Annals of Biomedical Engineering (© 2015)
DOI: 10.1007/s10439-015-1247-1

BMES BIOMEDICAL ENGINEERING SOCIETY™ www.bmes.org

MouthLab: A Tricorder Concept Optimized for Rapid Medical Assessment

GENE Y. FRIDMAN,[1,2] HAI TANG,[1] DAVID FELLER-KOPMAN,[3] and YANG HONG[1]

[1]Department of Otolaryngology Head and Neck Surgery, Johns Hopkins University, Ross Bldg. 833, 720 Rutland Ave, Baltimore, MD 21205, USA; [2]Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21205, USA; and [3]Division of Pulmonary and Critical Care Medicine, Johns Hopkins University, Baltimore, MD 21205, USA

(*Received 19 October 2014; accepted 8 January 2015*)

Associate Editor James Tunnell oversaw the review of this article.

Abstract—The goal of rapid medical assessment (RMA) is to estimate the general health of a patient during an emergency room or a doctor's office visit, or even while the patient is at home. Currently the devices used during RMA are typically "all-in-one" vital signs monitors. They require time, effort and expertise to attach various sensors to the body. A device optimized for RMA should instead require little effort or expertise to operate and be able to rapidly obtain and consolidate as much information as possible. MouthLab is a battery powered hand-held device intended to acquire and evaluate many measurements such as non-invasive blood sugar, saliva and respiratory biochemistry. Our initial prototype acquires standard vital signs: pulse rate (PR), breathing rate (BR), temperature (T), blood oxygen saturation (SpO_2), blood pressure (BP), and a three-lead electrocardiogram. In our clinical study we tested the device performance against the measurements obtained with a standard patient monitor. 52 people participated in the study. The measurement errors were as follows: PR: -1.7 ± 3.5 BPM, BR: 0.4 ± 2.4 BPM, T: -0.4 ± 1.24 °F, SpO_2: $-0.6 \pm 1.7\%$. BP systolic: -1.8 ± 12 mmHg, BP diastolic: 0.6 ± 8 mmHg. We have shown that RMA can be easily performed non-invasively by patients with no prior training.

Keywords—Tricorder, Vital signs monitoring, Medical assessment.

INTRODUCTION

Rapid medical assessment (RMA) is obtained from measuring vital signs at nearly every doctor's visit, emergency room intake, EMT call, home care nurse visit, and at least daily for hospitalized patients. Whenever the measurements are taken, they require time and attention from a trained nurse/technician who obtains each of the various measurements from different parts of the patient's body. The state of the art commercial technology in obtaining vital signs are all-in-one monitors that continuously or periodically measure blood pressure, pulse rate, temperature, blood oxygen level (SpO_2), electrocardiogram (ECG), and respiration rate. While these units consolidate the measurements for a unified display and storage, they are optimized for hospital patient monitoring. In this setting attaching the sensors to the different parts of the body is sensible because the patient is often in bed for a prolonged duration. However during a doctor's office visit some vital signs may not be obtained because they take time and effort to attach these sensors to the body and some may cause discomfort. For example, brachial cuff inflation used for measuring blood pressure is often uncomfortable for the elderly, the obese, and can be contraindicated in patients who have had prior lymph node dissection. ECG measurements require undressing the patient and positioning electrodes on the torso, and respiratory rate is obtained from the ECG electrode impedance in the patient monitors. Additionally, these all-in-one monitors are expensive, and generally not available for home use.

During the RMA event, because of the short time allocated to the task, vital signs are often condensed into single numbers (such as heart rate), ECG is not recorded, and the breathing rate is often estimated or computed by observation over a short time.[6] However, vital signs contain considerable information about the patient's health that is often overlooked during RMA. For example the patient's pulse rate contains information about the average heart rate, but one can also observe the strength of pulse and pulse regularity to monitor hyper/hypovolemia, and arrhythmia. Respiratory pattern is indicative of respiratory distress and

Address correspondence to Gene Y. Fridman, Department of Otolaryngology Head and Neck Surgery, Johns Hopkins University, Ross Bldg. 833, 720 Rutland Ave, Baltimore, MD 21205, USA. Electronic mail: gfridma1@jhmi.edu

Published online: 21 January 2015

potential hypoxemia. It also contains information not only in rate, but also in its pattern and can be observed over time on a patient monitor.

Considerable effort has been put into innovating wearable monitors to allow patients to be more active while they are recovering from an illness and be able to monitor the progress of their recovery.[1,5] These devices have been optimized for long term monitoring, and attaching the devices to the patient still requires time and effort, making them less appealing for the RMA applications.

Monitoring of patients in the hospital often occurs in specific contexts. For example, patients with diabetes will have their blood glucose monitored. In contrast, during RMA, much of the patient's medical history may be unknown. Therefore, the technology used for RMA should be optimized to produce as many as possible accurate measurements to assess the general health of the patient. Because the event is by definition short, it should also do this rapidly and simultaneously, while alerting the provider for medical irregularities and requiring minimal training for the person who obtains the measurements.

