Monitoring Hgb Concentration in Athletes

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Summary:

Ember is a new product, developed at Cercacor for the endurance athlete, which measures blood hemoglobin concentrations, [Hgb], non-invasively. The technology is meant to help athletes improve their athletic performance by measuring and tracking the impact training has on [Hgb].

The trend accuracy of the Ember device, defined as its ability to detect changes in [Hgb] when compared to changes in [Hgb] detected by an invasive method, was found to be within 0.7 g/dl at one standard deviation. This finding takes into consideration errors that could be introduced from placement of Ember sensors and, therefore, is indicative of real-world performance.

Background:

Ember is the world's first non-invasive hemoglobin tracking system for endurance athletes, which consists of a sensor and a device that connects to your smartphone. In order for Ember to have utility as a monitor for athletic performance, the device should be capable of accurately detecting changes in hemoglobin associated with intensity, elevation or duration of a particular exercise program. This report provides an overview of a study that examined the ability of the technology used in Ember to detect changes in [Hgb]. The changes measured non-invasively with the Ember system were compared with corresponding changes measured in blood using an invasive laboratory method. Since the technology used in Ember is an extension of the principles of pulse oximetry, it is prone to the same errors from sensor placement on a finger. The report, therefore, also includes a study of sensor placement errors. All studies discussed in this report were conducted in compliance with appropriate regulations and guidelines for studies involving human subjects.

Test Protocols:

Protocol 1 (Repeatability study)

In order to assess the variability in measurements from placement of the Ember sensor, thirty healthy adult volunteers were trained in applying the sensor. Subsequent to training, each of them took five [Hgb] readings on the Ember sensor by detaching and reattaching the sensor to a finger between attempts.

Protocol 2 ([Hgb] Trending study)

In order to assess the ability of Ember to track hemoglobin, 266 healthy adult volunteers were enrolled in a hemodilution study. In this type of study, a subject has approximately one pint of blood removed through an arterial or venous line, followed by a rapid infusion with isotonic intravenous fluid (such as Ringer's Lactate or Isolyte) to compensate for the loss of blood, and thereby reduce the concentration of hemoglobin. During the hemodilution process, blood was drawn at regular intervals to be analyzed for hemoglobin concentration using an ABL Radiometer blood gas analyzer and, simultaneously, measurements were made using 6 Ember sensors on 6 fingers (ring, middle and index fingers from both hands). Data from the hemodilution protocol was used to compare changes in [Hgb] between the two modalities – Ember device and invasive instrument.

Results and Analysis

Repeatability Data and Results

In all 150 data points were obtained from thirty subjects and five repeat measures from each of them. There was one 'measurement incomplete' point due to low perfusion.

The intraclass correlation coefficient (ICC, an index of reproducibility of measurements with an ideal value of 1) for the 5 repeated measurements was found to be 0.90 with a 95% confidence interval (CI) of [0.84, 0.94], indicating a close agreement of one Ember [Hgb] measurement with another.

In addition, the medians of each subject's 5 measurements were correlated with the average of the 5 placement errors (see Appendix A as defined above) in order to look at whether the size of placement errors depended on the [Hgb] values. The correlation between the two was found to be 0.27 and the P value of the regression coefficient was 0.071, indicating that the placement errors were independent of [Hgb] measurements.

Since the placement errors are independent of the level of [Hgb] values on a given subject, a statistical distribution similar to the one obtained from placement errors will be added to the errors in all comparative results for protocol 2. A statistically similar distribution is obtained by resampling the placement error data, with replacement. The number of resampled points equals the number of data points used to analyze Ember's trend accuracy, as shown in the following section. The resampled data points will eventually be added to all subsequent trend analysis of Ember in the report. The histograms in Figure 1 were obtained from the original placement error data (panel A) and from resampling the data (panel B). The data show low values of placement error (mean 0.01 and SD 0.39 g/dl).

