Cuff-Less Blood Pressure Monitoring Technologies

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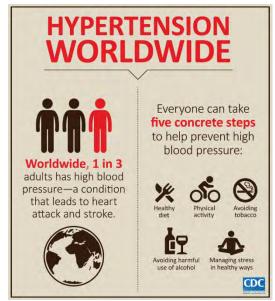
IEEE EMBS Baltimore Chapter Technical Meeting

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Blood Pressure (BP) Monitoring

- Hypertension
 - 1) The most prevalent chronic disease in US and globally
 - 2) 25% in the world's adult population
 - 3) Major risk factor for stroke and heart disease

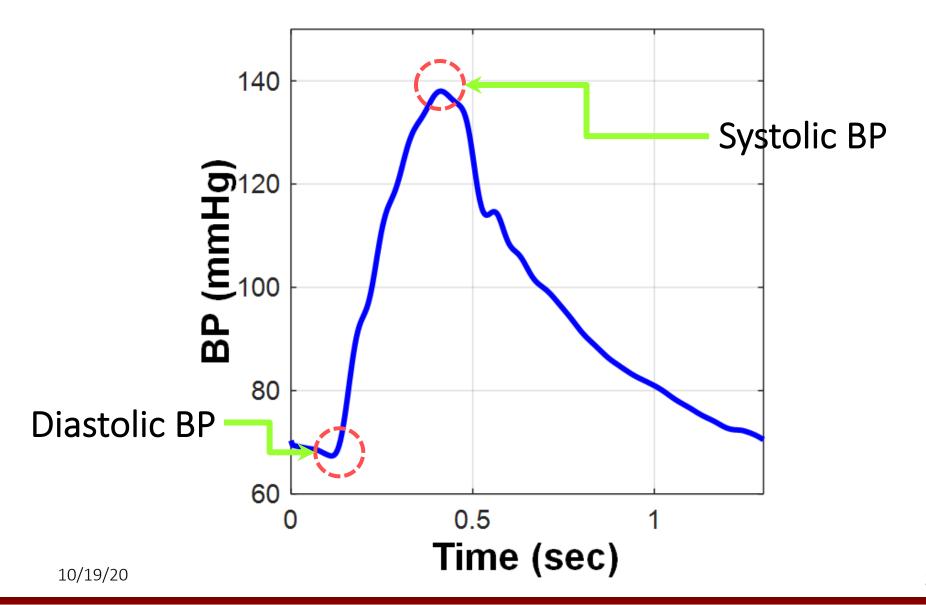


https://www.cdc.gov

- Hypertension can be treated w/ life style changes and medications;
 But, detection of hypertension is frequently missed
 - 1) 20% of hypertensives in US don't know they have hypertension
 - 2) BP in known hypertensives is often uncontrolled (50%)
- → Development of more accurate, ultra-convenient, and high-throughput BP monitoring technologies will drastically advance hypertension management and control!



Blood Pressure: Systolic & Diastolic



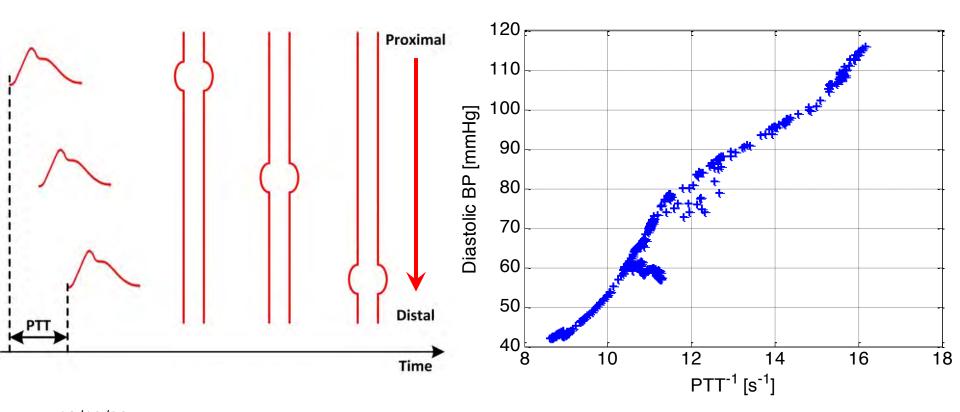
Blood Pressure Monitoring: Cuff-Based Devices