Figure 1 diagrams our realization of a "tricorder"—a fictitious rapid health assessment device popularized in the television show Star Trek. The MouthLab is intended to collect vital signs and ultimately to also obtain biochemical and biophysical measurements from the saliva and breath, and estimate blood sugar level non-invasively. Saliva can be monitored for biomarkers indicative of diseases such as cardiovascular disease, oral and breast cancers, and periodontal disease.[11,16] Respiratory gasses can be monitored for markers of airway inflammation, metabolic disorders, diabetes, and renal and liver failure.[9,10] Access to blood through the mucous membrane of the mouth could allow non-invasive blood composition measures (such as blood glucose level[2,13,16]) to be more accurate and less dependent on individual calibration as would be required through skin. In principle many non-invasive measurements could be obtained using light and RF impedance spectroscopy.

We built a prototype of the MouthLab to obtain vital signs and an electrocardiogram (ECG) and optimized the device function with both a healthy population and hospitalized patients suffering from cardiac and respiratory illnesses.

MATERIALS AND METHODS

MouthLab Prototype

System Design

The MouthLab consists of a 9-volt battery-powered hand-held unit and an individual comfortable mouthpiece. The mouthpiece is plugged into the hand-unit, and the patient holds the unit themselves with the mouthpiece just behind the lips, similar to a scuba mouthpiece (Fig. 2). The mouthpiece and the hand-unit both contain sensors that acquire biological signals (Fig. 3). The circuit board located in the hand unit contains analog electronics to amplify, filter, and sample the signals from the sensors. Microchip PIC18F2420 microcontroller records the data every 5 ms (200 samples/s) from all sensors. After the samples have been acquired, they are assembled into a data frame and sent to a laptop *via* Bluetooth.

Our custom-designed C# software on the laptop receives each data frame from the MouthLab and disassembles it into the sensor samples. The new samples are appended to each sensor's data stream and analyzed and displayed on the laptop screen in real time. The frames are simultaneously stored for *post hoc* analysis. The software displays the data from the individual sensors as well as the processed data (e.g., SpO_2 is based on data obtained from red and infrared optodetector measurements).

The mouthpieces and the hand-unit were designed with Solidworks CAD (Waltham, MA) tool and built using a MakerBot 3D Replicator 2 (Brooklyn, NY) 3D printer with polylactic acid (PLA) biocompatible plastic. The mouthpieces connect electrically and physically to the hand unit with an RJ45 Ethernet connector. While the mouthpieces are intended to be disposable in the commercial version of the MouthLab when they are produced in large volumes, our prototype mouthpieces were sterilized between uses.

The sensing components located on the hand unit consist of a zinc ECG electrode, red and infrared (IR) LEDs, an optodetector (photodiode), and two microphones. The sensing components located on the mouthpiece consist of two ECG zinc electrodes, IR LED and a photodiode, and a thermistor (Fig. 3).

Temperature Acquisition

The temperature is detected at the bottom inside of the lower lip using a thermistor positioned on the mouthpiece.

SpO_2 Blood Oxygen Saturation Acquisition

Pulse oximetry is captured using the IR and red LEDs positioned at the location of the thumb on the hand-held unit. As in a standard pulse-ox detection scheme, the blood oxygen saturation is monitored by the relative absorbance of the light intensity in the red vs. infrared wavelengths. The red wavelength is partially absorbed by oxygenated hemoglobin, while the intensity of the infrared wavelength is unaffected by the oxygenated hemoglobin concentration.[14] Mouth-

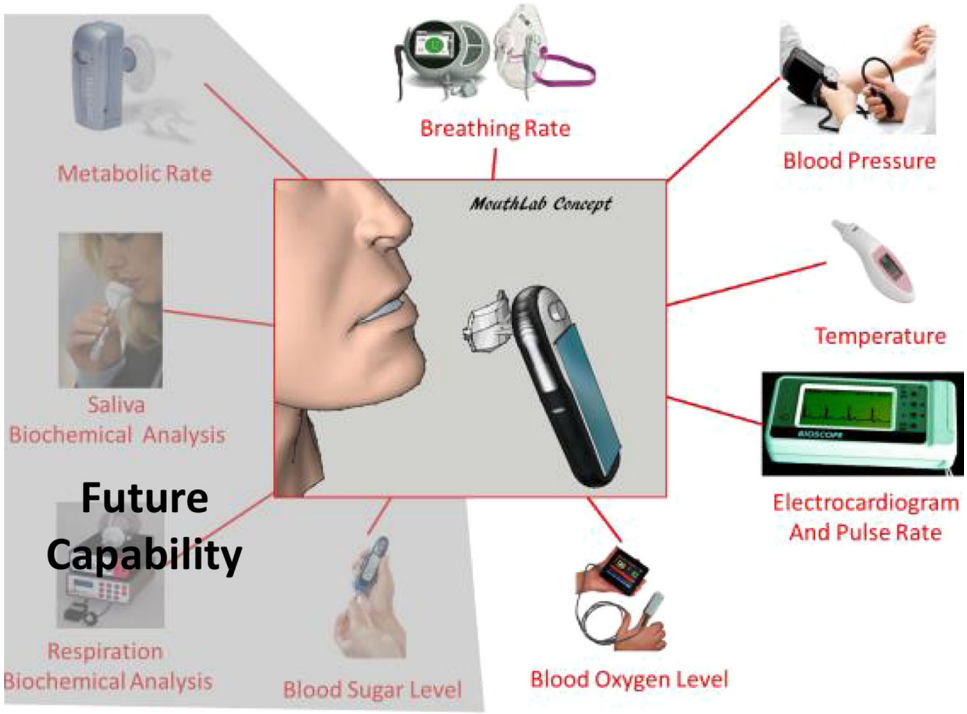

FIGURE 1. Our realization of a "tricorder"—a fictitious rapid health assessment device popularized in the television show Star Trek. The MouthLab is intended to collect vital signs and ultimately to also obtain non-invasive biochemical and biophysical measurements from the saliva and breath, and estimate blood sugar level. We built a prototype of this device to obtain vital signs and an electrocardiogram (ECG).

