Circulation: Cardiovascular Imaging

ORIGINAL ARTICLE

Smartphone-Based Blood Pressure Measurement Using Transdermal Optical Imaging Technology

See Editorial by Mukkamala

BACKGROUND: Cuff-based blood pressure measurement lacks comfort and convenience. Here, we examined whether blood pressure can be determined in a contactless manner using a novel smartphone-based technology called transdermal optical imaging. This technology processes imperceptible facial blood flow changes from videos captured with a smartphone camera and uses advanced machine learning to determine blood pressure from the captured signal.

METHODS: We enrolled 1328 normotensive adults in our study. We used an advanced machine learning algorithm to create computational models that predict reference systolic, diastolic, and pulse pressure from facial blood flow data. We used 70% of our data set to train these models and 15% of our data set to test them. The remaining 15% of the sample was used to validate model performance.

RESULTS: We found that our models predicted blood pressure with a measurement bias±SD of 0.39±7.30 mm Hg for systolic pressure, –0.20±6.00 mm Hg for diastolic pressure, and 0.52±6.42 mm Hg for pulse pressure, respectively.

CONCLUSIONS: Our results in normotensive adults fall within 5±8 mm Hg of reference measurements. Future work will determine whether these models meet the clinically accepted accuracy threshold of 5±8 mm Hg when tested on a full range of blood pressures according to international accuracy standards.

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CLINICAL PERSPECTIVE

Cardiovascular disease is a leading cause of death and disability, and elevated blood pressure is a leading contributor to disease risk. Screening for, diagnosing, and following the response to therapy for hypertension are constrained by current measurement methods that are subject to variability because of a wide variety of potential measurement conditions over the course of one's daily activities. Traditional brachial artery blood pressure measurement devices are inconvenient, uncomfortable, and require special equipment because of their reliance on inflatable cuff-based technology. This study reports on a new technology called transdermal optical imaging that measures blood pressure continuously and without contact from video of a person's face. In this initial study on normotensive subjects, we show that this technology exhibits comparable accuracy to traditional automated blood pressure monitors. However, transdermal optical imaging technology implemented on a smartphone would improve upon traditional cuff-based devices by being more convenient and more comfortable (eg, cuff-less). This is likely to encourage measurements in more places and with more regularity than before and provides a comprehensive picture of patients' blood pressure throughout the day, much like an ambulatory blood pressure monitor. Such a tool could revolutionize hypertension diagnosis and management and begin to address the incredible burden of cardiovascular disease worldwide.

Clinically significant elevated blood pressure (BP; hypertension) afflicts >25% of adults worldwide.[1] Hypertension also constitutes a major modifiable risk factor for cardiovascular disease.[2] Nonclinic BP monitoring in the form of standard automated BP monitors and ambulatory BP monitors is highly recommended in dealing with this epidemic.[3] It provides patients and health professionals with a representative picture of a patients' BP throughout the day[4,5] and reduces the cost and inconvenience associated with clinic visits[6,7] in the diagnosis and management of hypertension. Nevertheless, nonclinic BP monitoring has not reached its full potential because standard automated BP monitors are not convenient to use outside of the home, and because ambulatory BP monitors are uncomfortable to wear throughout the day.[8,9] Therefore, a tool is needed that can accurately measure BP comfortably and conveniently anywhere and anytime.

Smartphones equipped with transdermal optical imaging (TOI) technology may meet these requirements. TOI is a recently developed variant of remote photoplethysmography for imaging blood flow patterns from video of the face[10,11] (Figure 1). Video-based photoplethysmography capitalizes on the following facts. First, because of the translucent nature of facial epidermis, ambient light can penetrate the epidermis and reach the tissue below, with some of it reflected back out of the skin.[12] Second, the digital optical sensors in smartphones are highly sensitive and thus can capture re-emitted light and its small attenuations.[13] Third, the quantity of hemoglobin protein in the blood and melanin pigment in the skin determines the color of light that is reflected back out of the skin. Each has a different color signature, so it is possible to separate re-emitted light containing mostly hemoglobin information from light containing melanin information based on the differential absorbance characteristics of these 2 light-absorbing proteins.[12]

TOI technology uses several state-of-the-art techniques in photoplethysmography[14] with respect to extraction of raw signal (eg, region of interest tracking, multiple raw signals, 3 color channels) and estimation of plethysmographic signal (eg, bandpass filtering). However, unlike any other video-based technology, TOI separates each video image into multiple layers called bitplanes[15] in each of the 3 color channels. Then, using a machine learning-based algorithm developed using blood flow data collected concurrently from an Federal Drug Administration (FDA) cleared BP measurement system (Methods in the Data Supplement), TOI extracts hemoglobin-rich signals and discards melanin-rich signals from each image of the video sequence. Next, the hemoglobin signals from all bitplanes of each frame of the video are recombined to produce an image representing a map of hemoglobin concentration across the face. By linking all the images together in their original sequence, it produces a video of hemoglobin concentration changes representing facial blood flow oscillations. This unique methodology produces a robust signal with minimal noise and minimal susceptibility to variations in skin tone.