https://www.withings.com/

Cuff-Less Blood Pressure (BP) Monitoring via PTT

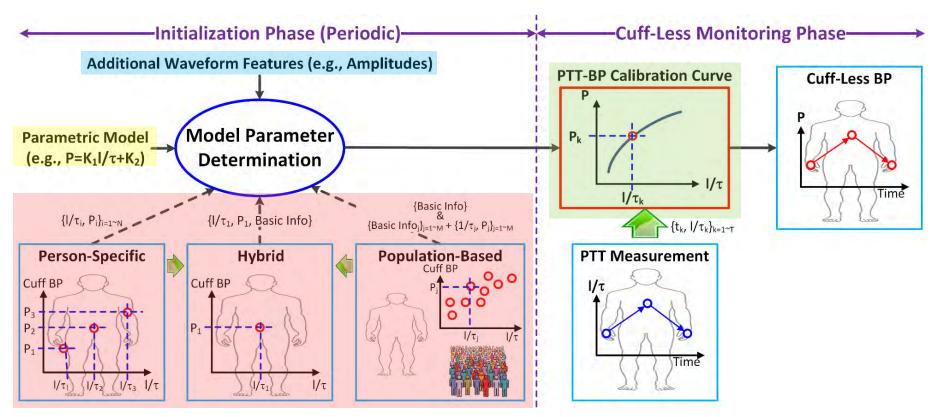
- PTT is time required for BP wave to travel b/w two sites in the artery.





Cuff-Less Blood Pressure (BP) Monitoring via PTT

- Estimating BP from PTT requires a PTT-BP calibration curve [ms ightarrow mmHg].
 - 1) Parametric model relating PTT to BP
 - 2) Model parameter determination methods



PTT-BP Calibration/Initialization

Calibration/Initialization: PTT [ms] → BP [mmHg]

$$\mathbf{P} = \mathbf{K}_1 \frac{\mathbf{l}}{\mathbf{\tau}} + \mathbf{K}_2$$

- K_1 and K_2 vary from person to person; change over time in a person; is even unknown for a given person \rightarrow must be determined w/ BP-PTT measurements
- Challenge arises from 2 unknowns to determine $(K_1 \text{ and } K_2)$
- Calibration/Initialization Procedure
 - 1) To define a parametric model
 - 2) To determine model parameters via simultaneous cuff BP-PTT measurements (requiring a proximal and a distal arterial waveforms)
 - 3) To periodically repeat initialization/calibration to account for changes in the calibration parameters (e.g., due to cardiovascular aging)

- Physiological Mechanisms underlying PTT –BP Relationship
 - 1) PTT decreases w/ increasing arterial elasticity due to fluid dynamic properties : BP wave travels faster through arterial wall when it is stiffer
 - 2) Arterial elasticity increases w/ BP due to arterial wall material properties

Bramwell-Hill Equation	Moens-Korteweg Equation		
$v = \frac{l}{\tau} = \sqrt{\frac{A}{\rho} \frac{dP}{dA}}$	$v = \frac{l}{\tau} = \sqrt{\frac{A}{\rho}} \frac{dP}{dA} \& C = \frac{dA}{dP} = \frac{2\pi r^3}{Eh}$ \downarrow $v = \frac{l}{\tau} = \sqrt{\frac{Eh}{2r\rho}}$		

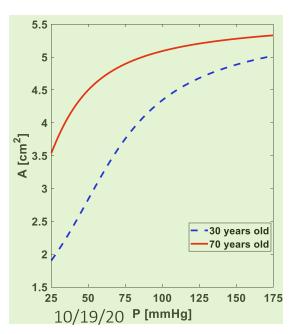
- Physiological Mechanisms in PTT –BP Relationship
 - 1) PTT decreases w/increasing arterial elasticity due to fluid dynamic properties
 - 2) Arterial elasticity increases w/ BP due to arterial wall material properties : Arterial wall gets stiffer as it expands when it is subject to higher BP

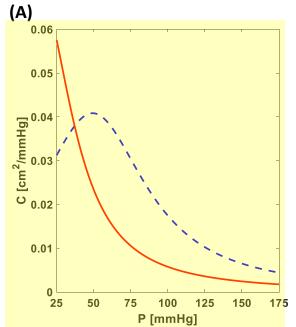
Hugh Model	Wesseling Model		
	$A(P) = A_{\text{max}} \left[\frac{1}{2} + \frac{1}{\pi} \tan^{-1} \left(\frac{P - P_0}{P_1} \right) \right]$		
$E = E_0 e^{\alpha P}$	$C(P) = \frac{dA}{dP} = \frac{A_{max}}{\pi P_1 \left[1 + \left(\frac{P - P_0}{P_1} \right)^2 \right]}$		

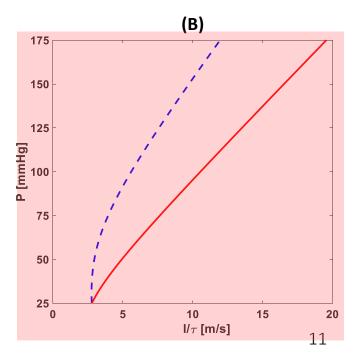
 PTT-BP Models can be derived by combining the models representing these two physiological mechanisms:

Model	Parameters	Incorporated Mechanisms	
$P = K_1 \ln \left(\frac{\tau}{l}\right) + K_2$	$K_1 = -\frac{2}{\alpha}, K_2 = \frac{1}{\alpha} \ln \left(\frac{2r\rho}{E_0 h} \right)$	M-K + Hugh	
$P = K_1 \frac{l}{\tau} + K_2$	$K_1 = \sqrt{\frac{2\rho P_1}{\pi + 2}}$, $K_2 = P_0$	B-H + Wesseling / High P	
$P = K_1 \left(\frac{l}{\tau}\right)^2 + K_2$	K ₁ , K ₁	B-H + Ma's A & C (PNAS, 2018)	
$\frac{\tau}{l} = \frac{2819.7}{\sqrt{\pi P_1 \left(1 + \left(\frac{P - P_0}{P_1}\right)^2\right) \left(\frac{1}{2} + \frac{1}{\pi} tan^{-1} \left(\frac{P - P_0}{P_1}\right)\right)}}$	P_0, P_1	B-H + Wesseling	

- PTT-BP Model: Insights (e.g., B-H + W $\frac{\tau}{l} = \frac{2819.7}{\sqrt{\pi P_1 \left(1 + \left(\frac{P P_0}{P_1}\right)^2\right) \left(\frac{1}{2} + \frac{1}{\pi} tan^{-1} \left(\frac{P P_0}{P_1}\right)\right)}}$
 - 1) (A) With aging, arterial cross-sectional area (A) becomes less dependent upon BP while arterial compliance (C) becomes more dependent upon BP
 - 2) (B) The shape of the PTT-BP relationship may be age-dependent and becomes nearly a line relationship in PWV in the elderly







PTT-BP Parametric Models: Empirical

 To achieve adequate fitting of PTT-BP data, w/o reference to physiological mechanisms

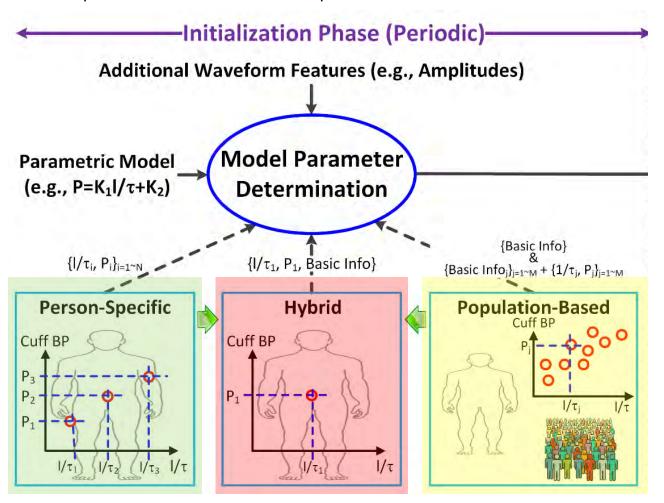
Linear Models	$P = K_1 \frac{\tau}{l} + K_2$
Nonlinear Models ($x = \frac{\tau}{l} \text{ or } \frac{l}{\tau}$)	$P = K_1 x^2 + K_2 x + K_3$ $P = K_1 x^p + K_2$ $P = K_1 e^{K_2 x}$
PP Models ¹	$PP = K \left(\frac{l}{\tau}\right)^2$
Models w/o Non-Physiological BP ²	$P = \frac{K_1}{\left(\frac{\tau}{l} - K_2\right)^2} + K_3$

¹: The model may not hold in general, as K depends on the difference in the arterial cross-sectional areas at systole and diastole and may thus vary considerably within a person; integrating the B-H equation yields $PP = \rho \left(\frac{1}{\tau}\right)^2 \ln \left(\frac{A_s}{A_d}\right) \approx \rho \left(\frac{1}{\tau}\right)^2 \left(\frac{A_s - A_d}{A_d}\right)$.

²: The model may be practical for initialization, but is still not physiological; physiologically correct limiting behavior is for PTT to be finite at zero BP and approach zero as BP approaches infinity.

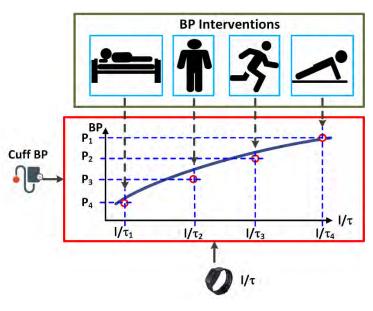
Cuff-Less Blood Pressure (BP) Monitoring via PTT

How can the parameters in PTT-BP parametric model be determined?



