figure 5, with the corresponding diffusion theory fits. The optical property spectra are shown in Figure 6 with the absorption spectrum of 70 % pure water included for comparison of spectral features.

The stability of μ_a and μ_s' are of interest for physiological monitoring applications. A series of measurements were performed on normal volunteers to investigate the stability of these coefficients at selected wavelengths. In these measurements, volunteers lay supine with the probe fixed to the abdomen. Reflectance was sampled at 960 nm, 1060 nm, and 1250 nm for 1 hour or more at approximately 30 s intervals. The volunteer lay as still as possible during the measurement, and no food or beverages were consumed. The temporal behavior of the estimated optical properties varied between measurements, but common features found in most scans can be noted. First, the scattering coefficient was usually observed to increase during the first 30-45 minutes of the scan by about 2 - 5 %, after which it remained fairly stable. The magnitude of the initial relative increase for a given volunteer was about the same at 960 nm and 1060 nm, and lower at 1250 nm. Second, the absorption coefficient was often observed to increase significantly throughout the measurement, by as much as 30%. As was observed with the scattering coefficient, the magnitude of these absorption increases was usually comparable at 960 nm and 1060 nm, and lower at 1250 nm. A sample of the temporal behavior of the optical properties for one volunteer is shown in Figure 7.

The sensitivity of the optical properties of skin to changes in temperature is also a concern for monitoring applications. Experiments were performed on human volunteers to investigate the temperature dependence of optical properties. The measurement protocol was similar to the baseline stability measurements described above. In order to produce controlled changes in temperature, a small aluminum collar was placed on the skin and fit loosely around the probe. Water from a heating and refrigerating water bath was circulated through the collar. The collar temperature was held constant for 45-60 minutes at 37° C, then 20° C, then 45° C, and finally 37° C. The reflectance was sampled at 960 nm, 1060 nm, and 1250 nm. The estimated optical properties based on reflectance measured during a typical temperature series are shown in Figure 8. The behavior observed in a total of 10 measurements showed several qualitative trends. Both μ_s' and μ_a increase and decrease with increases and decreases in temperature, but with different relative magnitudes and temporal response. The changes in μ_s' are somewhat comparable at the three wavelengths studied, while the changes

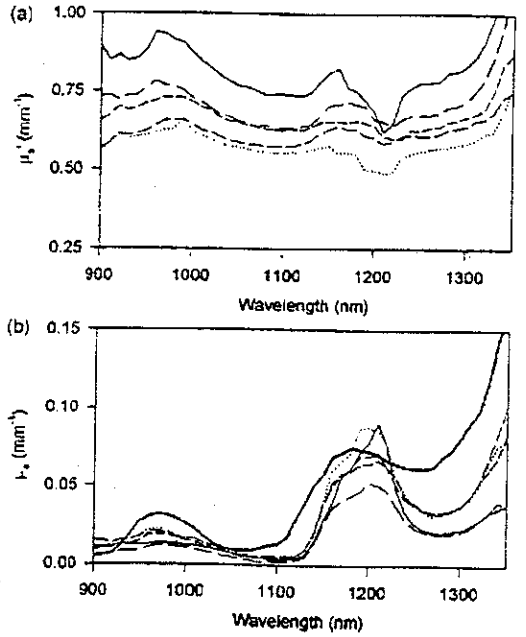

Figure 5 Optical property spectra measured *in vivo* on human volunteers. (a) μ_s' for 5 volunteers measured on the abdomen or the lower back. (b) μ_a for 5 volunteers measured on the abdomen or the lower back. The absorption spectrum for 70% water (thicker line) is shown for comparison[16].

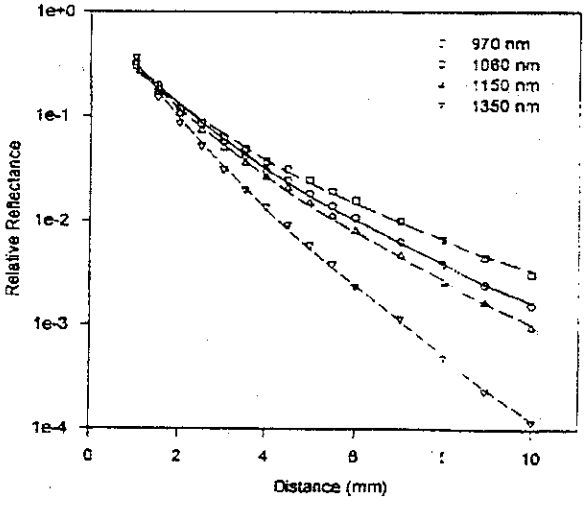

Figure 6 Measured relative reflectance versus distance for human abdomen, *in vivo*, at selected wavelengths. Markers represent measured data, and lines represent theoretical reflectance based on nonlinear fits to a diffusion model.