Feasibility and Performance of a Continuous Ketone Monitoring Sensor

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Conflicts of Interest

Shridhara Alva is an employee of Abbott Diabetes Care.

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Diabetic Ketoacidosis and Type 1 Diabetes

DKA is a leading cause of death among children and adults with diabetes[1]

• Prevalence

Annual DKA prevalence among T1D adults across countries[1]

3-10%

• High risk T1D populations

- Youth and adults with suboptimal insulin management

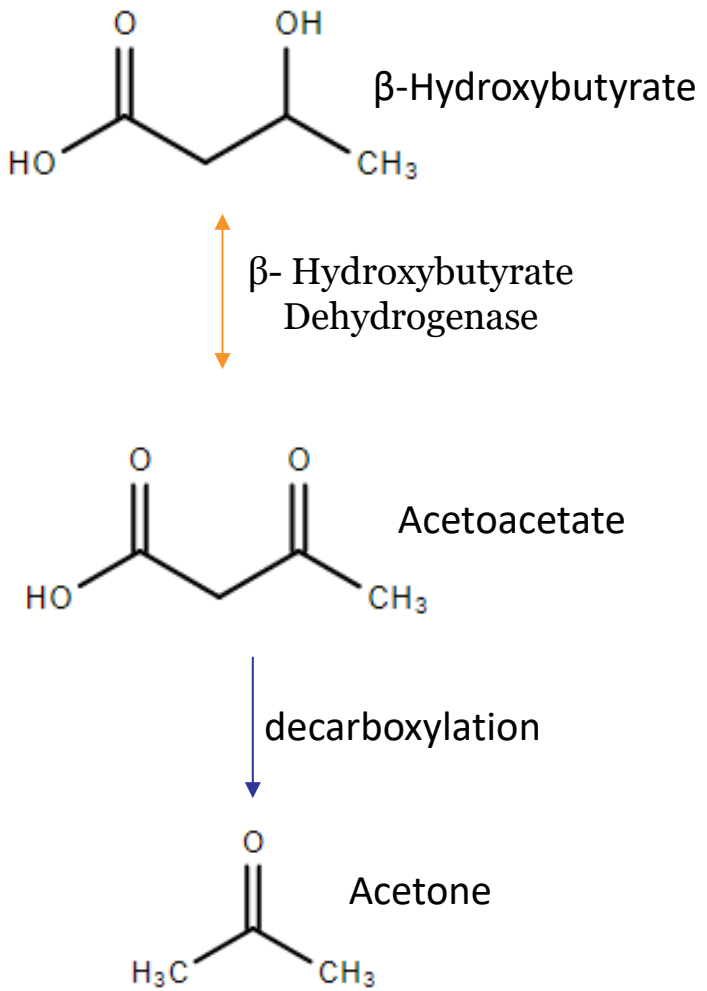
- Patients using insulin pumps

- Patients using SGLT2 therapies

1. Nguyen et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211042656

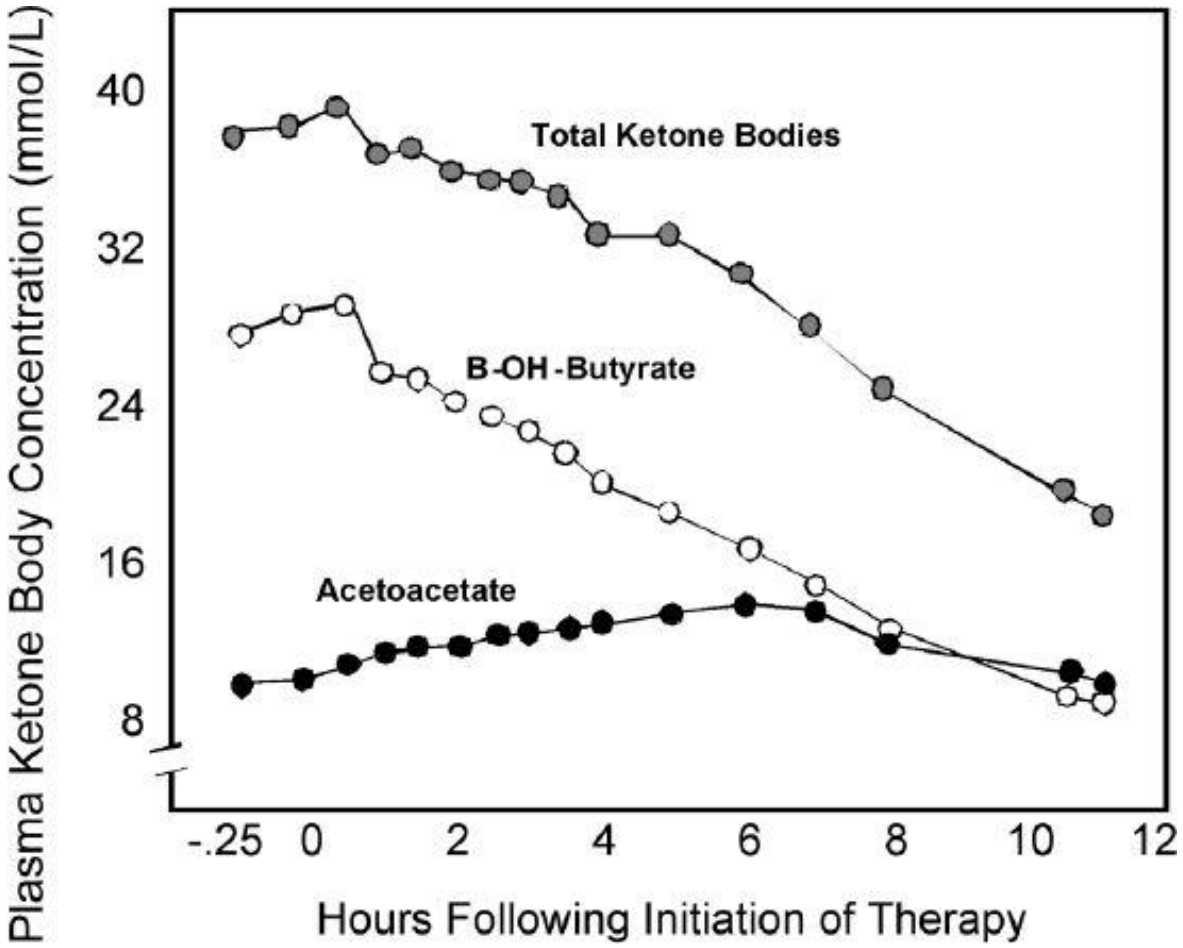
Ketone Bodies and Ketone Assays

- Urine ketone
  - Compare color after 30 – 60 sec with color chart
  - Urine ketone (acetoacetate) is 2-4 hours behind blood values
- Blood Ketone - laboratory
  - Laboratory Assay using Nitroprusside test
  - Measures Acetoacetate
- Blood ketone – Point of Care/Home Test
  - Whole blood test
  - Measures β-hydroxybutyrate



Misra & Oliver, *Diabetes Medicine* (2015): https://doi.org/10.1111/dme.12604

Clearance of Ketone Bodies Following Initiation of Therapy



- Upon initiation of therapy
  - B-hydroxy butyrate level drops steadily
  - Acetoacetate level increases initially and stays elevated for much longer period
  - Persistent urine ketonuria despite resolution of blood ketonemia

Laffel, L *Journal of Diabetes Science & Technology* (2007): https://doi.org/10.1177/193229680700100122

Ketone Monitoring is inconvenient and ineffective.