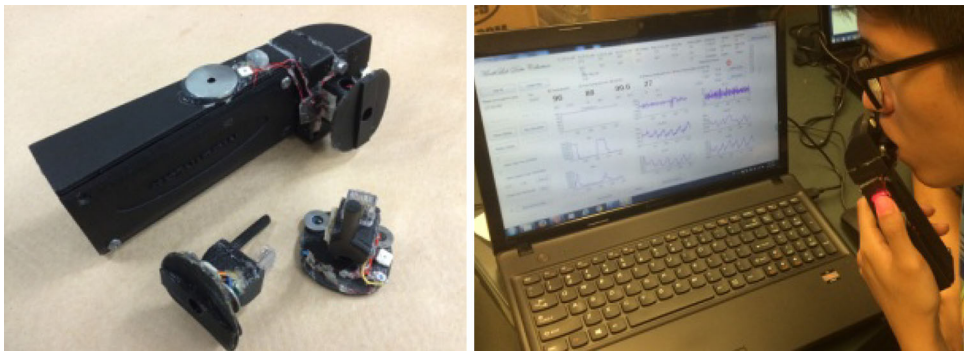

FIGURE 2. MouthLab hand-held unit with one attached mouthpiece, and two other mouthpieces (of the 25 total produced) on the left panel. The right panel shows the MouthLab being used by a subject with the data from the MouthLab sensors and vital signs estimates displayed on the laptop in real time.

Lab turns on the IR (850 nm) and the red (650 nm) LEDs sequentially for 200 μs each during the 5 ms acquisition window and samples the intensity of each wavelength with the optodetector as the light passes through the tissue.

To simplify the mechanical design of the hand unit, unlike the standard pulse oximeters that have the LEDs located on one side of the finger and the opto-detector on the opposite side, the optodetector is located on the same side of the thumb as the red and IR LEDs.

Pulse Rate Acquisition

Although the entire photoplethysmography (PPG) and ECG waveforms are available for more thorough analysis, pulse rate is measured by the inverse of the periodicity of the upper lip IR based pulse oximetry waveform.

Electrocardiogram Acquisition

The ECG is detected using a standard three-lead ECG circuit *via* three metal electrodes (ECG−,

ECG+, and ECGref). Instead of the typical placement of the electrodes on the leg and the torso however, the ECG+ electrode is positioned on the thumb, with the ECG− and ECGref electrodes positioned on the mouthpiece. The ECG− is in contact with the inner upper lip and the ECGref is in contact with the inner lower lip.

Breathing Rate Acquisition

The breathing rate is detected using two microphones positioned on the hand-held unit. One is used to acquire breathing signal from the nose and the other from the mouth after the breath passes through the stem of the mouthpiece. The information from the two microphones is added together in the software to allow the breathing pattern detection to be independent of whether the subject was breathing from the nose or the mouth.

Blood Pressure Acquisition

Systolic and diastolic blood pressure have been previously correlated with some success to the relative timing of the ECG and the finger-based PPG waveforms,[15] and to the blood flow velocities at the toe vs. the ear-lobe.[3,4] While these and other PPG and ECG based methods have not been universally successful in estimating blood pressure, there appears to be a relationship between the parameters extracted from these waveforms and blood pressure. Because this relationship is not well understood, we extracted all of the potentially relevant parameters from these waveforms and then used an artificial neural network to correlate these parameters to blood pressure.

MouthLab obtains blood pressure estimate as a function of 12 parameters that reflect the post-heart-contraction blood flow through the upper lip and the thumb (6 identical parameters each). The parameters are diagrammed in Fig. 4 on the close-up of the actual data recorded from the MouthLab. After the heart contracts (indicated by the R-wave of the ECG), the blood rushes to the upper lip and the thumb. This blood volume is monitored using an IR LED and an optodetector from the thumb (same ones used for the SpO_2 measurement) and the upper lip. In the figure, the two blood volume measurements are shown in black. We calculate the derivative of the volume waveform to obtain blood flow rate in the thumb and in the upper lip (only upper lip blood flow rate waveform is shown in the figure by a red dashed line).

The parameters used in BP estimation are the following: (A) time from heart contraction to the start of blood filling the tissue, (B) time from the start of blood filling the tissue to the peak blood flow into the tissue, (C) maximum rate of blood flow, (D) duration of blood flow (defined as being greater than half of the maximum blood flow rate), (E) time from completion of blood in-flow to the next heart contraction, (F) normalized integral of the blood volume.