In this study, we tested the hypothesis that information contained within these facial blood flow oscillations can indicate systolic, diastolic, and pulse BPs. This hypothesis is based on the following 3 existing sets of evidence. First, TOI already detects heart rate with accuracy equal to an ECG[11] and heart rate variability with comparable accuracy. This demonstrates that blood flow changes revealed by TOI technology correspond with the systemic cardiovascular changes engendered by the pulsating heart. Second, studies using photoplethysmography have shown that hemoglobin changes in the fingers contain important information about arterial pressures in the form of photoplethysmography waves.[13,16,17] While the information obtained from finger photoplethysmography is relatively homogeneous, TOI of the face is able to obtain such information from mul-

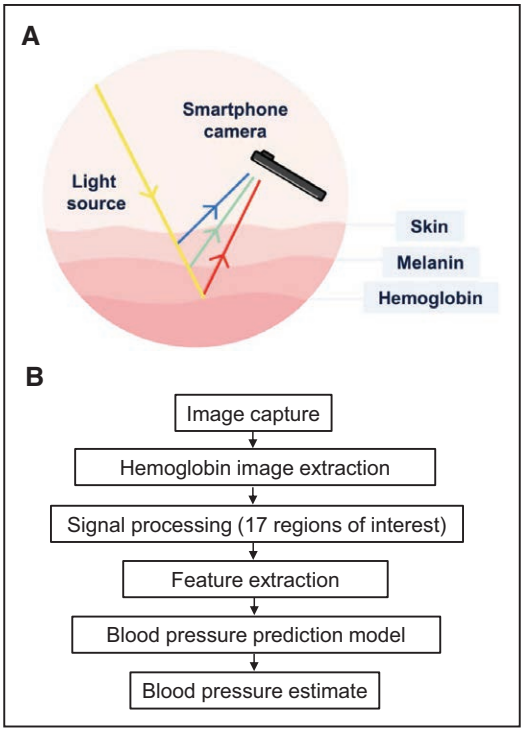

Figure 1. Schematic of transdermal optical imaging.
A, In transdermal optical imaging, light from the visible spectrum travels beneath the skin surface and is re-emitted before being captured by the camera sensor. Transdermal optical imaging technology capitalizes on subtle changes in skin color from the difference in re-emitted light between hemoglobin and melanin chromophores to detect blood flow pulsation in the cardiovascular system. **B**, The process of transdermal optical imaging involves (1) capturing video of the face using a conventional camera, (2) extracting spatiotemporal images of hemoglobin concentration from the bitplanes of the red, green, and blue image channels using advanced machine learning, (3) processing the hemoglobin signal from 17 different regions of interest, (4) extracting features from these signals, and (5) using a blood pressure prediction model trained with advanced machine learning algorithms to indicate blood pressure from these signals.

tiple locations simultaneously, thus taking into account differential microvascular control of the face by sympathetic and parasympathetic vasomotor neurons.[18] TOI should, therefore, provide richer information about BP and thus produce more accurate measures than finger photoplethysmography. Third, a recent study combined photoplethysmography and a smartphone to determine brachial systolic, diastolic, and pulse BP accurately without calibration by a brachial cuff.[13] This technology used a finger photoplethysmography sensor to detect blood flow as the subject presses their finger against the sensor with progressively greater levels of force. A finger pressure sensor guided the application of that force, and the smartphone used force and blood flow information to compute BP oscillometrically. The study demonstrates that absolute brachial pressures can be accurately estimated using photoplethysmography elsewhere on the body and without calibration with a brachial cuff. Like photoplethysmography, TOI optically captures blood flow data and then uses it to determine BP. Furthermore, it does so remotely, using only camera hardware that is already ubiquitous on existing smartphones without the need for a photoplethysmography instrument or pressure sensor.

This proof-of-concept study used a smartphone to video-record the faces of subjects while simultaneously collecting their systolic and diastolic BP reference measurements using an FDA-cleared continuous BP monitor. This monitor measures upper arm (brachial artery) BP continuously, thus providing an objective and continuous characterization of BP changes that occur throughout the video recording session. After applying TOI data processing algorithms (see methods) to the face video, we obtained blood flow signals that track transdermal blood oscillations in multiple locations of the face frame by frame. Then, we divided the sample into a training set (70%), a testing set (15%), and a validation set (15%). We used an advanced machine learning algorithm to train and test computational models to predict reference BP from these signals using data from the training and testing sets. The remaining validation set was never used in training or testing. This independent data set was thus used to evaluate how well the trained models would generalize to predict systolic, diastolic, and pulse pressures in new subjects that they had never seen before. This study recruited subjects with normotensive BPs, with the high BP cut-off defined by Eighth Joint National Committee general population criteria.[19] Subjects had a systolic pressure between 100 and 139 mm Hg and a diastolic pressure between 60 and 89 mm Hg. This range was sufficient to build computational BP models and determine whether TOI technology can be used to measure BP.

MATERIALS AND METHODS

Data and Code Disclosure Statement

Sample data are available from the corresponding author on reasonable request. The full data set (including videos) contains personally identifying information from human subjects and is not available because of privacy considerations. In general, computer code is available from open source software libraries as described. Where custom computer code is used, its function is clearly described in the methods.