Limitations of Current Ketone Monitoring

Urine Testing

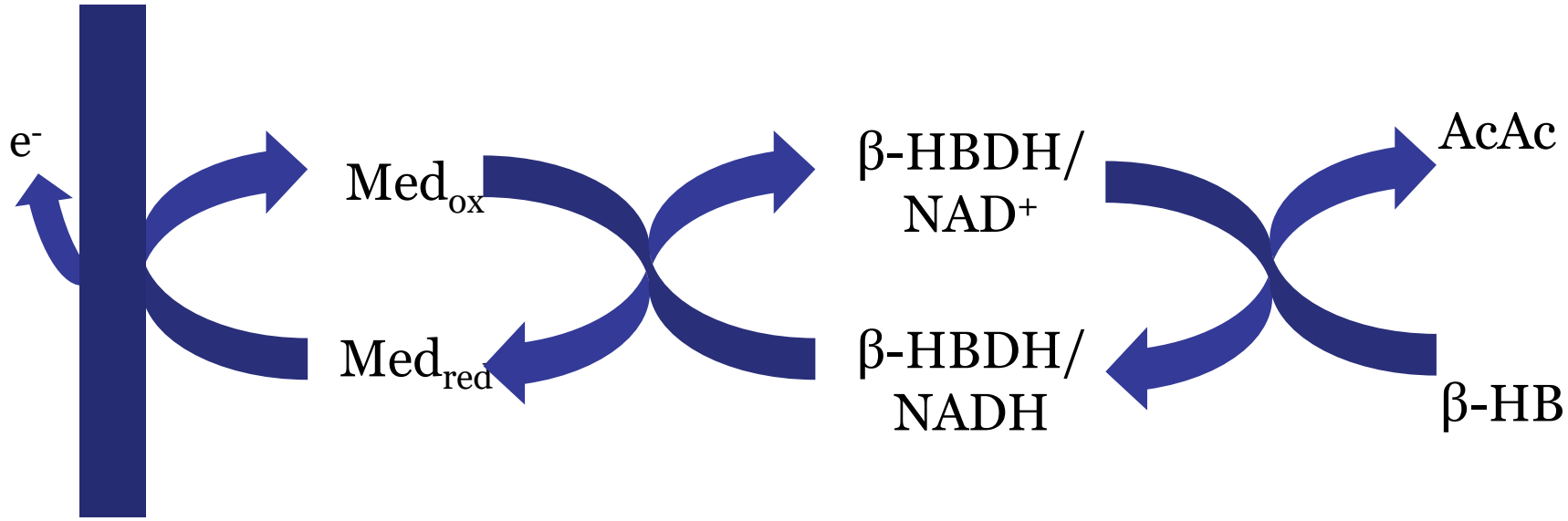
Blood ketone testing

- Current ketone monitoring confirms ongoing DKA versus detecting its onset
- Patients rarely check their ketone levels as recommended due to cost and burden[1]
  - Only 20% own home ketone monitoring[2] and 33% of patients own out-of-date strip[3]
  - Patients avoid fingerprick blood testing[1]

1. Nguyen et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/1932296821104265
2. Foster et al, *Journal of Diabetes Technology and Therapeutics* (2019): https://doi.org/10.1089/dia.2018.0384
3. Larsson et al, *Internal Medicine Journal 2018):* https://doi.org/10.1111/imj.13798

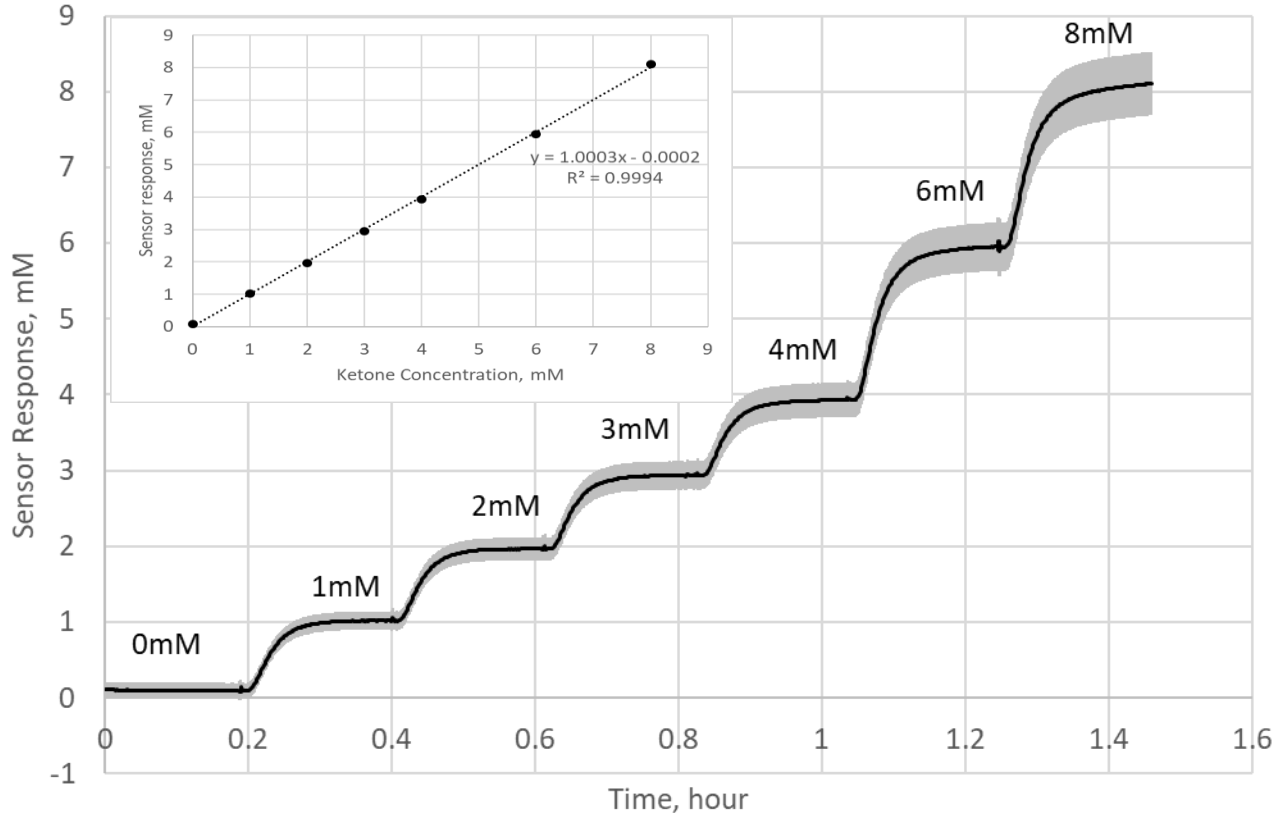
Continuous Ketone Monitoring – *In Vitro* Data

