# Hemoglobin Validation

## *Introduction*

**Hemoglobin (Hb)** molecules are a set of very closely related proteins. Each Hb protein contains four iron atoms and can therefore carry four molecules of oxygen (O2). Hb attaches to red blood cells and delivers oxygen throughout the body with blood flow. The main function of Hb in mammals is to transport oxygen from the lungs to the organs and tissues. Moreover, it also specifically interacts with the 3 other gases, carbon dioxide (CO2), carbon monoxide (CO), and nitric oxide (NO), that have important biological roles. Hb also plays a role in helping red blood cells obtain their disc-like shape, which helps them move easily through blood vessels.[1–3]

Hb levels are usually assessed by a Hb blood test. A low level of Hb in the blood means there is also a low level of oxygen. This can result in a condition called anemia. Patients with anemia typically present with vague symptoms such as lethargy, weakness, and tiredness. Severe anemia may present with syncope, shortness of breath, and reduced exercise tolerance. Hb is usually measured in grams per deciliter (g/dL) of blood. Normal Hb levels are usually 13-18 g/dL in males and 12-15 g/dL in non-pregnant females.[4,5]

To obtain a blood sample for Hb evaluation, an invasive blood test measurement is needed. Replacing this method with a non-invasive, cheap, and remote technique is highly advantageous for availability, affordance, and usability.

PPG (photoplethysmography) is a non-invasive, simple, and low-cost tool that can reflect blood flow and blood volume changes in blood vessels. The PPG waveform comprises a pulsatile ('AC') physiological waveform attributed to blood volume changes with each heartbeat and is superimposed on a slowly varying ('DC') baseline with various lower frequency components attributed to respiration, sympathetic nervous system activity, and thermoregulation. PPG technology has been used in a wide range of commercially available medical devices to measure blood pressure, oxygen saturation, cardiac output, and to assess autonomic function.[6] Hb can also be evaluated by devices using PPG technology. FDA approved such a device in a range of 8-17 gr/dl with a measurement error of ±1 gr/dl.[7]

Camera-based approaches make it possible to derive remote PPG (rPPG) signals, and therefore might enable a remote and non-invasive measurement of blood parameters. Binah.ai’s Hb algorithm uses the rPPG signal recorded from facial skin tissue. The algorithm extracts face video images, produces an rPPG signal, analyzes the data using AI, and provides the end user with a Hb measurement in real-time.

This report describes the results of validation experiments that compare Binah.ai’s Hb evaluations with the results of regular, invasive blood tests.

## *Methods*

Binah.ai's Hb measurements were compared to the Hb values received in regular blood tests of healthy participants.

**Measurement set-up:**

Each participant was instructed to sit as stably as possible. Recordings were conducted in a testing room located in Binah.ai's offices, with controlled and fixed artificial ambient light. A mobile device was placed on a stand in front of the participant. The participant's face filled over 20% of the frame's area (distance of about 30cm) and was positioned in the center of the frame. The camera was set at the level of the forehead and positioned perpendicular to the face. Participants were instructed to look at the screen during the whole recording and to avoid any movement (including talking). Each recording lasted approximately 60 seconds.

**Statistical analysis:**

Accuracy was calculated using the following parameters:

$$AE\ (Absolute\ Error) = App_i - Ref_i$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^{N} (App_i - Ref_i)^2}{N}}$$

$$MAE = \frac{1}{n}\sum_{i=1}^{n} |App_i - Ref_i|$$

When,

*N* is the number of data points.

*App* is the measurement of the Binah.ai's application.

*Ref* is the reference results.

*i* is the index number of the measurements.

Confidence intervals (CI) were calculated using the bootstrap method and indicate where the estimator (i.e., RMSE) would fall in 95%, for future samples.

Participants with outlier AE (defined as 3 standard deviations or more above the mean) and participants with invalid reference device values were excluded from analysis.

For this report, the Binah.ai's SDK 4.10.1 version was used.
The measurements were recorded by the mobile device models listed below.
iOS: iPhone 11 Pro, iPhone 13 Pro, iPhone 13 Pro Max.
Android: Samsung S21 Ultra, Pixel 6 Pro.

## *Results*

**Demographic Data:**

**Table 1** includes participants' demographic data for each operating system (iOS and Android).

| Operating System | Number of Participants | Age Range (average) | Sex | Fitzpatrick Skin Tone * |
|---|---|---|---|---|
| **iOS** | 43 | 20-61 (30) | F (59%), M (41%) | 2 (41%), 3 (53%), 4 (6%) |
| **Android** | 42 | 20-61 (30) | F (57%), M (43%) | 2 (37%), 3 (56%), 4 (7%) |

**Table 1:** Demographic data for experiments using phones with an iOS and Android operating systems.
* Fitzpatrick skin tone classifications are: 1- Pale white, 2- white, 3- Darker white, 4- Light brown, 5- Brown, 6- Dark brown or black.

