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Short Communication

Sweat test for cystic fibrosis: Wearable sweat sensor vs. standard laboratory test☆

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Abstract

Background: Sweat chloride testing for diagnosis of cystic fibrosis (CF) involves sweat induction, collection and handling, and measurement in an analytical lab. We have developed a wearable sensor with an integrated salt bridge for real-time measurement of sweat chloride concentration. Here, in a proof-of-concept study, we compare the performance of the sensor to current clinical practice in CF patients and healthy subjects.
Method: Sweat was induced on both forearms of 10 individuals with CF and 10 healthy subjects using pilocarpine iontophoresis. A Macroduct sweat collection device was attached to one arm and sweat was collected for 30 min and then sent for laboratory analysis. A sensor was attached to the other arm and the chloride ion concentration monitored in real time for 30 min using a Bluetooth transceiver and smart phone app.
Results: Stable sweat chloride measurements were obtained within 15 min following sweat induction using the wearable sensor. We define the detection time as the time at which the standard deviation of the real-time chloride ion concentration remained below 2 mEq/L for 5 min. The sweat volume for sensor measurements at the detection time was 13.1 ± 11.4 μL (SD), in many cases lower than the minimum sweat volume of 15 μL for conventional testing. The mean difference between sweat chloride concentrations measured by the sensor and the conventional laboratory practice was 6.2 ± 9.5 mEq/L (SD), close to the arm-to-arm variation of about 3 mEq/L. The Pearson correlation coefficient between the two measurements was 0.97 highlighting the excellent agreement between the two methods.
Conclusion: A wearable sensor can be used to make real-time measurements of sweat chloride within 15 min following sweat induction, requiring a small sweat volume, and with excellent agreement to standard methods.

Keywords: Sweat test; Cystic fibrosis; Sweat rate measurement; Wearable sweat chloride sensor; Personalized medicine

1. Introduction

Determination of sweat chloride concentration is the gold standard bioassay for diagnosis of cystic fibrosis (CF) and involves: sweat induction, sweat collection, transportation to a laboratory, and laboratory analysis [1]. The goal of this work is to develop a wearable sweat chloride sensor to enable real-time measurements and eliminate the need for sweat collection, handling, and laboratory analysis.

Recently, several groups, including us, have reported wearable sweat chloride sensors for CF diagnosis [2–6]. We have developed a potentiometric sweat sensor with integrated salt bridge to enable reliable measurements over extended periods of time [2,3] (Fig. 1). Here, we compare real-time

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Fig. 1. Wearable sweat sensor and mobile app. (A) Schematic illustration of the sweat chloride sensor. (B) Sweat sensor with integrated salt bridge, Bluetooth wireless transceiver, and mobile application on a smart phone. (C) Captured image of the mobile application during a sweat test.

measurement using the wearable sensor with Bluetooth transceiver and a mobile app (Fig. 1A,B), to a conventional sweat test in 10 individuals with CF and 10 healthy subjects. The Bluetooth transceiver connects the wearable sensor to a smart phone, and the mobile app converts the sensor output to sweat chloride concentration in real time (Supplementary video 1). In this proof-of-concept, we compare the time of the measurement, the sweat volume required to make a measurement, and the measurement accuracy between the wearable sweat sensor and the conventional sweat test.

2. Methods

Simultaneous measurements of sweat chloride were performed using the wearable sensor and a standard clinical protocol (Fig. 2A) on 10 individuals with CF and 10 healthy subjects (CF: male = 4, female = 6, age = 28.9 ± 7.4 years (SD); healthy individuals: male = 1, female = 9, age = 35.0 ± 12.1 years (SD)). First, pilocarpine iontophoresis was performed on both arms for sweat induction (Fig. 2B and E). A Macroduct (Wescor) was attached to one arm for sweat collection (Fig. 2C). Sweat collection was stopped after 30 min or when Macroduct was filled. The sweat sample was transferred to a 0.2 mL PCR tube and sent to the Johns Hopkins Chemical Laboratory and analyzed by coulometric titration (Wescor ChloroCheck® Chloride meter) (Fig. 2D) using the same protocol as clinical samples. A sensor was attached to the other arm using an adhesive bandage (Fig. 2F). The sweat chloride concentration from the sensor was monitored in real time using the smart phone app (Fig. 2G).

All sensors were calibrated before each trial at room temperature (25 °C), and adjusted to skin temperature (31.5 °C) using the Nernst Equation [2]. Calibration curves were obtained by sequentially immersing the sensor in 10, 50 and 100 mEq/L of NaCl for 3 min at each concentration. For each sensor, the results from two calibration curves were averaged. To measure sweat volume as a function of time, we took images of the Macroduct during the tests. From calibration tests and using custom software (Supplementary Information), we determined the sweat volume as a function of time. In our analysis, we assume that the sweat rates on the left and right forearms are the same [7,8]. All

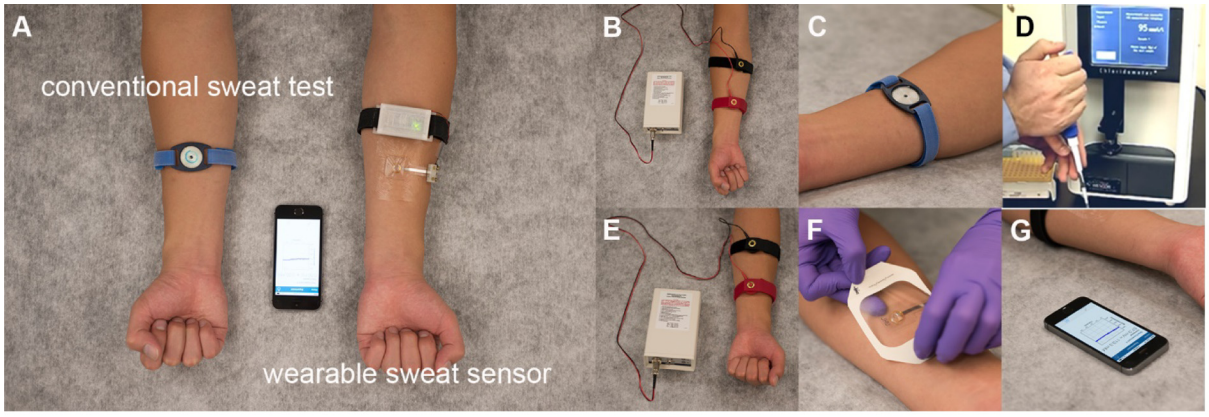

Fig. 2. Assessment of the performance of the wearable sensor. (A) Measurement of sweat chloride using the wearable sensor and standard clinical practice. (B–D) Protocol for conventional sweat testing: (B) pilocarpine iontophoresis, (C) sweat collection using a Macroduct (Wescor), and (D) laboratory-based sweat chloride analysis. (E–F) Protocol for testing using the wearable sensor: (E) pilocarpine iontophoresis, (F) wearable sensor and Bluetooth wireless transceiver, and (G) monitoring sensor results in real time using a smart phone app.

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