- Sensor structure and dimensions similar to FreeStyle Libre Sensor with ketone specific chemistry
- NAD^+ dependent β-HBDH and a proprietary redox mediation chemistry containing Osmium complex



Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

In vitro Performance Across Ketone Range



Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

First Human Continuous Ketone Monitoring

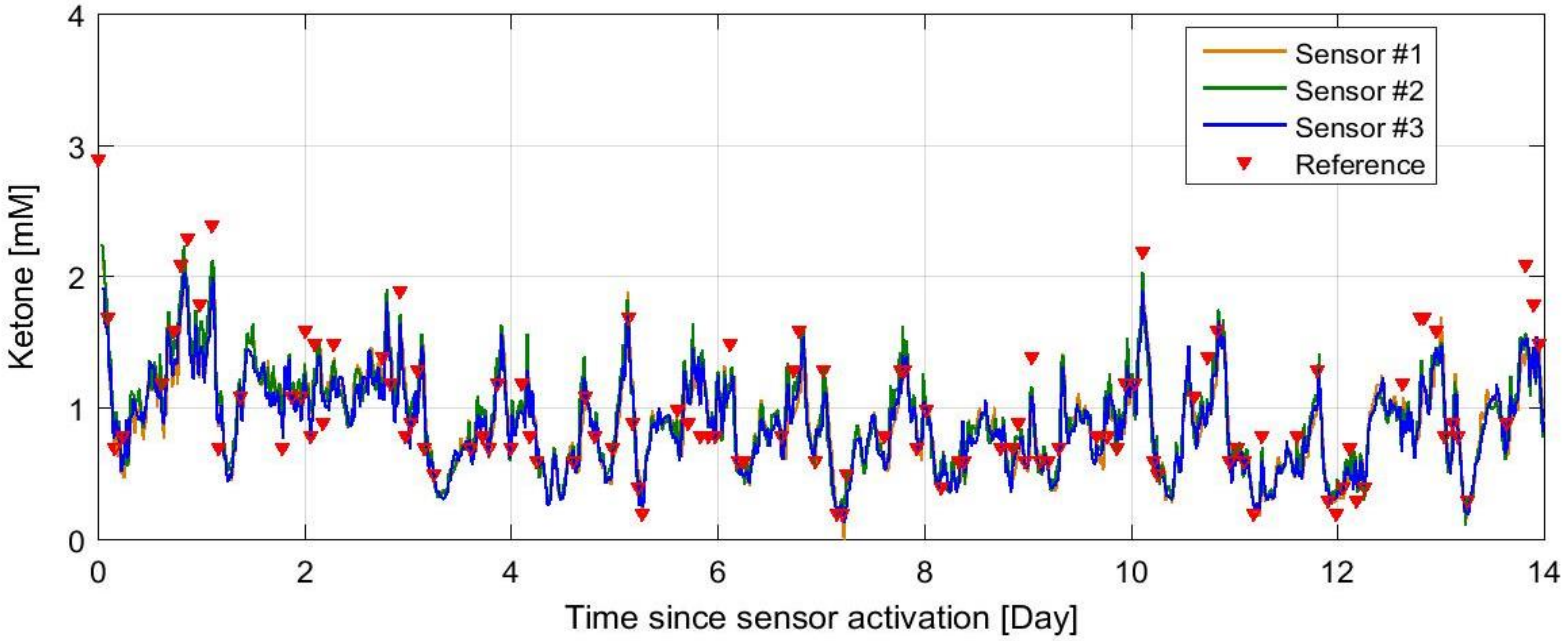
- First human study of Continuous Ketone sensor reported in 2021
- Study involved 12 participants practicing low carbohydrate diet
- Sensor in the FreeStyle Libre 2 form factor was used in the study
- Data reported with a single retrospective calibration of the sensor
- Demonstrated that ISF ketone levels track capillary ketone levels and can be measured over a 14-day period with these sensors

Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

In vivo Performance Over 14 Days

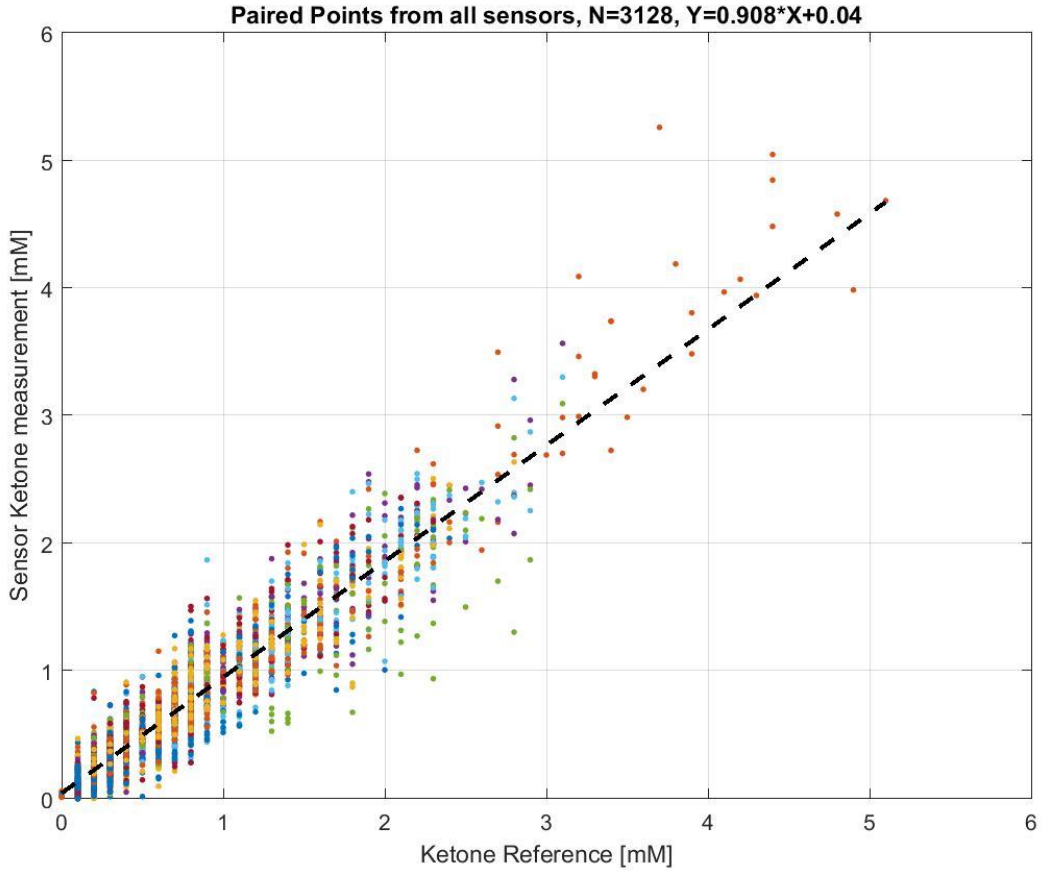
three sensors simultaneously worn by one subject

Capillary ketone reference



Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

In vivo Performance: Correlation with Capillary Ketone



Range	Percentage Within 0.3mM/ 30%	Mean MAD/ MARD	Paired Data Points
<1.5mM	91.7%	0.129 mM	2724
>= 1.5 mM	89.7%	14.4%	408
Combined	91.4%		3132