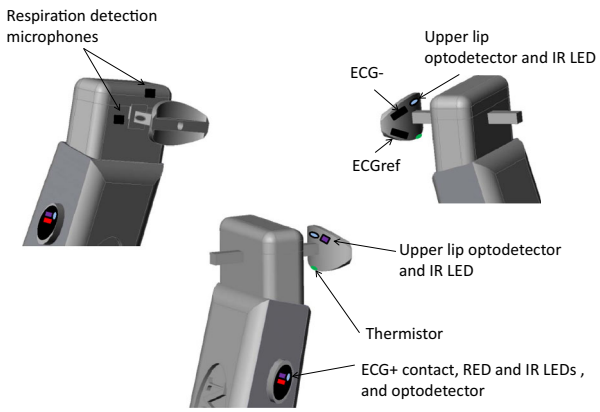

FIGURE 3. LED and sensor locations on the MouthLab hand-held unit and the mouthpiece.

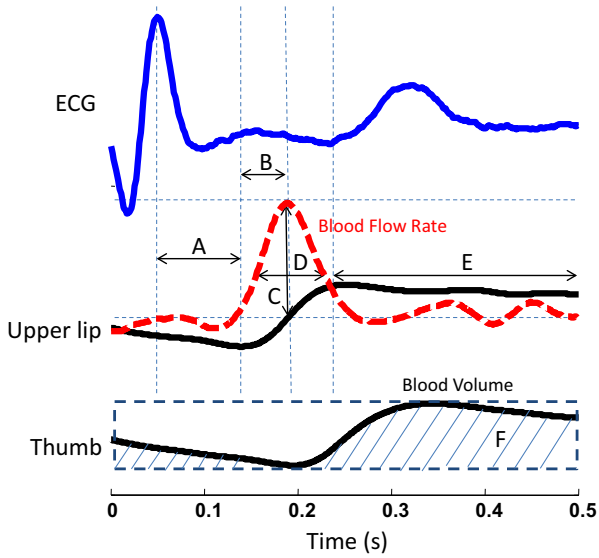

FIGURE 4. Parameters used for blood pressure estimation are acquired from the ECG and the simultaneously recorded blood volume measurements from the upper lip and the thumb. The black lines indicate the blood volume measurements and the red-dashed line, shown here for the upper lip only indicates the blood flow rate as the derivative of the blood volume. Six parameters are obtained at the upper lip and another six are obtained at the thumb. The five parameters A–E are diagrammed for the upper lip only. (A) time from heart contraction to the start of blood filling the tissue, (B) time from the start of blood filling the tissue to the peak blood flow into the tissue, (C) maximum rate of blood flow, (D) duration of blood flow (defined as being greater than half of the maximum blood flow rate), (E) time from completion of blood in-flow to the next heart contraction. The sixth parameter (F), relative integral of the blood volume to the total area of the rectangle is diagrammed for one cycle of the IR measurement on the thumb only.

We compute both systolic and diastolic blood pressure using a feed-forward artificial neural network with eight hidden nodes.[8] The inputs to the network are the blood volume and flow parameters recorded with the MouthLab and the output are the systolic and the diastolic blood pressure estimates. The actual blood pressure measurements used for comparison were obtained using a standard brachial sphygmomanometer from the DRE Waveline EZ+ (DRE Inc. Louisville, KY) patient monitor.

Experimental Methods for Human Studies

The human study protocol was reviewed and approved by the Johns Hopkins Institutional Review Board as IRB# NA_00080624. The protocol allowed us to recruit up to 200 adults for this study.

The purpose of the study was to optimize the performance of the MouthLab. In all cases we obtained the vital signs and the ECG using a standard FDA approved patient monitor and we then obtained the measurements using the MouthLab. This allowed us to optimize the hardware design as well as the algorithms used to extract vital signs measurements from the device.

While we were not attempting to diagnose any specific disorder, we recruited both ill and healthy subjects to broaden the range of all measurements that would be observed by the MouthLab. The healthy adult (18–65 years old) subjects were recruited through flyers posted throughout our research building. The ill adult subjects suffering from cardiac and pulmonary disorders were recruited by individually approaching the patients in the hospital wards. During the study, the healthy subjects were seated in a chair and the hospitalized subjects were reclining in their hospital bed. In all cases, the DRE Waveline EZ+ (DRE Inc. Louisville, KY) patient monitor was used to obtain actual measurements from the subjects. After obtaining informed consent, the ECG leads, blood pressure cuff, and pulse oximeter from the patient monitor were attached to the subject. The patient monitor measured the breathing rate *via* the impedance measurements obtained with the ECG electrodes. We acquired the temperature using a standard ear thermometer (Braun Thermoscan, Braun GmbH, Kronberg, Germany). After obtaining the standard measurements we instructed the subject on how to use the MouthLab and recorded the data for up to 15 min.

We manufactured and instrumented 25 mouthpieces for these studies. The mouthpieces used in the study were always washed and sterilized using benzalkonium chloride (Benz-All) chemical disinfectant. The mouthpieces were subsequently rinsed in sterile water and dried in a dedicated oven at low temperature (40 °C) for at least an hour and then individually packaged in sterile plastic bags.

After we obtained sufficient data from the study to complete hardware optimizations, we conducted a limited-scale study with the subsequent 52 subjects during which we suspended making any changes to the MouthLab hardware.