Subjects

Adults (≥18 years) were recruited at the University of Toronto (Toronto, Canada) and at the Physical Examination Center of the Affiliated Hospital of Hangzhou Normal University (Hangzhou, China). The use of human subjects in this study was approved by institutional review committees at both institutions (University of Toronto Social Sciences, Humanities and Education Research Ethics Board, and Affiliated Hospital of Hangzhou Normal University Research Ethics Board). We collected data from 2348 subjects throughout all seasons of the year over 2 years. Then, we selected the 2242 subjects with an average reference systolic BP between 100 and 139 mm Hg and a diastolic pressure between 60 and 89 mm Hg. In

the sample, we found the number of participants with systolic BP between 130 and 139 mm Hg to be substantially under represented. To ensure a more even distribution of subjects across the full range of systolic BP between 100 and 139 mm Hg, we randomly downsampled the number of subjects with systolic BP between 100 and 129 mm Hg. According to best practice in machine learning, downsampling ensures that models predict well across the full data range.[20] Consequently, we had 1328 subjects for creating and validating BP prediction models (for subject characteristics, including reference BP distribution, Table I in the Data Supplement).

Data Collection Procedure

Subjects provided informed written consent before commencing the study. Additional consent was obtained for publication of the subject photos displayed herein. On receiving consent, experimenters measured height and weight and administered a prestudy questionnaire to collect demographic information. Subjects were then directed to a quiet study room and seated at the data collection apparatus (Figure 2; full description in the Data Supplement) where they could acclimatize for at least 5 minutes. Experimenters adjusted chair height so that the subject's feet were flat on the floor. During the acclimatization period, the continuous BP monitor was calibrated for use, as described in the Data Supplement. The ambient room temperature varied by season and ranged from 14°C to 26°C (mean±SD: 19±4°C; Methods in the Data Supplement).

On reaching 5 minutes of acclimatization, the experimenter opened the camera application on the iPhone and selected video mode and the front camera. They locked the camera's focus and exposure control to the subject's face by placing their finger on the subject's forehead in the digital viewfinder until focus and exposure locked. The experimenter then remotely started the video recording, which simultaneously inserted a marker into the BP recording to synchronize the reference BP recording with the video recording. The recording proceeded for exactly 2 minutes, at which time the video recording and BP recording was stopped. This corresponded to the end of data collection.

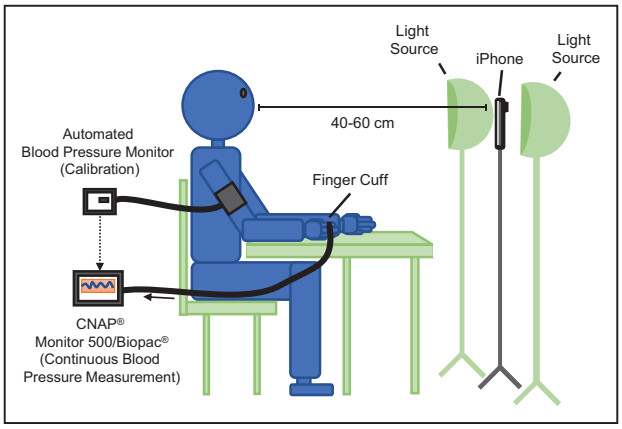

Figure 2. Data collection set-up.
Subjects were seated at a table with their back, elbow, and forearm supported, legs uncrossed, and feet placed flat on the floor. A front-facing uniform light source was used to ensure sufficient lighting. An upper-arm calibrating cuff was placed on the right arm at the approximate level of heart (right atrium) and was used to calibrate the CNAP Monitor 500 continuous finger blood pressure reading for brachial blood pressure. A camera (iPhone 6 Plus front camera) was mounted in front of the subject to record video simultaneously with continuous blood pressure during data collection.

Signal Processing

Our video recordings of the face captured light re-emitted by blood hemoglobin (Figure 1A). The amount of light captured by the camera was, therefore, inversely proportional to hemoglobin concentration near the skin surface. It is widely acknowledged that this pulsation of light reflects the pulsation of arteries under the skin.[21] However, these changes in re-emitted light are essentially imperceptible in conventional videos. For this reason, it was necessary to use signal processing techniques to extract and amplify cyclical blood pulsations within the human facial vasculature.[15] See Methods in the Data Supplement for signal processing about TOI and reference BP signal.

Features Extracted From Subject Data

We extracted 155 unique features from participant data. The first 126 of these features were extracted from facial transdermal blood flow signals from each subject's 17 regions of interest. These features fall into the following categories: pulse amplitude, heart rate band pulse amplitude, pulse rate, pulse rate variability, pulse transit time, pulse shape, and pulse energy. The remaining 29 features consisted of meta-features that help normalize for different imaging conditions, as well as features pertaining to ambient room temperature and subject physical characteristics (eg, age, weight, and skin tone). For details, see Methods and Figure I in the Data Supplement.