No adverse events reported

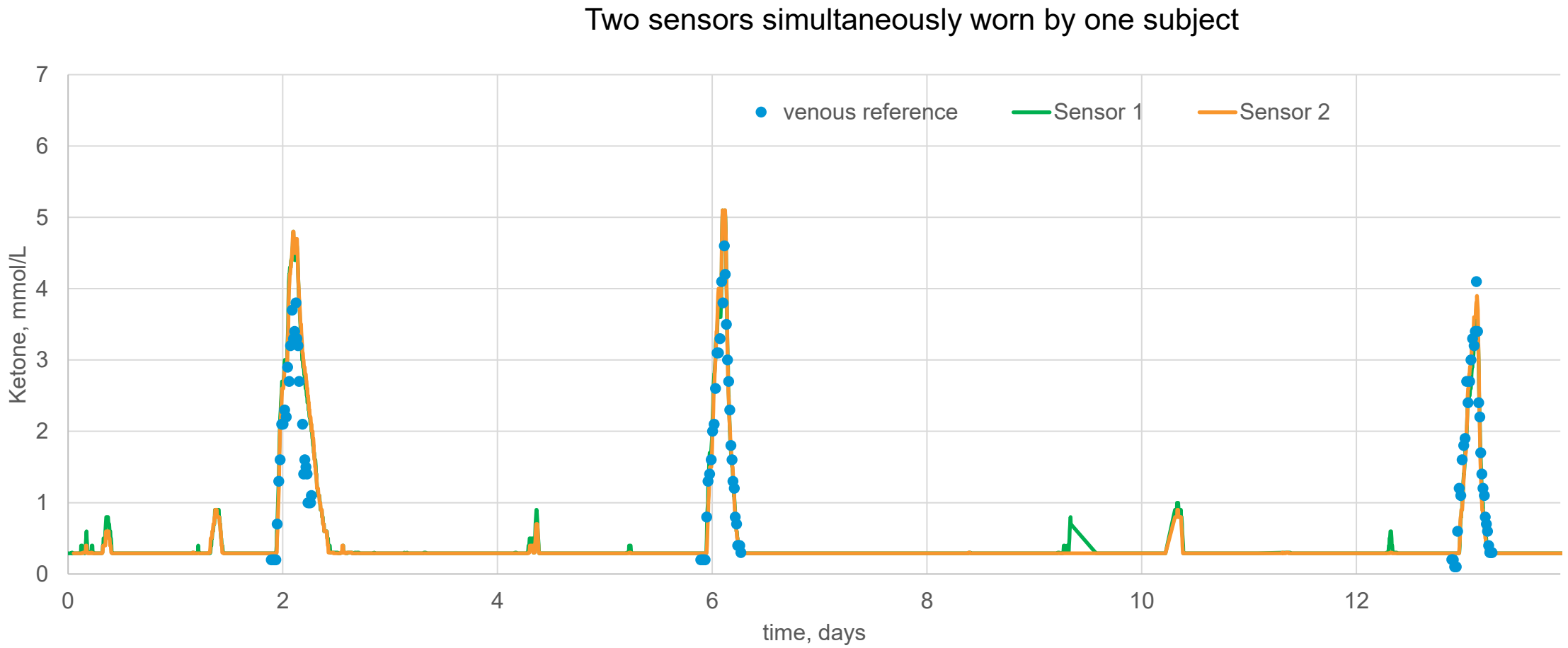
Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

In vivo Performance – Factory Calibration

- Study enrolled 36 participants with or without low carbohydrate diet
- Sensor in the FreeStyle Libre 2 form factor was used in the study
- Data collected with three unique factory calibration of the sensor lots
- Study participants consumed exogenous ketone to generate elevated ketone levels in a clinic setting
- Reference measurements with ketone strips were performed using venous blood using Precision Xtra ketone strip.

