Integrating Ketone and Glucose Monitoring for Optimized Diabetes Management

Beyond the Strip: Innovations in Ketone Monitoring and Clinical Applications

Stay ahead of the curve—explore cutting-edge ketone monitoring systems and clinical trial insights shaping the future of patient care

Current methods for ketone measurement include urine, capillary blood, or breathalyzer testing, which all come with certain limitations:[1-3]

- Urine ketone strips, while inexpensive, only measure acetoacetate and not ß-hydroxybutyrate (BHB), making urine ketone testing unreliable for monitoring progression or resolution of diabetic ketoacidosis (DKA).
- Blood ketone monitors for BHB, while the preferred test for self-monitoring during illness and hyperglycemia, can be inconvenient, potentially painful, and relatively expensive.
- Breath analyzers, while convenient and less painful than finger sticks, do not measure BHB, are expensive, and lack an evidence base for their accuracy and dynamic range.

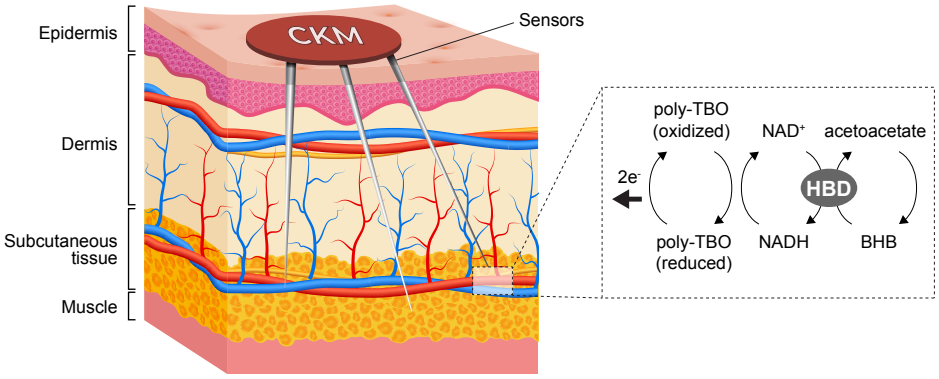
Therefore, continuous ketone monitors (CKMs), an emerging technology that offers real-time tracking of ketone levels, are under development to improve early detection of clinically significant ketosis and ketoacidosis, which will allow for timely intervention and improved metabolic control.[1]

CKMs detect BHB in interstitial fluid (ISF) rather than in blood or urine.[4]

Two types of CKM sensors have been proposed so far:

- **Electrochemical sensors:** measure ketone levels in ISF using enzymatic reactions that generate an electrical signal proportional to ketone concentration.[4]
- **Optical sensors:** optical methods analyze changes in light absorption caused by ketone bodies.[7]

Schematic illustration of continuous monitoring of BHB in ISF using a microneedle sensor[5,6]



β-hydroxybutyrate dehydrogenase (HBD) reduces NAD+ into NADH and oxidizes BHB to acetoacetate. NADH is in turn oxidized at the electrode surface to generate a current proportional to BHB concentration.

CKM=continuous ketone monitor; HBD=β-hydroxybutyrate dehydrogenase; Poly-TBO=electropolymerized toluidine blue O.

Recent studies have demonstrated the feasibility of CKMs:

- A combined continuous glucose monitor (CGM) and CKM system using subcutaneous electrochemical sensors that measure BHB levels is currently under development and has received US Food and Drug Administration (FDA) breakthrough device designation.[4,8]
- Another device measuring ISF ketone levels includes a microneedle sampling method with a sensor array. A pilot study demonstrated the ability of this sensor to detect BHB levels with similar correlation trends to standard blood BHB profiles.[6]
- An implantable near-infrared spectroscopy sensor measuring optical transmittance in ISF was well tolerated and produced accurate measurements of ketones, as well as glucose, lactate, and ethanol, in an early feasibility study (GLOW, NCT04782934).[7]

Populations likely to benefit most from CKMs include:[9]

- Children with type 1 diabetes (T1D)
- Pregnant women with T1D
- Individuals with recurrent DKA
- Individuals on SGLT inhibitors or low-carbohydrate diets
- Individuals performing high-intensity exercise
- Individuals with diabetes living in rural areas, away from emergency rooms/hospitals
- Individuals fasting for procedures

KEY MESSAGES

- Current methods for ketone measurement, including urine, capillary blood, and breathalyzer testing, all come with certain limitations.
- Integrating CKMs with traditional glycemic control measures, such as CGMs, holds substantial promise for improving metabolic safety and treatment precision in diabetes management.
- Ongoing research and technological improvements are expected to address current challenges, paving the way for the integration of CKMs into standard diabetes management protocols.

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