Eigenvectors Used for BP Prediction

After extracting these features, we used SPSS (Version 24) to conduct principal component analysis[22] on extracted features to reduce feature dimensions. We used the varimax rotation[22] to produce 30 orthogonal eigenvectors.

Training of BP Prediction Models

These 30 decorrelated eigenvectors were then input into a multilayer perceptron machine learning algorithm (SPSS, Version 24) to generate models that best predicted: (1) systolic BP, (2) diastolic BP, and (3) pulse pressure.

We randomly divided the sample into a training set (70%), a testing set (15%), and a validation set (15%). We trained and tested our multilayer perceptron models with the training and testing sets. We then validated these models on the independent validation set that was not used in training or testing. This independent data set was used as an objective indicator to evaluate how well the trained models would generalize to predict systolic, diastolic, and pulse pressures in new subjects that they had never seen before. We trained, tested, and validated the models with 200 iterations for each type of model to generate statistical estimates of model performance (see below for information on statistical estimation of model performance; see Methods in the Data Supplement for rationale behind multiple iterations).

For comparison purposes, we also created separate control models for systolic, diastolic, and pulse pressure using only age, height, weight, skin tone, sex, race, and heart rate

as predictors. By doing so, we were able to ascertain whether our models based all features were able to predict BP above and beyond the contribution of demographics features independent from video features. The rationale for doing so was that the demographic features could be readily obtained without using TOI. For the same reason, we added heart rate as a predictor in these control models. Note that although here we used heart rate measurements based on TOI, such measurements could also be readily obtained without TOI (eg, palpation, smartwatch, and ECG).

Statistics: Testing Performance of the BP Prediction Models

We quantified the accuracy and precision of each of the 200 iterations of systolic, diastolic, and pulse pressure models as a percentage accuracy, a mean bias±SD, as an intraclass correlation, and as a Pearson correlation. These calculations were performed on each of the 200 iterations for each type of BP model, and the mean and 95% CI was reported for the 200 iterations of each model. All accuracy statistics were calculated on the validation set only. For percentage accuracy, we took the absolute difference (error) between the predicted BP and the reference BP for a given subject and divided it by the reference BP of the subject to get a proportion of error. We then subtracted this value from 1 to convert this proportion error to a proportion accuracy and multiplied it by 100 to obtain a percentage accuracy. We then calculated the mean accuracy across all subjects to arrive at a percentage accuracy for each model. For mean bias and SD, we calculated the difference between the reference and predicted pressure for each subject for the systolic, diastolic, and pulse pressure prediction models. We then calculated the mean and SD of this difference for all subjects in each respective model. Intraclass correlation estimates and their 95% CI were based on single measure absolute agreement in a 2-way mixed-effects model. Pearson correlations and their 95% CIs were also calculated. A plot of reference versus predicted pressures was constructed using the mean of 200 predicted values for each model to display predictive ability across the range of reference BPs.

We further determined the degree of information gain attained by each predictive model to determine the predictive power of each model beyond that of simply predicting the mean. Theoretically, the SE of the predictions when the measurement bias is zero will equal the SD of the reference pressures if the mean is predicted every time. A greater reduction in the SD of the residual (prediction error) relative to reference BP SD demonstrates a greater degree of correct predictive ability. To quantify predictive ability, we took the absolute difference of these 2 values and divided it by the SD of the reference BP. We converted to a percentage by multiplying by 100. Thus, a greater percentage corresponds to greater information gain for that model relative to reference SD.

To assess eigenvector importance in each iteration of the systolic, diastolic, and pulse pressure models, we determined the relative importance of each of the 30 eigenvectors normalized against the most important eigenvector. We averaged eigenvector importance across all 200 iterations of the model to rank each eigenvector according to its average importance for each model. Although eigenvectors represent abstract dimensions in our data, to help readers understand what these dimensions may represent, we highlighted the most representative features of each eigenvector, which had the highest values in the rotated component matrix.

RESULTS

Our study tested the hypothesis that TOI accurately detects BP from video of the face. We tested this hypothesis in 2 parts. First, we determined whether oscillations in TOI signal reflected oscillations in continuously measured BP. We did this to determine whether TOI captures BP on a qualitative level. We then quantitatively assessed our BP prediction models against reference systolic, diastolic, and pulse BP measurements.

TOI Signal Resembles Reference BP Pulses

We anticipated that TOI signal would reflect hemoglobin concentration in the face. This signal would, therefore, serve as a surrogate for blood volume and ultimately BP. To identify regions in the face with robust hemoglobin signal, we constructed a spatiotemporal map of TOI signal in the face (Figure 3A). This full facial map allowed us to examine areas of the face where subcutaneous vasculature was either under the control of the sympathetic nervous system (eg, lips and nose) or the parasympathetic nervous system (eg, forehead, chin, and lower jaw)[18]; we anticipated both could provide useful information. Using this spatiotemporal map, we identified the 17 regions on the face that could provide robust hemoglobin signals (Figure 3B).