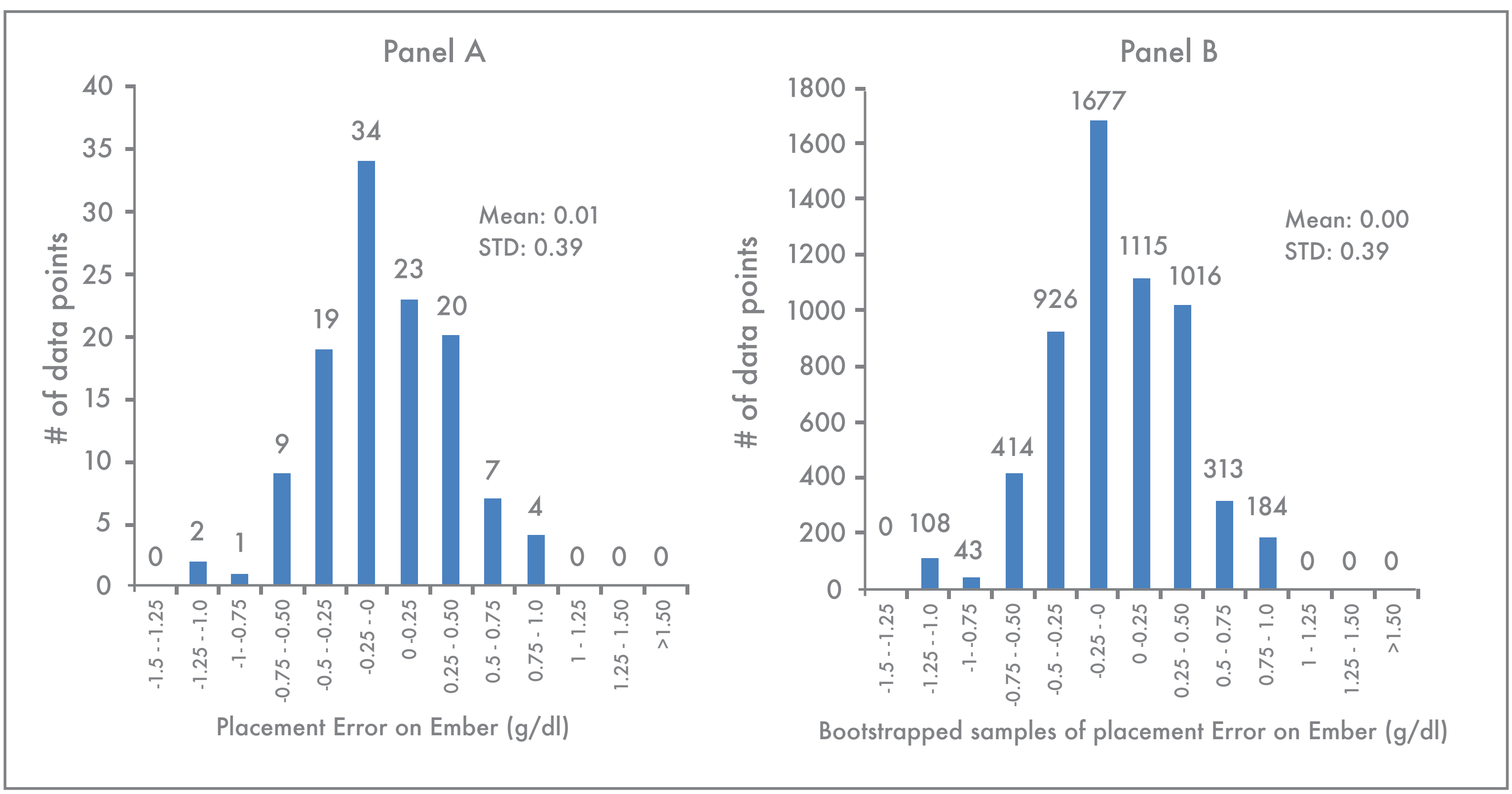

Figure 1. Distribution of placement error of Ember on a finger based on the original data (A) and resampled data (B).