**Accuracy data:**

**Table 2** includes accuracy data for iOS and Android (RMSE, RMSE CI 95%, MAE±SD).

| Operating System | Blood Parameter | Number of measurements | RMSE | RMSE CI 95% | MAE±SD |
|---|---|---|---|---|---|
| **iOS** | Hb (g/dl) | 98 | 1.1 | [0.9, 1.2] | 0.9±0.6 |
| **Android** | Hb (g/dl) | 81 | 1 | [0.9, 1.2] | 0.8±0.6 |

**Table 2:** RMSE, RMSE CI 95%, and MAE±SD for experiments using phones with iOS and Android operating systems, when compared to the reference results. CI were calculated using the bootstrap method. Abbreviations: RMSE - Root Mean Square Error, CI - Confidence Intervals, MAE -Mean Absolute Error, SD - Standard Deviation.

Pearson correlations between Binah.ai's Hb estimations versus the results of regular invasive blood tests were calculated and presented in **Figure 1**. Pearson correlation coefficients (R values) are presented on the plots.

The Bland-Altman plots for comparison between measurements of the two methods (Binah's and the reference results) are presented in **Figure 2**.

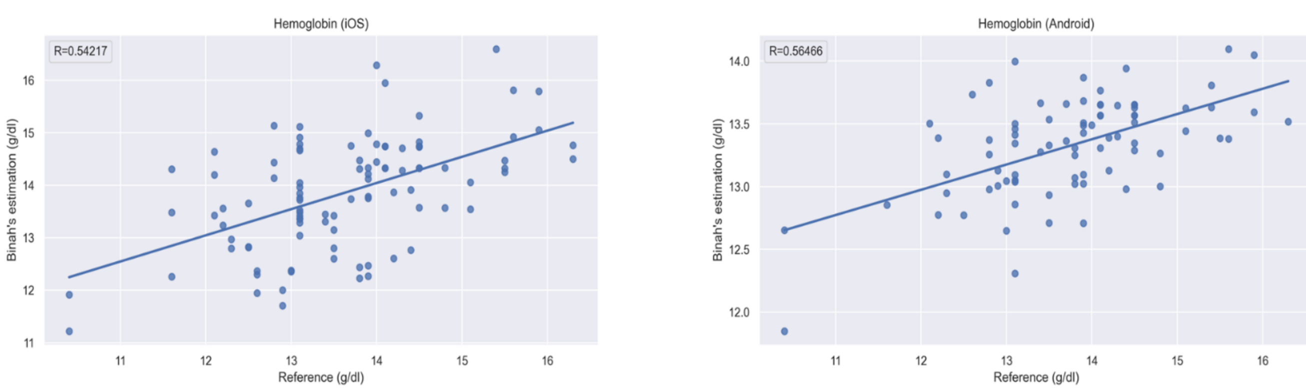


**Figure 1:** Binah.ai's Hb estimation vs. reference results. Pearson correlation was calculated, and correlation coefficients are presented on each plot (R). Plots describe measurements conducted with both operating systems (iOS and Android).

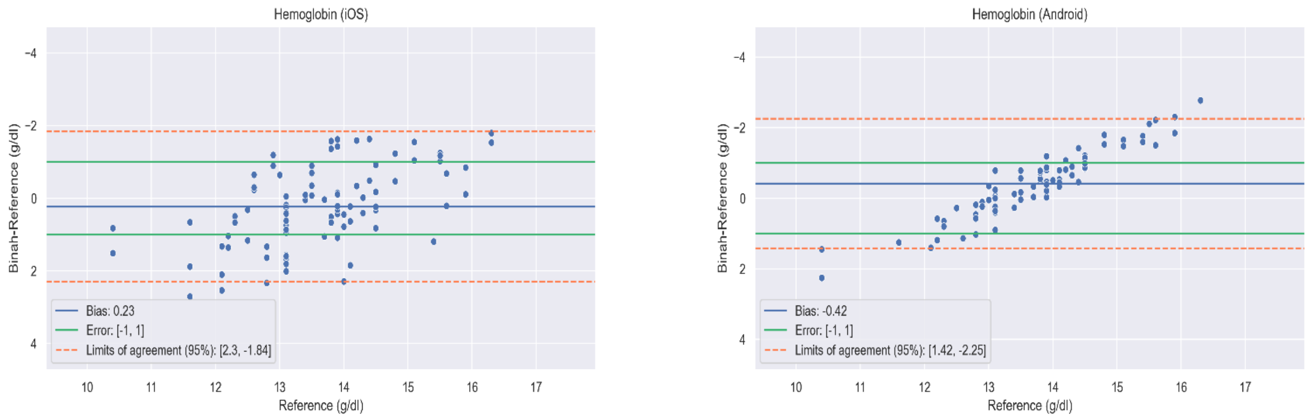


**Figure 2:** Bland-Altman plots for comparison between Hb measurements of the two methods (Binah's and the reference results). Plots describe measurements conducted with both operating systems (iOS and Android). The "Bias" line stands for the mean difference between measurements of Binah.ai and the reference results, the "Error" lines represent the value of the accuracy criterion, the "Limits of agreement" lines mark the limit of 95% of the samples.

## *Conclusions*

This report summarizes the results of validation experiments in which Binah.ai's Hb estimations were correlated with blood test results and had MAE, which is similar to an FDA-approved device[7].

## *References*

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