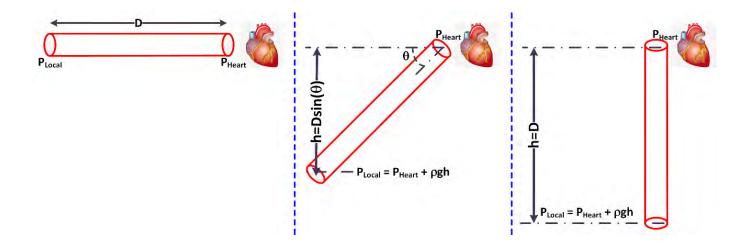
- <u>Person-Specific Method</u>: A person-specific method intends to determine all the model parameters in the calibration model. It involves measuring cuff BP and PTT during multiple interventions that perturb BP in the person.
 - 1) Employ one or more interventions to perturb BP in the person
 - 2) Measure cuff BP and PTT during the baseline period and each intervention
 - 3) Fit the model to the multiple PTT-BP data pairs to determine all parameters

Intervention	BP Effect [mmHg]	Convenience Level	
Slow Breathing	< 5 /< 5	High	
Supine to Standing	< 10 /+4	High	
Cold Pressor	+16/+14	Low	
Exercise	+40/+40 to -9/-4 (1-hr later)	Moderate (could be incorporated in daily life)	
Sustained Handgrip	+45-50/+40	Low	
Mental Arithmetic	+20/+11	Low (requires person adherence)	
Valsalva Maneuver	-15/-15	Low (requires special cuff to detect fast chang	
Hydrostatic Maneuver Hand Lowering/Raising Supine to Seated	-50/-50 to +50/+50 +30/+30	High (but requires heart level detection)	





- Person-Specific Method: Hydrostatic Maneuver
 - 1) High convenience + large BP change
 - 2) Use of the weight of blood column: ~7 mmHg for 10 cm height change



- Local wrist/hand PTT: ~50 mmHg BP change
- PAT: ~25 mmHg (effective BP measurement site may be ~ midpoint of the arm)
- C-F PTT: ~30 mmHg w/ supine to standing (effective BP measurement site may be ~ abdomen)

- Person-Specific PTT-BP Calibration: Other Considerations
 - 1) Leveraging natural BP variations that occur over time in a person due to stress, physical activity, meals, and other factors: ~5 mmHg DP / ~6-9 mmHg SP [BP change is small and timing is unknown]
 - 2) Different BP interventions change BP via different physiological mechanisms

 > Employing a multitude of interventions that invoke an array of physiological mechanisms may provide a good balance for more effective calibration
 - 3) SP or DP? One PTT may be used to calibrate both DP and SP, b/c usually there is modest correlation b/w DP and SP:

$$P_s = G_1 P_d + G_2$$

 W/G_1 and G_2 functions of age and gender.

Yet, models relating one time delay to SP and DP will obviously break down when the two BP values diverge!

 <u>Population-Based Method</u>: A population-based method determines all the model parameters in the calibration model w/o using any BP-perturbing interventions. It involves making the model parameters functions of basic information of the person (e.g., age and gender) using a training dataset comprising cuff BP and PTT measurements from a cohort of subjects.

Example: B-H equation + Wesseling model

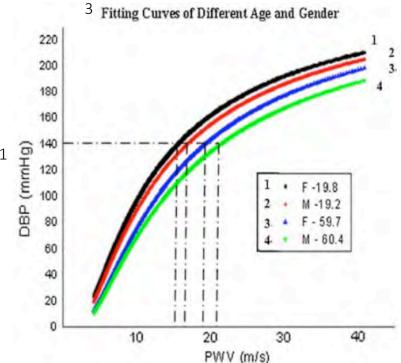
$$\frac{\tau}{l} = \frac{2819.7}{\sqrt{\pi P_1 \left(1 + \left(\frac{P - P_0}{P_1}\right)^2\right) \left(\frac{1}{2} + \frac{1}{\pi} tan^{-1} \left(\frac{P - P_0}{P_1}\right)\right)}}$$

$$W/P_0 = 72 - 0.89age (F)/P_0 = 76 - 0.89age (M), P_1 = 57 - 0.44age$$

Population-Based Method: Examples

$$\frac{1}{\tau}$$
 = (0.00131age - 0.0168)P_d + 3.35¹ (r²=0.71)

$$P_d = (22 \pm 14) \frac{1}{\tau} + K_2^2$$



The efficacy of the models remains controversial

¹Carroll, J. D., Shroff, S., Wirth, P., Halsted, M. & Rajfer, S. Arterial Mechanical Properties in Dilated Cardiomyopathy. J. Clin. Invest. 87, 1002–1009 (1991).