Estimating blood pressure required training the neural network (i.e., setting the weights). Because of the large number of weights in the neural network (112), we required the data from as many subjects as possible to train this network using the standard back-propagation algorithm.[8] A valid test data for any system (generally referred to as the "test set") must be independent from the data that were used to create the system ("training set") to avoid the system bias to work only with the data used to create it. In our application, it means that the accuracy of the neural network blood pressure prediction must be tested on subjects whose data were not used to obtain the weights of the network. Because we only had 52 subjects in our study, to maximize both the training set to create the most accurate neural network and the test set to be able to evaluate the accuracy of this neural network we used a standard statistical *bootstrapping* technique.

The bootstrapping technique in *post hoc* analysis was conducted as follows: The 12 parameters from the MouthLab (Fig. 4) plus the measured blood pressure for all subjects except one were used to obtain the artificial neural network weights using a back propagation algorithm. The neural network was then used to estimate the blood pressure from the MouthLab data for the one subject that was removed from the training set. We repeated this procedure for each subject enrolled in the study. In this way, the neural network blood pressure prediction was always tested on the MouthLab data from a subject whose data were NOT in the training dataset.

To ensure that we had as much training data as possible, we extracted seven 60 s-timeframes from the MouthLab data recordings for each of the 52 subjects. During the bootstrap, the training sets included all of the seven timeframes from each subject and none from the test subject. Of the seven collected timeframes, one random one was used to estimate the test subject's blood pressure during the test portion of the bootstrap procedure.

While the bootstrap technique is a standard statistical procedure, we wanted to assure ourselves that the tested blood pressure estimates were not dependent on of the bootstrapping technique itself. To conduct this control we repeated the entire bootstrapping procedure after we randomized the blood pressure measurements for all subjects. Our expectation was that the blood

pressure estimates from the scrambled dataset should not give a good prediction of the measured blood pressure unless the procedure itself somehow erroneously induced this result.

RESULTS

Prior to conducting the device accuracy study with the 52 subjects, we optimized the performance of the MouthLab with the help of approximately 80 other volunteers. In this first part of the study we freely made changes to the MouthLab hardware and electronics to improve the performance of the device. For example the use of the thumb (rather than the original sensor position at the lower lip) for acquiring ECG and pulse oximetry and the positioning of the IR LEDs and the optodetectors resulted directly from this optimization study. The more optimal locations of these sensors improved the noise tolerance for ECG detection and pulse oximetry by reducing the measurement artifacts due to varying lip thickness and lip muscle motion.

For the limited clinical trial we stopped making changes to the MouthLab hardware. Figure 5 shows a typical set of simultaneous sensor measurements obtained with the MouthLab. The respiration traces are overlaid to show the respiration data obtained by each microphone. The panel on the right shows the details of the traces, including the details of the ECG and pulse oximetry waveforms. The blood volume changes indicated in the IR and the red wavelength waveforms obtained from the thumb and the upper lip show the tissue filling with blood following each heart contraction seen in the ECG trace.

The temperature, SpO_2, pulse rate, and respiration rate obtained by the MouthLab for the study subjects are compared against the actual data obtained by the standard monitoring equipment Fig. 6. The measurement errors across population are as follows: PR: -1.7 ± 3.5 beats per minute, SpO_2: $-0.6 \pm 1.7\%$, BR: 0.4 ± 2.4 breaths per minute, T: -0.4 ± 1.24 °F, American National Standard ANSI/AAMI EC13:2002 cardiac monitor standard requires ±5 beats per minute accuracy. SpO_2 standard is ±4% in the range of 70–100% provided by ISO 9919:2005(E). The accuracy of breathing rate and temperature are typically stated relative to other FDA approved devices that exist on the market (e.g., Ramsey *et al.* [12]). Our FDA approved patient monitor that we used for data comparison had the specified accuracy of ±3 breaths per minute for respiration rate monitoring and ±0.2 °F for temperature.

Of the 52 subjects enrolled in the study, we could not use the data from seven of the subjects for the blood pressure estimates, resulting in 45 subjects that were included in the blood pressure study. We encountered hardware problems associated with the positioning of the IR LED and the optodetector on the mouthpiece and with the thumb pressure and its position relative to the sensors for some subjects. These problems prevented the PPG and the ECG parameters from stabilizing for the use in the blood pressure estimation algorithm. While we subsequently developed the solutions to these problems, we decided to not address them during the study in an effort to maintain study consistency.

Figure 7 shows the results of the blood pressure estimates obtained with the MouthLab compared to the cuff-based recordings obtained with the DRE patient monitor. For all subjects the average error in systolic measurement was -1.8 ± 12 mmHg, $R^2 = 0.7$, and the average error in the diastolic measurement was 0.6 ± 8 mmHg, $R^2 = 0.7$. The FDA accepted standard for blood pressure measurement devices is ±13 mmHg based on American National Standard ANSI/AAMI SP10:2002/A2:2006/(R)2008. As the measure of confidence in our blood pressure estimation, when we scrambled the blood pressure measurements for all subjects we obtained the expected high error of -3 ± 25 and -2 ± 16 for systolic and diastolic pressures respectively. The high error in BP estimates in this control indicates that the bootstrapping method per-se was NOT responsible for higher accuracy that we obtained with the MouthLab and supports the validity of the accuracy test.

Table 1 summarizes the statistical results for each of the measurements obtained in this human study. With the exception of SpO_2 that had a p value less than 0.05 ($p = 0.04$), p values for each measurement type do not reject the null hypothesis that there is no significant difference between the measurements obtained with standard equipment vs. those obtained with the MouthLab.

