# Calibration of a non-invasive Raman spectroscopy device realized using pre-collected clinical data

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## Introduction

The combination of spectroscopy and multivariate analysis is the ideal approach for non-invasive glucose measurement, but the required calibration stability and accuracy was only recently demonstrated by RSP Systems [1]. This study demonstrates that a Raman-based device can be calibrated with a short calibration period (if any), thus further underlining Raman spectroscopy as a promising technology for the non-invasive era in diabetes management [2]. While the complexity and multivariate nature of skin Raman spectra have historically imposed demanding calibration requirements, the application of pre-collected clinical data to device calibration now reduces that limitation hereby allowing for a shorter and more convenient calibration.

Using paired Raman spectra and reference blood glucose concentrations from past studies, a regression model is trained and then tailored to individual users, based on 10 calibration points collected over an initial 4-hour period. To test this new calibration scheme, a clinical study was conducted involving 50 subjects with type 2 diabetes measuring over a period of 2 days. Glucose excursions were achieved through meal challenges.

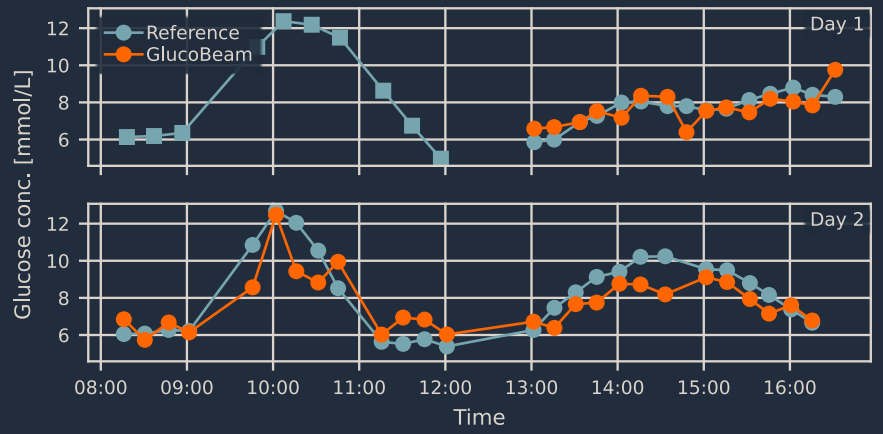


***Figure 1*** *– Example of a participant's intermittent measurements using GlucoBeam vs. reference method (Contour Next) over a two-day period. The first 10 measurements on day 1 (square markers) correspond to calibration, which are used to tailor the model to the specific user.*

## Results

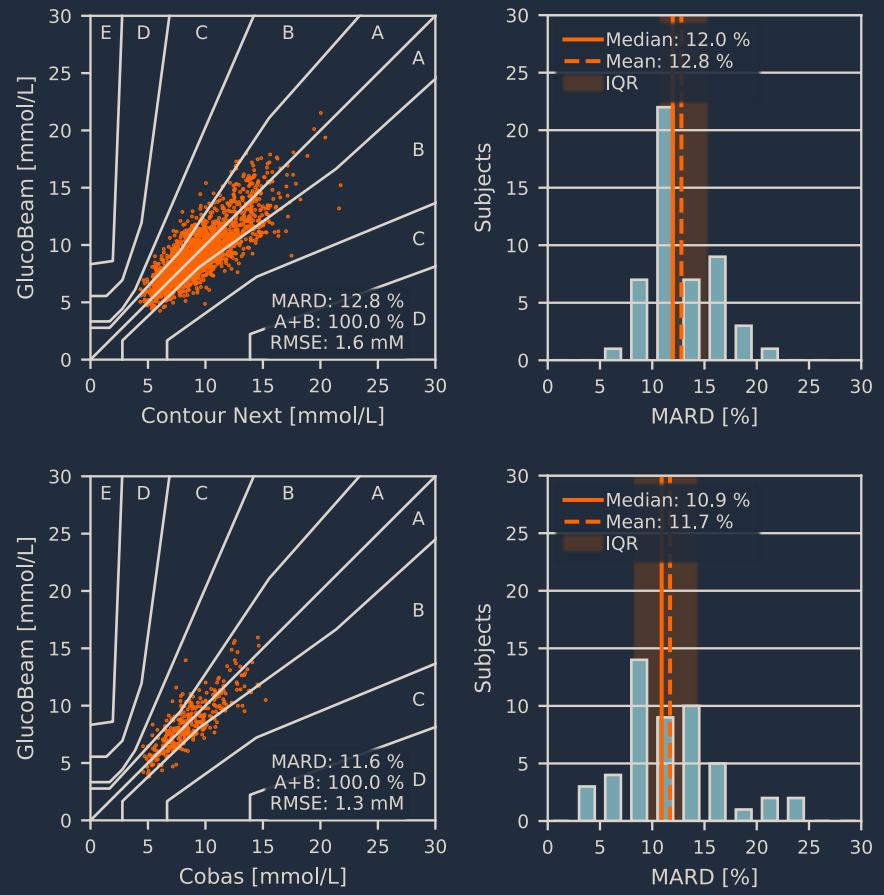


***Figure 2*** *– Summary of study results. Left: Consensus Error Grid (CEG) analysis of pooled GlucoBeam measurements when the comparator is Contour Next (top, 1918 data points) and Cobas (bottom, 346 data points). Using Cobas as reference gives an overall better performance. Right: Histogram of the Mean Absolute Relative Difference (MARD) for individual subjects, highlighting the median value and interquartile range (IQR), when the reference is Contour Next (top) and Cobas (bottom).*

## Conclusion

This study has successfully demonstrated that Raman spectroscopy, paired with a pre-trained regression model, offers non-invasive glucose monitoring after a short initial calibration period. With 100% of the measurements within zones A and B of the CEG plot and a mean/median MARD of 11.7/10.9%, the performance results are promising for future use in diabetes management. It is expected that accurate factory calibration can be reached as more data is collected and algorithms are refined.

The current performance is based on intermittent measurements, further developments shall improve measurement accuracy by exploiting time series analysis. This becomes particularly relevant when the technology is miniaturized to a wearable form.

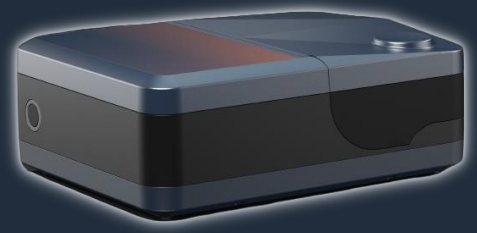

***Figure 3*** *– GlucoBeam. A portable, Raman-based non-invasive glucose monitor that measures the glucose concentration in the interstitial compartment of the skin.*

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[1] A. Pors et al., "Accurate Post-Calibration Predictions for Noninvasive Glucose Measurements in People Using Confocal Raman Spectroscopy," *ACS Sens.*, 1272-1279, 2023.
[2] B. Todaro et al., "Is Raman the best strategy towards the development of non-invasive continuous glucose monitoring devices for diabetes management?," *Front. Chem.* 10, 994272, 2022.