[Hgb] Trend Data and Results

For the purpose of comparing changes in [Hgb] between consecutive arterial or venous blood samples (designated κ and κ + 1) in the hemodilution study, as measured with the Ember, to those measured with the ABL blood gas analyzer, the ΔΔ[Hgb] was calculted as follows:

ΔΔ[Hgb] = Δ[Hgb]Ember* – Δ[Hgb]ABL = ([Hgb]Ember, κ + 1 – [Hgb]Ember, κ) – ([Hgb]ABL, κ + 1 – [Hgb]ABL, κ)

*Resampled placement error data were added to all Δ[Hgb]Ember values before being used for analysis

In addition to the changes between consecutive blood samplings, changes from the first sample to all subsequent samples in a row were also compared. The combination of 266 subjects, 1-6 sensors, and 4-5 blood samples per subject during the hemodilution process yielded a total of 7039 samples.

Results from Protocol 2

Correlation analysis showed that the ICC was 0.71 with a 95% CI of [0.70, 0.72] (Figure 2). A frequency plot of ΔΔ[Hgb] is presented in Figure 3. The data show that the mean ΔΔ[Hgb] was 0.14 g/dl with an SD of 0.65 g/dl, resulting in a trend accuracy, defined quantitatively as √(mean^2+SD^2) , of 0.66 g/dl. These results indicate good agreement of Ember with the reference instrument.