Next, we examined the TOI signal in the 17 regions to determine whether it is representative of BP. We qualitatively compared this signal with the reference BP waveforms from the FDA-cleared continuous BP monitor. As expected, TOI signal displayed periodicity corresponding to the reference BP pulses. Furthermore, a characteristic feature of the BP pulse—the dichrotic notch[23]—can be distinguished in the TOI signal (see Figure 3C for examples). These results, therefore, suggest that TOI methodology can measure facial blood flow changes that correspond to systemic cardiovascular activity.

TOI Accurately Determines BPs

As shown in Table 1, all of our computational models based on multilayer perceptron are highly accurate in terms of predicting the reference BPs of our validation cohort. On average, our models predicted systolic BP with an accuracy of 94.81%, diastolic BP with an accuracy of 95.71%, and pulse pressure with an accuracy of 95.75%. The average prediction biases±error SDs were 0.39±7.30 mm Hg for systolic BP, –0.20±6.00 mm Hg for diastolic BP, and 0.52±6.42 mm Hg for pulse pressure. These SDs represent information gains of 25.5%,

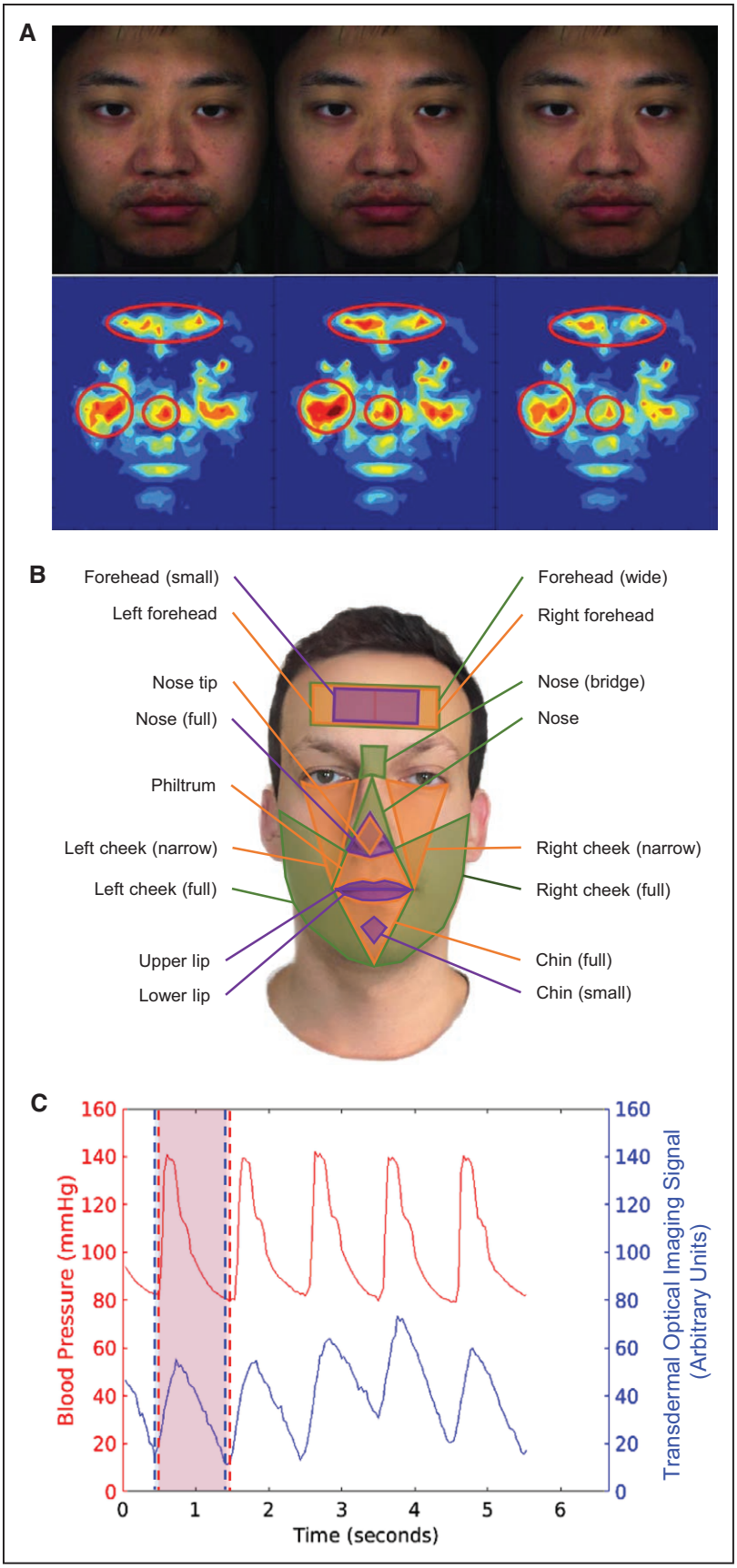

Figure 3. Extracted transdermal optical imaging signal, regions of signal extraction, and comparison with blood pressure signal.
A, Subject's face (top) with corresponding visualization of hemoglobin signal using transdermal optical imaging technology (bottom). Transdermal optical imaging signal intensity is presumed to reflect hemoglobin concentration. Circles indicate spikes in hemoglobin signal. **B**, Seventeen regions of interest of varying sizes are located on the forehead, nose, cheek, lip, chin, and philtrum. **C**, Simultaneously recorded transdermal optical imaging signal from one individual (raw signal from green channel; presumed hemoglobin signal in the forehead [wide] region of interest) and continuous reference blood pressure signal (CNAP Monitor 500) exhibit temporally congruent oscillations and occur at ≈1 per second—characteristic of blood pressure pulse. Consent was obtained for use of patient photos.