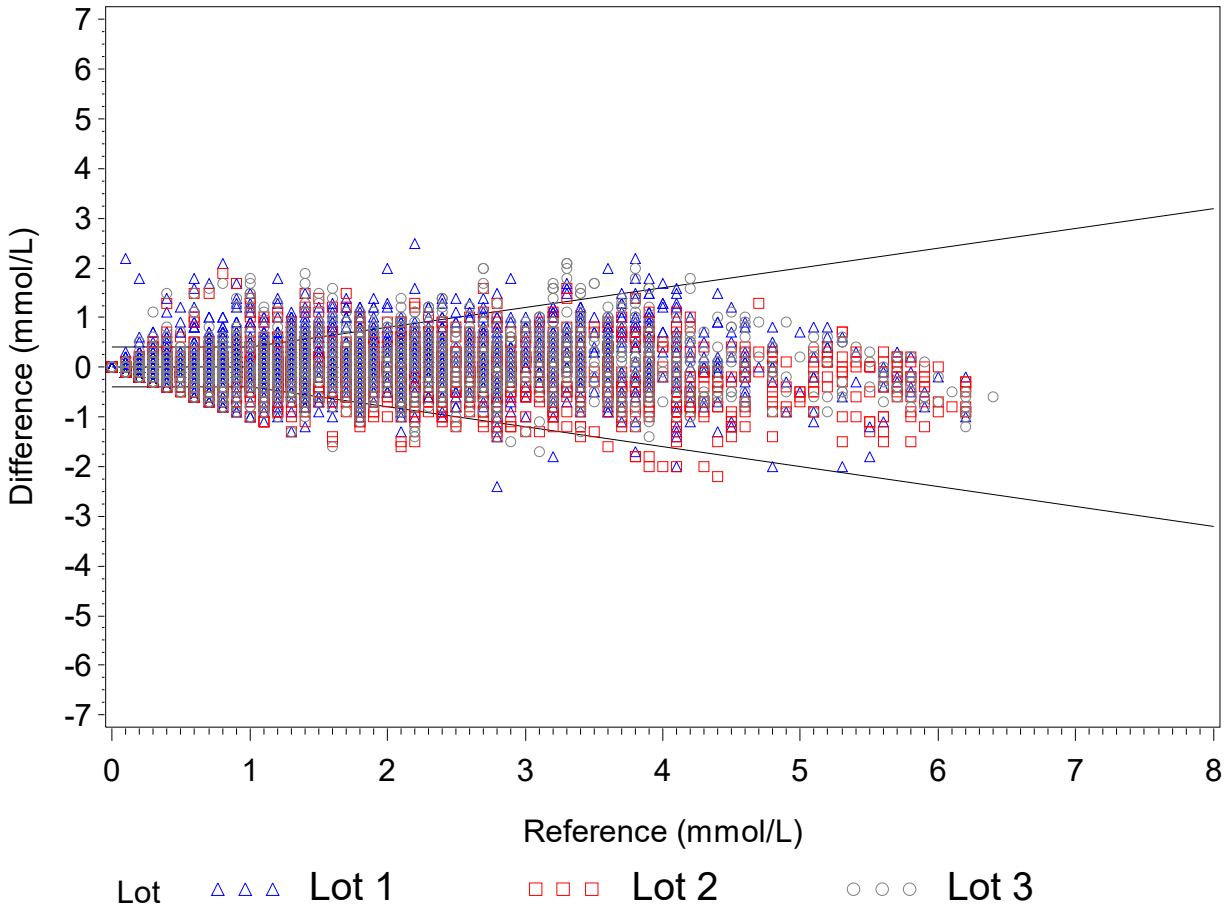
Data on file

In vivo Performance with Exogenous Ketone



Data on file

Sensor Performance against Venous Strip Reference



Percentage Within 0.3mM/ 30%	Percentage Within 0.4mM/ 40%	Mean Absolute Difference, mmol/L	Paired Data Points
85.0%	91.1%	0.30 ± 0.32	8922

Lag time is ~4 mins

No serious adverse events

3 mild application site symptoms
(pain and bruising)

Data on file

Integrated Continuous Glucose and Ketone Monitoring System

Integrated Continuous Glucose and Ketone Monitoring

- Designed to continuously monitor glucose and ketones levels every minute without scan
- Provide alarms for elevated and high ketone levels
- Leverages FreeStyle Libre 3 form factor
- Achieved US FDA breakthrough designation

Integrated continuous glucose and ketone monitoring system under development. Smartphone imagery for illustration purposes only. Not real patient data.

Current Status and Next Steps

- Ability to measure β-hydroxybutyrate in ISF has been demonstrated with good correlation between the sensor and blood ketone levels
- Sensor is stable over the wear duration
- The sensor can be factory calibrated and responds quickly to changing ketone concentrations.