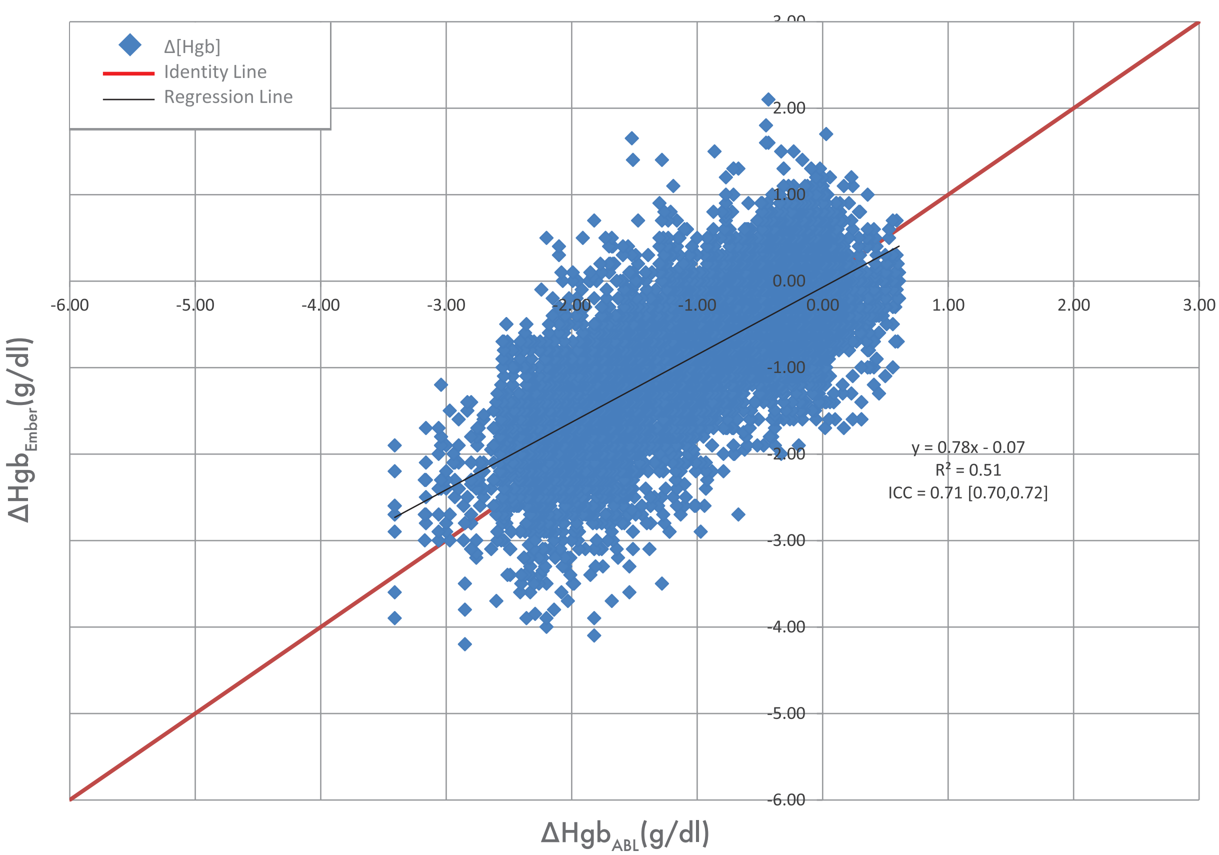

Figure 2. Scatter plot comparing [Hgb] changes as measured by Ember with [Hgb] changes as measured using an invasive method (ABL).