Table 1. Accuracy and Precision of Full Blood Pressure Prediction Models Containing All Features

Model	Accuracy (%)	Error Bias (mm Hg)	Error SD (mm Hg)	Information Gain vs Reference SD (%)	Intraclass Correlation	Pearson Correlation
Systolic blood pressure	94.81 (94.79 to 94.83)	0.39 (0.35 to 0.44)	7.30 (7.28 to 7.32)	25.5(25.3 to 25.7)	0.60 (0.60 to 0.60)	0.67 (0.67 to 0.67)
Diastolic blood pressure	95.71 (95.69 to 95.73)	−0.20 (−0.23 to −0.17)	6.00 (5.98 to 6.02)	12.0 (11.7 to 12.3)	0.37 (0.32 to 0.42)	0.47 (0.46 to 0.48)
Pulse pressure	95.76 (95.74 to 95.78)	0.52 (0.46 to 0.58)	6.42 (6.39 to 6.45)	21.8 (21.5 to 22.1)	0.56 (0.55 to 0.57)	0.63 (0.63 to 0.63)

Mean accuracy and precision with 95% CI of 200 systolic, diastolic, and pulse pressure prediction models (N=202). Intraclass correlation is 2-way mixed effects model showing absolute agreement for single measures.

12.0%, and 21.8%, respectively. Our findings corresponded to average intraclass correlations of 0.60, 0.37, and 0.56 and average Pearson correlations of 0.67, 0.47, and 0.63 for systolic, diastolic, and pulse pressures, respectively.

Table 2 shows the accuracy and information gain of the control models trained on demographic features and heart rate only. These systolic, diastolic, and pulse pressure models demonstrated information gains of 8.8%, 8.8%, and 11.1% versus the reference standard, respectively. As shown by the 95% CIs for all measures (Tables 1 and 2), these results were significantly lower than the results obtained from the full models.

Figure 4 shows the scatter plots of reference versus predicted pressures as well as the line of identity. At low reference pressures predicted pressures tend to fall above the line of identity and at high reference pressures predicted pressures tend to fall below the line of identity. Thus, there is some degree of overprediction at low reference pressures and some degree of underprediction at high reference pressures.

Eigenvector and Feature Importance in Predicting BPs

The relative importance of each eigenvector in predicting systolic, diastolic, and pulse pressure is provided in Tables II, III, and IV in the Data Supplement, respectively. The majority of predictive power in all 3 models came from eigenvectors representing blood flow features. Pulse rate features were not a major contributor to any eigenvector. With respect to subject physical characteristics in the meta feature category, it should be noted that neither age, sex, skin tone, or room temperature had any appreciable influence on any eigenvector and thus were not considered significant determinants of BP prediction. Height and weight were top features of eigenvector 15.

In a feature-specific analysis outside of eigenvectors, we found that age, sex, height, weight, heart rate, and skin tone did not significantly correlate with prediction accuracy in systolic, diastolic, or pulse pressure models (*P*s>0.05).

DISCUSSION

This study tested the hypothesis that TOI technology can extract blood flow patterns from the face and then use them to accurately predict BP. Our results support this hypothesis. We observed that TOI signal obtained in the face very closely corresponds to BP wave oscillations obtained simultaneously in the finger. Furthermore, we demonstrated that systolic and diastolic BPs predicted from TOI fall within 5±8 mm Hg of reference measurements. A bias and SD of 5±8 mm Hg are a key accuracy threshold when testing proceeds according to the Association for the Advancement of Medical Instrumentation (AAMI) standard. The present study thus demonstrates that TOI technology can determine BP in normotensive participants with an accuracy that is comparable to clinical standards. True validation, however, will require that testing proceeds according to the methodology outlined in this standard, which includes the testing of non-normotensive participants.

Our findings suggest that blood flow in the facial vasculature contains information about BP as measured elsewhere in the body by an FDA-cleared continuous BP monitor. The way in which TOI extracts and process-

Table 2. Accuracy and Precision of Control Prediction Models Based on Demographics and Heart Rate Only

Model	Accuracy (%)	Error Bias (mm Hg)	Error SD (mm Hg)	Information Gain vs Reference SD (%)	Intraclass Correlation	Pearson Correlation
Systolic blood pressure	93.64 (93.63–93.65)	−0.5 (−0.6 to −0.5)	8.9 (8.9 to 8.9)	8.8 (8.8 to 8.8)	0.34 (0.34 to 0.34)	0.42 (0.42 to 0.42)
Diastolic blood pressure	95.45 (95.44–95.46)	−0.4 (−0.4 to −0.4)	6.2 (6.2 to 6.2)	8.8 (8.6 to 9.0)	0.31 (0.25 to 0.37)	0.41 (0.40 to 0.42)
Pulse pressure	95.01 (95.00–95.02)	0.0 (0.0 to 0.1)	7.3 (7.3 to 7.3)	11.1 (10.8 to 11.4)	0.41 (0.41 to 0.41)	0.46 (0.46 to 0.47)

Demographics features consisted of age, height, weight, skin tone, sex, and race. Mean accuracy and precision with 95% CI of 200 systolic, diastolic, and pulse pressure prediction models (N=202). Intraclass correlation is 2-way mixed effects model showing absolute agreement for single measures.