²Butlin, M., Shirbani, F., Barin, E., Tan, I., Spronck, B. & Avolio, A. P. Cuffless Estimation of Blood Pressure: Importance of Variability in Blood Pressure Dependence of Arterial Stiffness across Individuals and Measurement Sites. IEEE Trans. Biomed. Eng. 65, 2377–2383 (2018).

³Chen, Y., Wen, C., Tao, G., Bi, M. & Li, G. Continuous and Noninvasive Blood Pressure Measurement: A Novel Modeling Methodology of the Relationship between Blood Pressure and Pulse Wave Velocity. Ann. Biomed. Eng. 37, 2222–2233 (2009).

- Hybrid Method: A hybrid method involves measuring cuff BP and PTT in the person to determine a single model parameter and using the person's basic information and a training dataset to determine the remaining parameters.
 - 1) PAT to Mean BP, $P = K_1 \ln \left(\frac{\tau}{l}\right) + K_2$, $K_1 = -64.5$ mmHg, K_2 determined w/baseline PAT-cuff BP measurement (healthy subjects)¹
 - 2) PAT to Mean BP, $P = K_1 \ln \left(\frac{\tau}{l}\right) + K_2$, $K_1 = -22.2$ mmHg, K_2 determined w/baseline PAT-cuff BP measurement (old hypertensive subjects)²
 - 3) PAT to SP, 5-parameter model, 4 parameters determined w/ training dataset, intercept determined w/ baseline PAT-cuff BP measurement³
- → Essentially a mixture of person-specific method and population-based method Trade-off b/w accuracy and convenience

¹Zheng, Y.-L., Yan, B. P., Zhang, Y.-T. & Poon, C. C. Y. An Armband Wearable Device for Overnight and Cuff Less Blood Pressure Measurement. IEEE Trans. Biomed. Eng. 61, 2179–2186 (2014).

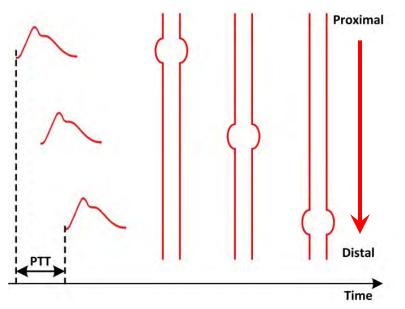
²Zheng, Y., Poon, C. C. Y., Yan, B. P. & Lau, J. Y. W. Pulse Arrival Time Based Cuff-Less and 24-H Wearable Blood Pressure Monitoring and its Diagnostic Value in Hypertension. J. Med. Syst. 40, 195 (2016).

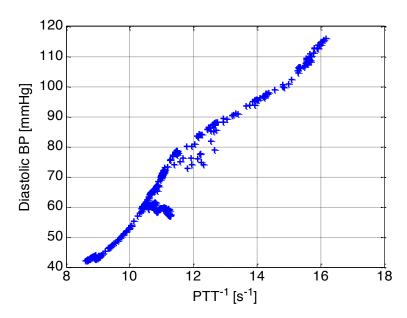
³Gesche, H., Grosskurth, D., Küchler, G. & Patzak, A. Continuous Blood Pressure Measurement by using the Pulse Transit Time: Comparison to a Cuff-Based Method. Eur. J. Appl. Physiol. 112, 309–315 (2012).



Cuff-Less Blood Pressure (BP) Monitoring via PTT

PTT is inversely associated with BP due to (i) BP \propto arterial elasticity and (ii) arterial elasticity \propto PTT⁻¹.