While conducting our evaluation of the MouthLab prototype we made qualitative observations of how the subjects used the devices and the potential difficulties that they encountered. One clear observation was that the subjects did not know where to put the mouthpiece in their mouth and they were apprehensive about the size of the mouthpiece. Many voiced a concern that their mouth was too small to accommodate the device. Once instructed to put the mouthpiece just behind the lips however, virtually all subjects readily accommodated and only two voiced subsequent concerns regarding the comfort of the device.

The thumb sensors (ECG, optical IR and red wavelength measurements) were affected by the pressure of the thumb on the detectors and skin hardness and temperature. Excessive pressure on the detectors increased the noise and reduced the signal fidelity for

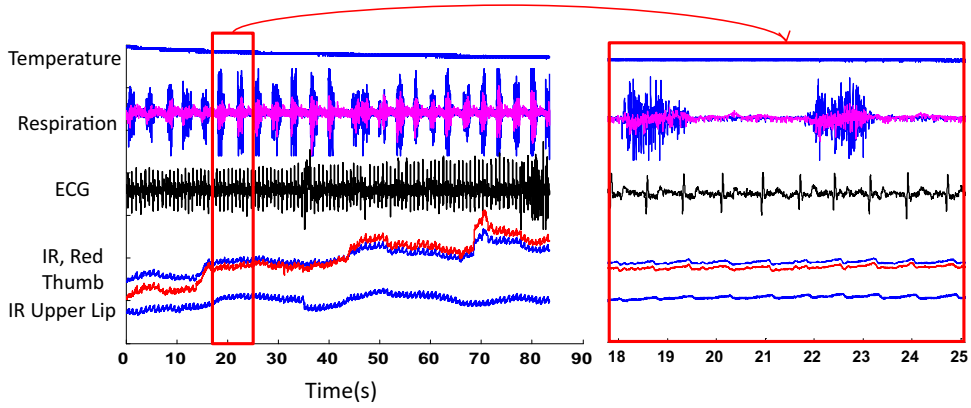

FIGURE 5. Typical set of sensor measurements obtained by the MouthLab. Respiration waveform shows the data from the microphone that acquires the breathing from the mouth superimposed on the data from the microphone that acquires breathing data from the nose. The waveforms sampled by the optodetector positioned on the thumb are shown for the IR and the red wavelengths in blue and red respectively.

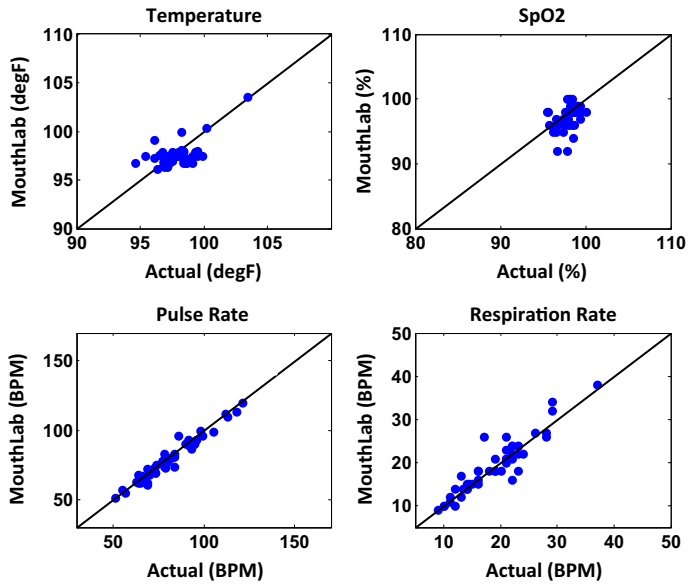

FIGURE 6. Comparison of vital signs acquired by the MouthLab to those acquired by the standard patient monitor. MouthLab measurements that exactly match the measurements obtained from the standard monitor will be located on the 45° line.

both ECG and optical measurements. These were possibly due to the restricted blood flow to the thumb due to excessive pressure. Cold skin (especially for hospitalized subjects in bed and perhaps indicative of poor circulation) resulted in low fidelity of the optical readings. In support of the poor circulation hypothesis, we also had trouble collecting the SpO_2 measurements using our standard equipment for these subjects. Hard skin on the thumb (perhaps due to lack of skin moisture) resulted in reduced amplitude of the ECG signal.

The optical and ECG detectors in the upper lip could suffer from reduced signal amplitude and increased noise due to lip movement or lack of contact between the inside of the lip and the detectors. The lack of contact was seen in cases in which a subject was missing teeth, but did not have dentures and in about 10% of the subjects in which the angle of the lip did not match well the curvature of the mouthpiece.

We did not encounter difficulties in the recording of the respiration or the temperature, except in the cases in which the subject had a breathing tube in either the nose or the mouth.

DISCUSSION

We developed a novel platform that is optimized for conducting rapid medical assessment. The key innovation of the MouthLab as a self-contained device is the ready access to saliva, breath, and the mucous

membrane. Access to these within one device could dramatically increase the number of possible biochemical and biophysical medical measurements obtained during rapid medical assessment in the future.