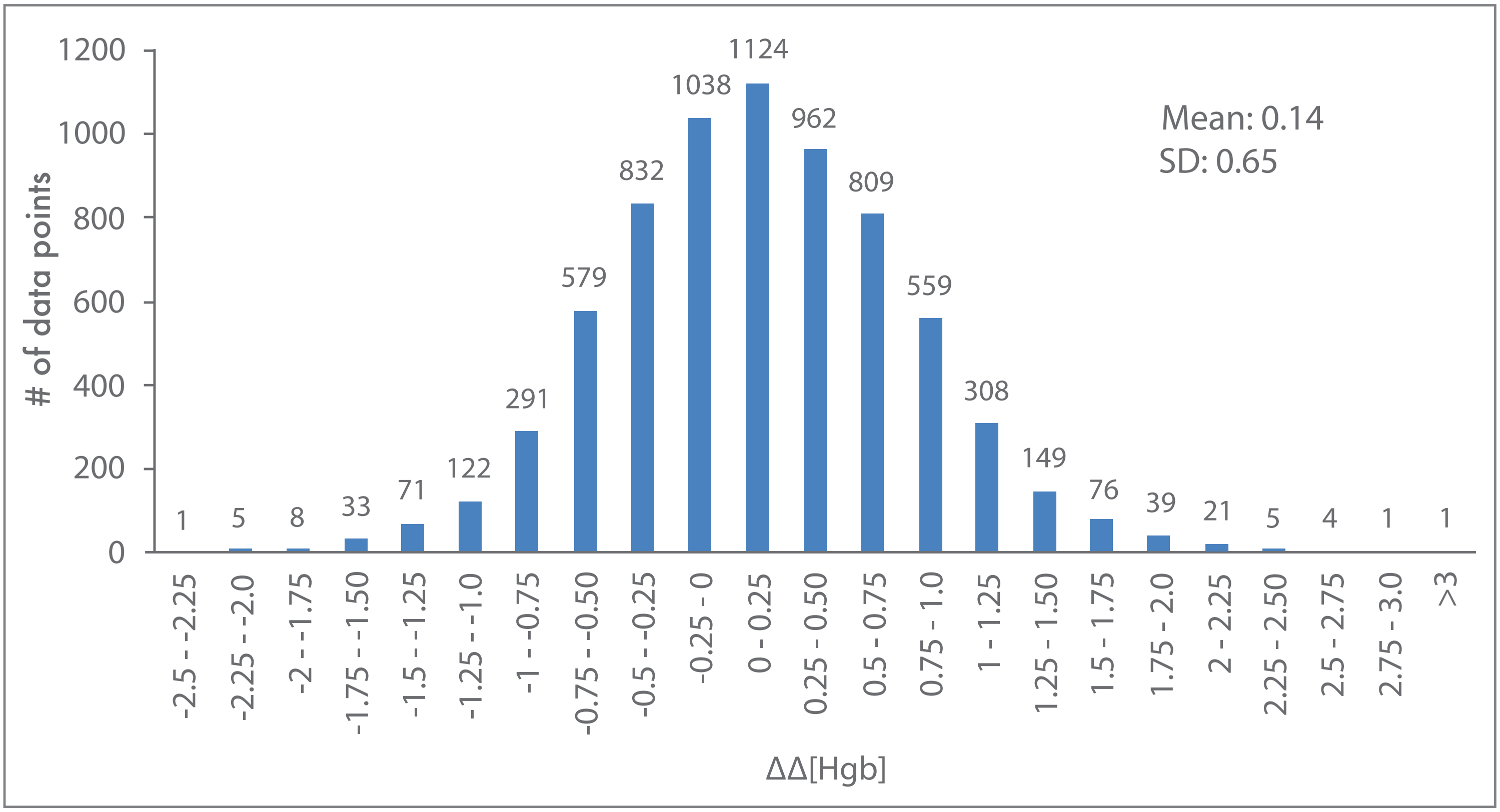

Figure 3. Histogram of error in measuring [Hgb] changes using Ember.

Conclusions

- Ember was shown to have low placement error, with high reproducibility of repeated measurements that involved attaching, detaching, and reattaching the sensor to a finger.
- Ember displayed good trend accuracy in measuring [Hgb] non-invasively when compared to an invasive reference.
- The above findings encourage further research to understand the potential use of Ember in measuring athletic performance.

Bibliography

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Appendix A:

Error introduced while placing an Ember sensor

Error introduced from placement was calculated by subtracting each of the 5 [Hgb] values measured on a subject from their median. Table 1 shows the data collected to assess placement errors from the Ember sensors.

Subject	Ember [Hgb] Placement 1	Ember [Hgb] Placement 2	Ember [Hgb] Placement 3	Ember [Hgb] Placement 4	Ember [Hgb] Placement 5
1	13.6	13.2	12.8	12.7	13.1
2	NA*	12.6	12	12.8	12.7
3	15.3	15.2	15	14.6	14.7
4	13.7	13.2	13.5	13.4	13.4
5	14	13.9	13.9	13.8	13.8
6	14.9	14.7	14	13.6	14.1
7	12.3	12	11.9	11.6	11.9
8	15.1	14.8	14.5	14.6	13.9
9	16.6	16.4	15.9	16.4	15.6
10	13.5	13.2	13.4	13.5	12.9
11	14.7	14.1	14	13.6	14
12	12.9	13.3	13.4	13.4	13
13	14.5	14.6	13.9	13.7	14.1
14	17.1	16	16.9	15.9	16.4
15	14.6	14.5	14.2	14.1	14.2
16	12.8	12.8	12.9	13.1	13.2
17	13.5	13.3	13.2	13.7	13
18	15.8	15	14.9	15	15.9
19	16.6	15.7	15.8	16.4	16.5
20	14	14.3	13.9	13.9	14.5
21	15.8	15.3	15.2	15	14.2
22	15.1	14.4	14.4	13.9	14
23	15.1	14.8	13.8	14.4	14.2
24	14.7	14.5	14.1	14	13.7
25	15.6	15.2	15.2	14.5	14.2
26	14.3	14.1	13.8	13.7	13.9
27	12.7	12.5	12.5	12.6	12.7
28	13.4	13.2	12.8	13.5	13.2
29	12.8	12.3	11.9	11.5	11.6
30	14.4	14	14	13.9	13.7

Table 1. Ember [Hgb] data (in g/dl) from 30 subjects, with 5 repeat measurements on each.

*Value was not displayed within the specified measurement time.