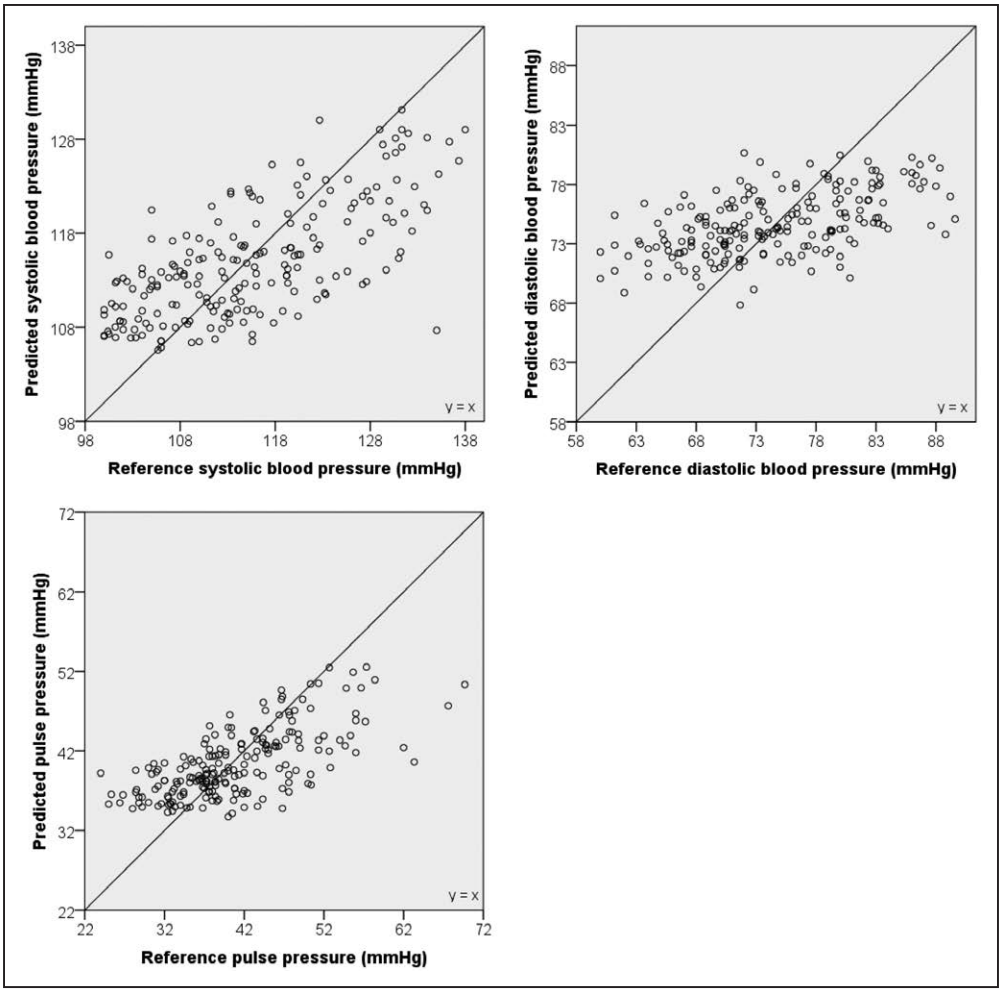

Figure 4. Reference vs predicted pressures for systolic, diastolic, and pulse pressure prediction models.
Scatter plots depicting the reference vs the mean predicted blood pressures (BPs) for systolic, diastolic, and pulse pressure prediction models in subjects within the normotensive BP range (systolic BP 100–139 mm Hg; diastolic BP 60–89 mm Hg). The line on each plot represents a line of identity (y=x).

es this information allows for accurate predictions of systolic, diastolic, and pulse BP. These models exhibit significant predictive ability over and above simply predicting the mean. Furthermore, our findings suggest that blood flow patterns from different parts of the body exhibit robust relationships with one another. Just like finger BP is highly related to upper arm BP (as in the case of the continuous BP monitor), blood flow patterns from the face are highly related to upper arm BP.

Our results also show that systolic, diastolic, and pulse pressure control models trained on demographics and heart rate alone show some degree of predictive ability. However, these models were significantly inferior to the corresponding full models trained on all facial video features in addition to demographics and heart rate. For example, the full models based on both facial video and demographics features had almost 3 times the information gain in the systolic model, twice the information gain in the pulse pressure model, and a third more information gain the diastolic model than the control models trained on demographics and heart rate alone. Thus, the facial video features are highly important for BP prediction overall and demographics plus heart rate features are insufficient for obtaining a high level of information gain. However, for developing a BP prediction model, one must use as many BP-predictive features as possible to maximize prediction accuracy and information gain.