We built two prototypes of this device intended to measure vital signs. We conducted human studies in which we improved the location of the sensors, the shape of the mouthpiece, and the electronics of the device. We then conducted a limited clinical trial in which we compared the MouthLab estimates of the vital signs to those obtained using a standard patient monitor.

While the location and consolidation of the sensors near the mouth and the hand used to hold the device is novel, the technology used by the MouthLab to obtain SpO_2, pulse rate, breathing rate, ECG, and temperature is not new. SpO_2 and pulse rate commonly measured from the index finger, are instead collected from the thumb using the same optical measurement technology. ECG commonly obtained from the electrodes positioned on the torso, are instead collected the electrodes positioned on the thumb and the lip. Respiratory patterns commonly measured using the torso ECG electrodes' impedance, or by observations, are instead collected by the microphones positioned near the mouth and nose on the device. The temperature obtained from the mouth is quite analogous to that obtained by an oral thermometer. It is not surprising therefore that our results closely matched those obtained using standard means.

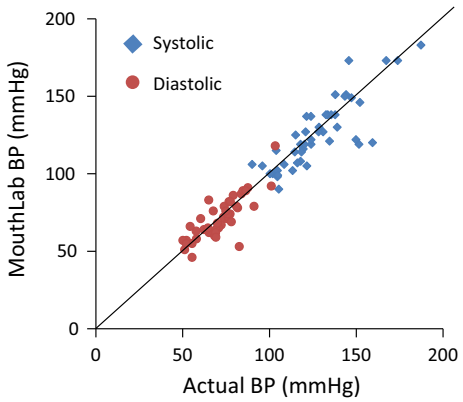

FIGURE 7. Blood pressure estimates obtained by the MouthLab compared to those acquired using a cuff from a standard patient monitor. For the 45 subjects the average error in systolic measurement was −1.8 ± 12 mmHg, R^2 = 0.7, and the average error in the diastolic measurement was 0.6 ± 8 mmHg, R^2 = 0.7.

Alternatively, developing a method for measuring blood pressure from the mouth and the thumb required considerably more effort than repositioning a sensor. The blood pressure is obtained from monitoring the timing and the patterns of the ECG and the blood volume and flow in the thumb and the upper lip. For this reason we devoted much of this manuscript to the description of both the measurement technique and the testing of the MouthLab blood pressure estimate accuracy. The device nearly matched the accuracy for blood pressure measurements that is standardized for sphygmomanometers, while not requiring the user to wear a brachial cuff. Because we used an artificial neural network is a general purpose computational algorithm to estimate blood pressure from optically observed blood volume and flow and ECG parameters, the physiological explanation of the mechanism behind blood pressure estimate is not clear and will need to be addressed in the near future.

One important advantage of using MouthLab for blood pressure assessment is removing the variety of extraneous factors that can affect the accuracy of the measurement. The error in blood pressure measurements can be high in RMA situations because of the inadequate medical training required to obtain the measurement accurately.[7] A variety of extraneous factors routinely affect both systolic and diastolic blood pressure accuracy by as much as 50 mmHg for systolic (cuff over clothing) and by as much as 11 mmHg for diastolic (unsupported arm).[7] Having

TABLE 1. Statistical comparison between the standard patient monitor measurements (Standard) and those obtained by the MouthLab.

	Standard	MouthLab	*p* value	Error
Pulse rate ($N = 52$)	80 ± 16 bpm	82 ± 16 bpm	0.65	−1.7 ± 3.5 bpm
SpO_2 ($N = 52$)	97 ± 2%	98 ± 1%	0.04	−0.6 ± 1.7%
Breathing rate ($N = 52$)	19 ± 6 bpm	19 ± 6 bpm	0.23	0.4 ± 2.4 bpm
Temperature ($N = 52$)	98 ± 1 °F	98 ± 1 °F	0.12	−0.4 ± 1.24 °F
Systolic blood pressure ($N = 45$)	128 ± 21 mmHg	126 ± 22 mmHg	0.69	−1.8 ± 12 mmHg
Diastolic blood pressure ($N = 45$)	72 ± 12 mmHg	71 ± 13 mmHg	0.83	0.6 ± 8 mmHg

The *p* value is the result of the two-tailed *t* test analyzing the null hypothesis that there is no significant difference between measurements obtained with the Standard equipment vs. those obtained with the MouthLab. *P* value less than 0.05 indicates a significant statistical difference between the two measurements. For each row, the errors are computed between the corresponding Standard and MouthLab measurements of each individual subject and then averaged to produce the Error estimate.

the subject take their own measurement with a device that is self-positioning like the MouthLab would make the measurements more consistent.

The qualitative challenges that we observed during the clinical trial will need to be addressed in the next version of the MouthLab. These can be addressed by improving the consistency and reliability of the device. To improve signal detection problems associated with inconsistent thumb pressure, we will develop a spring-loaded button that must be pressed to collect the measurements. To improve the lip-based measurements we will reshape the mouthpieces to more closely match the descending angle of the upper lip. Additionally we will improve optical signal fidelity to account for the users' anatomical mouth differences. We will add an automatic brightness control to the optical measurement circuitry to shine the LEDs brighter or darker depending on the amplitude and the fidelity of the observed signal.