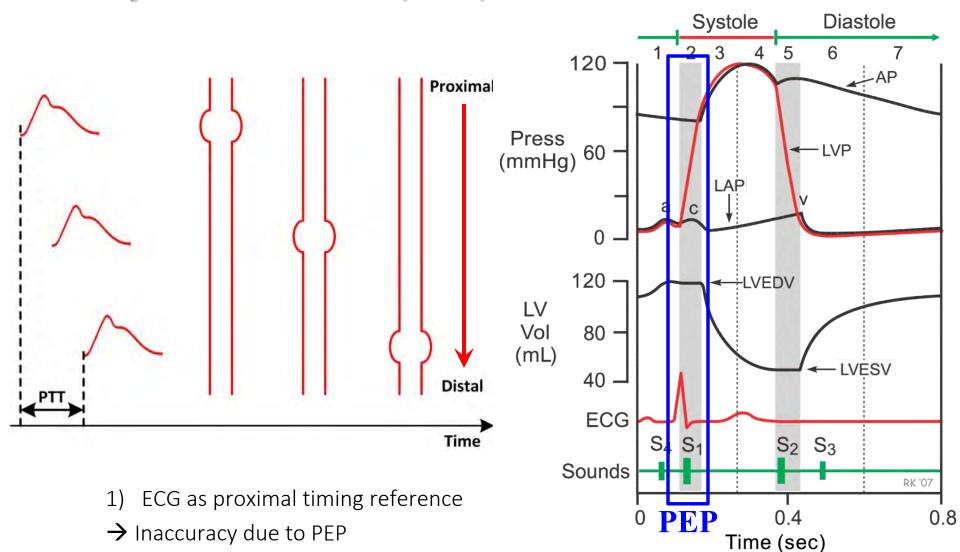
- In practice, PTT principle is inappropriately used in cuff-less BP monitoring for the sake of convenience
 - ECG as proximal timing reference \rightarrow inaccuracy due to pre-ejection period
 - Finger pulse as distal timing reference \rightarrow inaccuracy due to smooth muscles