Limitations

Although the present study showed that TOI is a robust method for determining patient BP, additional work is needed. For example, we only included subjects in the normotensive systolic (≥100 to <140 mm Hg) and diastolic (≥60 to <90 mm Hg) BP ranges and did not include a cohort with hypertensive or hypotensive BPs. Thus, a crucial next step is to recruit hypertensive or hypotensive subjects with and without having taken any medication to test the robustness of the current computational BP models based on normotensive subjects.

A further limitation of the subject base is racial homogeneity. The vast majority of subjects used were of East

Asian descent. Nevertheless, our participants displayed a reasonable degree of skin tone variation and this factor did not impact model prediction accuracy. The lack of skin tone influence was likely because of the unique ability of TOI to remove skin melanin information from video signals. However, it should be noted that the current sample still lacked a sufficient number of subjects with either very dark or very fair skin tones. Future studies should incorporate a robust mix of participants from diverse skin tones and races to ensure that results generalize to individuals from all races and skin tones.

Also, the present study trained the computational BP models against reference BP measures from a continuous BP monitor. Although this monitor was validated against the internationally recognized gold standard measurements, our models were not. Thus, future model training and cross-validation must be done using gold standard techniques. Such techniques require either invasive intra-arterial pressure for continuous measurement or auscultation involving a mercury sphygmomanometer for discrete measurements by 2 independent nurses for the measurement of reference BP. Furthermore, this technology should be further tested in the intended environmental conditions (ie, dynamic lighting conditions, held in the hand). Such conditions would fully test the capabilities of the technology, including its ability to track the face in the presence of motion and compensate for changing lighting conditions.

It should be noted that to demonstrate proof-of-concept that TOI can measure BP, our study adopted the key accuracy criteria required by the Association for the AAMI standard as a point of reference. The 81060–2 standard put forth by the AAMI, however, is not for smartphone-based BP monitoring. Instead, it is one of several standards governing the validation of noninvasive sphygmomanometers for clinical use.[24] It also forms the basis of the United States Federal Drug Administration evaluation criteria for such devices. The AAMI standard does not explicitly encompass pulse pressure, but we measured it as well to determine the degree to which facial blood flow features are suited for measuring pulse pressure, and because pulse pressure measurements provide clinical value.[25] Importantly, the AAMI standard was never designed for assessing the validity of BP measurements using smartphones. In fact, no such international standards and related protocols currently exist. Thus, future development and wide usage of smartphone-based BP monitors call for specific international standards.

Potential Applications and Other Directions of Future Research

Notwithstanding the above-noted limitations, the present study demonstrated the potential of TOI technology for monitoring BP conveniently. This technology could be implemented on any modern smartphone. A video of the user's face could be captured by a smartphone application where the resource nonintensive task of extracting hemoglobin signal from video would be performed. Then, the signal could be transmitted via internet to the cloud where the resource-intensive task of computing BP could be performed. BP predictions could then be returned to the user's phone. This process would reduce the quantity of data transmitted to and from the cloud, as well as protect user privacy by preventing personally identifiable data from being sent to the cloud.

A smartphone application based on TOI technology would be more comfortable than existing cuff-based devices because it would function remotely through video without contact with the user. A software-based solution build on TOI technology is convenient because it accompanies the user wherever they may be with their smartphone, thus allowing for BP measurements at more times and places than is possible with a cuff-based device.

It should be noted that in this study, we focused on assessing BP prediction in individuals at rest since in the clinic resting measurements are used to diagnose hypertension and hypotension. Furthermore, our study took place under controlled conditions. However, future studies need to explore whether TOI can be used to monitor BP in different environments (eg, outdoors, in a moving vehicle, under low light). Additionally, it needs to be examined whether it can track BP during physical activity. Such BP measurement could be useful for applications like fitness tracking, exercise science, and cardiac stress testing. These are situations where BP measurement has traditionally been challenging with traditional forms of BP measurement. The field of video photoplethysmography has traditionally struggled to deal with situations where motion is present. Moment-to-moment variation in camera angles may also present an issue. It has yet to be determined whether TOI technology is more robust under these conditions. Furthermore, specifically designed studies are needed to examine whether BP prediction models based on resting measurements can be adapted to predict BP during physical activity, or whether special BP prediction models specifically designed for physical activity are needed.

In summary, we have presented proof-of-concept that TOI technology can accurately determine BP. We acknowledge that a significant body of work remains to be done in developing and validating this technology to the AAMI standard or another relevant standard. However, this technology has shown great promise in this initial phase of the validation process, and we think that the likelihood of successful validation is high. The realization of this technology would enable the creation of convenient and widely available BP measurement tools in smartphones. Such tools would have several advan-

tages over cuff-based BP devices currently on the market. The added convenience and availability of these tools are likely to promote more frequent BP measurements in more people and thus facilitate the detection and management of abnormal BP in the population.

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Disclosures

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