Even with the added enhancements the user can still inadvertently compromise the measurement quality for example by erroneously holding the mouthpiece behind the teeth rather than behind the lips. We will provide an audiovisual feedback in form of a blinking LED and a tone to indicate low quality of the measurements. Finally, the user interface will have an indication for any measurement that is suspected of being low quality.

We envision that a near-term commercialization step in developing the MouthLab vital signs device will provide a summarized simple user display on the hand unit. It will also stream the sensor data *via* a cellular network to central cloud storage, rather than to the laptop PC as was the case with our prototypes. To make the MouthLab functionality independent of the cellular network availability, we will implement the algorithms in the firmware of the hand unit but with the ability to update the software *via* the cell network. The MouthLab will enable patients themselves with no required medical training to obtain a more complete rapid general health assessment in a doctor's office, emergency room, or at home. The results associated with this RMA event will immediately be available to the healthcare provider *via* internet access.

We believe that MouthLab as a concept provides a portable platform that could be extended further to acquire more biochemical and biophysical medical data from the saliva, breath, and mucous membrane. Ultimately with new measurements and more intelligent algorithms MouthLab will be able to not only record more data, but extract important aspects from the dataset (e.g., ECG and breathing irregularities), conduct basic diagnosis (e.g., possible heart attack in progress from an elevated ST ECG segment, or internal bleeding from increased Lactate saliva concentrations) and report potential health concerns using onboard expert system analysis.

ACKNOWLEDGMENTS

We thank Sunny Smith, Charles Della Santina, and Lani Swarthout for material support, helpful discussions, and contribution to the logistics associated with prototype development and human studies. We thank Divya Kernik, Lucas Fridman, and Alexandra Della Santina for their contribution to the early prototype designs.

REFERENCES

[1]Banaee, H., M. U. Ahmed, and A. Loutfi. Data mining for wearable sensors in health monitoring systems: a review of recent trends and challenges. *Sensors (Basel)* 13(12):17472–17500, 2013. doi:10.3390/s131217472.

[2]Caduff, A., M. S. Talary, M. Mueller, F. Dewarrat, J. Klisic, M. Donath, L. Heinemann, and W. A. Stahel. Non-invasive glucose monitoring in patients with Type 1 diabetes: a multisensor system combining sensors for dielectric and optical characterisation of skin. *Biosens. Bioelectron.* 24(9):2778–2784, 2009.

[3]Chen, W., T. Kobayashi, S. Ichikawa, Y. Takeuchi, and T. Togawa. Continuous estimation of systolic blood pressure using the pulse arrival time and intermittent calibration. *Med. Biol. Eng Comput*. 38(5):569–574, 2000.

[4]Chen, Y., C. Wen, G. Tao, and M. Bi. Continuous and noninvasive measurement of systolic and diastolic blood pressure by one mathematical model with the same model parameters and two separate pulse wave velocities. *Ann. Biomed. Eng* 40(4):871–882, 2012.

[5]Custodio, V., F. J. Herrera, G. Lopez, and J. I. Moreno. A review on architectures and communications technologies for wearable health-monitoring systems. *Sensors (Basel)* 12(10):13907–13946, 2012. doi:10.3390/s121013907.

[6]Elliott, M., and A. Coventry. Critical care: the eight vital signs of patient monitoring. *Br. J. Nurs.* 21(10):621–625, 2012.

[7]Handler, J. The importance of accurate blood pressure measurement. *Perm. J.* 13(3):51–54, 2009.

[8]Haykin, S. Neural Networks A Comprehensive Foundation. New York: IEEE Press, 1994.

[9]Martinez-Lozano, S. P., R. Zenobi, and M. Kohler. Analysis of the exhalome: a diagnostic tool of the future. *Chest* 144(3):746–749, 2013. doi:10.1378/chest.13-1106.

[10]Nair, P. Update on clinical inflammometry for the management of airway diseases. *Can. Respir J.* 20(2):117–120, 2013.

[11]Pfaffe, T., J. Cooper-White, P. Beyerlein, K. Kostner, and C. Punyadeera. Diagnostic potential of saliva: current state and future applications. *Clin. Chem.* 57(5):675–687, 2011. doi:10.1373/clinchem.2010.153767.

[12]Ramsay, M. A., M. Usman, E. Lagow, M. Mendoza, E. Untalan, and V. E. De. The accuracy, precision and reliability of

measuring ventilatory rate and detecting ventilatory pause by rainbow acoustic monitoring and capnometry. *Anesth. Analg.* 117(1):69–75, 2013. doi:10.1213/ANE.0b013e318290c798.

[13]Vashist, S. K. Non-invasive glucose monitoring technology in diabetes management: a review. *Anal. Chim. Acta.* 750:16–27, 2012. doi:10.1016/j.aca.2012.03.043.

[14]Webster, J. G. Medical Instrumentation Application and Design (4th ed.). Hoboken: Wiley, 2009.

[15]Yoon, Y., J. H. Cho, and G. Yoon. Non-constrained blood pressure monitoring using ECG and PPG for personal healthcare. *J. Med. Syst.* 33(4):261–266, 2009.

[16]Zloczower, M., A. Z. Reznick, R. O. Zouby, and R. M. Nagler. Relationship of flow rate, uric acid, peroxidase, and superoxide dismutase activity levels with complications in diabetic patients: can saliva be used to diagnose diabetes? *Antioxid. Redox Signal.* 9(6):765–773, 2007.