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SYMPOSIUM

Requirements for Calibration in Noninvasive Glucose Monitoring by Raman Spectroscopy

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Abstract

Background:
In the development of noninvasive glucose monitoring technology, it is highly desirable to derive a calibration that relies on neither person-dependent calibration information nor supplementary calibration points furnished by an existing invasive measurement technique (universal calibration).

Method:
By appropriate experimental design and associated analytical methods, we establish the sufficiency of multiple factors required to permit such a calibration. Factors considered are the discrimination of the measurement technique, stabilization of the experimental apparatus, physics–physiology-based measurement techniques for normalization, the sufficiency of the size of the data set, and appropriate exit criteria to establish the predictive value of the algorithm.

Results:
For noninvasive glucose measurements, using Raman spectroscopy, the sufficiency of the scale of data was demonstrated by adding new data into an existing calibration algorithm and requiring that (a) the prediction error should be preserved or improved without significant re-optimization, (b) the complexity of the model for optimum estimation not rise with the addition of subjects, and (c) the estimation for persons whose data were removed entirely from the training set should be no worse than the estimates on the remainder of the population. Using these criteria, we established guidelines empirically for the number of subjects (30) and skin sites (387) for a preliminary universal calibration. We obtained a median absolute relative difference for our entire data set of 30 mg/dl, with 92% of the data in the Clarke A and B ranges.

Conclusions:
Because Raman spectroscopy has high discrimination for glucose, a data set of practical dimensions appears to be sufficient for universal calibration. Improvements based on reducing the variance of blood perfusion are expected to reduce the prediction errors substantially, and the inclusion of supplementary calibration points for the wearable device under development will be permissible and beneficial.

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Abbreviations: (ISF) interstitial fluid, (NAS) net analyte spectrum

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