Laboratory for Control & Information Systems

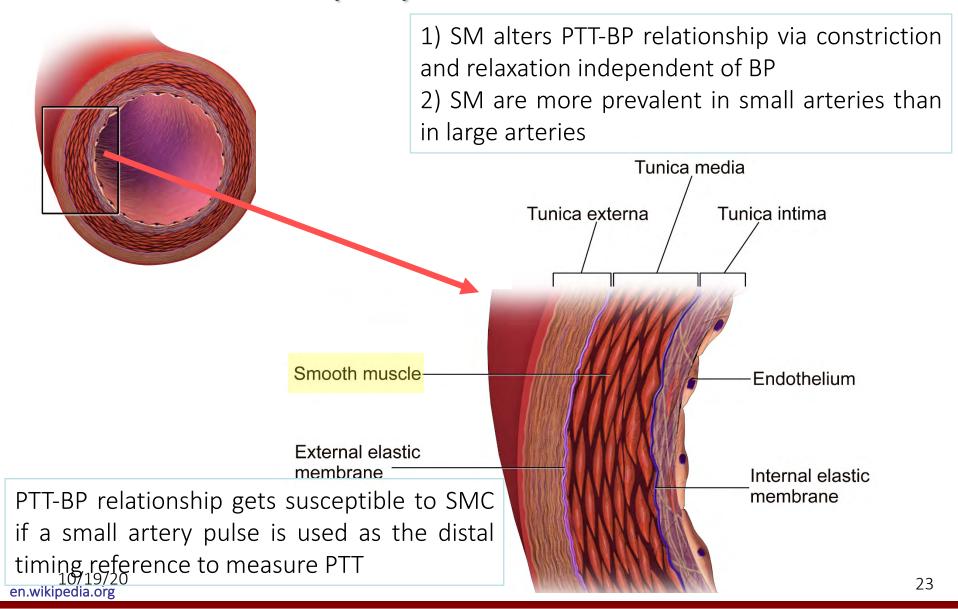


Pre-Ejection Period (PEP) as Disturbance

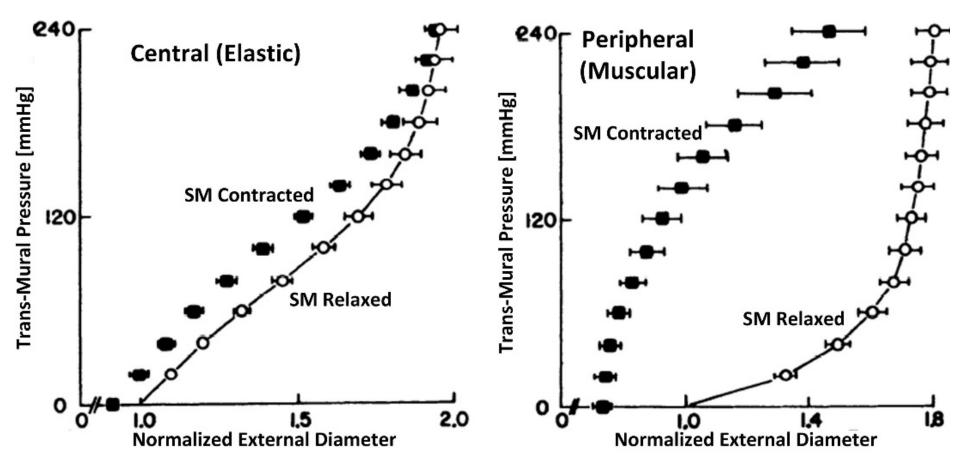


https://www.cvphysiology.com/

Smooth Muscle (SM) as Disturbance



Smooth Muscle Contraction as Disturbance

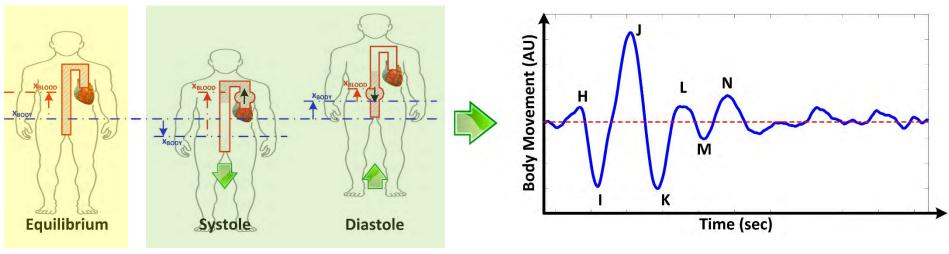


Cox, American Journal of Physiology (1978)

Finger pulse as distal timing reference \rightarrow Inaccuracy due to smooth muscles

Ultra-Convenient Cuff-Less BP Monitoring via BCG

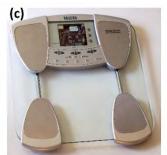
- Ballistocardiogram (BCG): Heartbeat-Induced Body Movement
 - For ~150 years, it has been known that heartbeat induces body movement

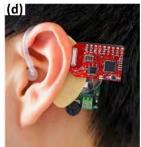


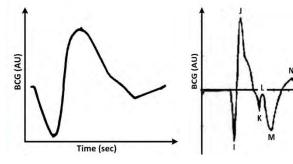
- BCG is amenable to ultra-convenient instrumentation
- Mechanism underlying the BCG waves has remained mysterious





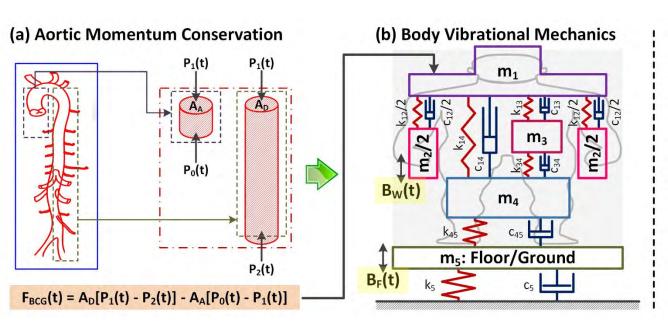


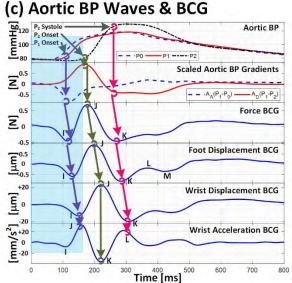




BCG: Elucidating Physiological Mechanism

- Physiological mechanism underlying the genesis of the BCG is elucidated, for the first time, by developing a simple lumped-parameter model
 - 1) BCG $F_{BCG}(t)$ originates from ascending & descending aortic BP gradients
 - 2) The limb BCG signals are the responses of compliant body to the BCG
 - 3) BCG waves (+/- peaks) elucidate timing/amplitude characteristics in BP waves







BCG: Physiological Interpretation & Insights

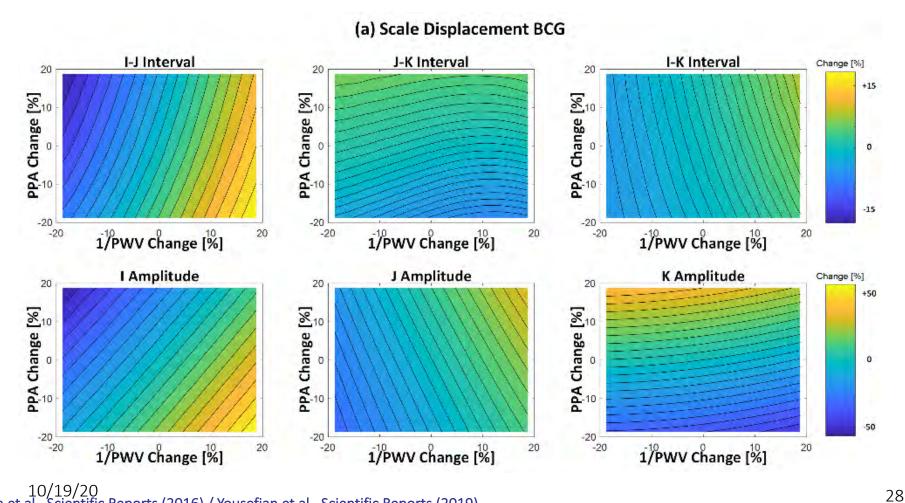
- The BCG waveform elucidates timing/amplitude info on aortic BP waves
- The BCG waveform exhibits meaningful changes in response to BP changes

Relationship b/w BCG and Timing/Amplitude Characteristics of Aortic BP Waves

Arterial BP	Arterial BP Gradients	Foot Displacement BCG	Wrist Acceleration BCG
Aortic Inlet BP (P ₁) Onset	Peak, P ₀ -P ₁	I	J
Aortic Outlet BP (P ₂) Onset	Peak, P ₁ -P ₂	J	K
Aortic Outlet BP (P ₂) Systole	Valley, P ₁ -P ₂	K	L
Aortic Inlet BP (P_1) Amplitude	Positive Amplitude, P ₁ -P ₂	J Amplitude	K Amplitude
Aortic Outlet BP (P ₂) Amplitude	Peak-Peak Amplitude, P ₁ - P ₂	J-K Amplitude	K-L Amplitude

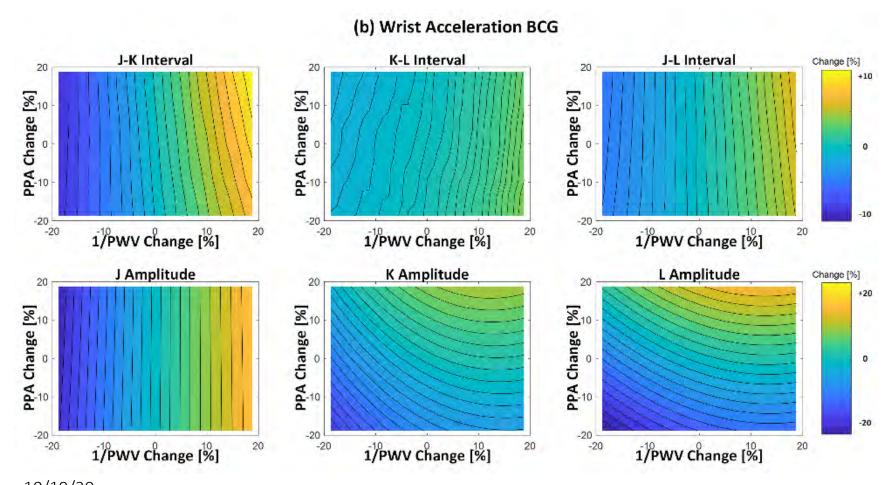
BCG: Physiological Interpretation & Insights

- The BCG waveform elucidates timing/amplitude info on BP waves
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BCG: Physiological Interpretation & Insights

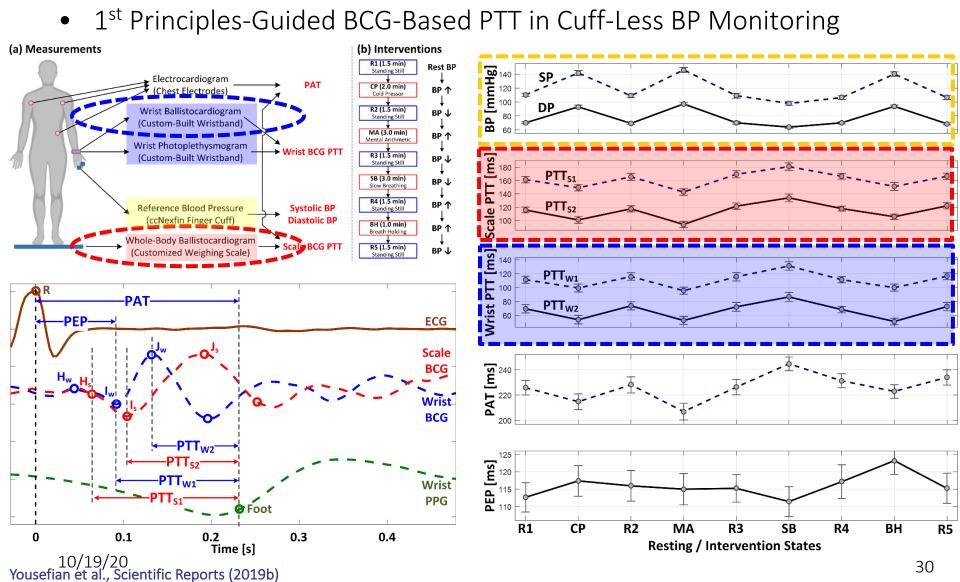
- The BCG waveform elucidates timing/amplitude info on BP waves
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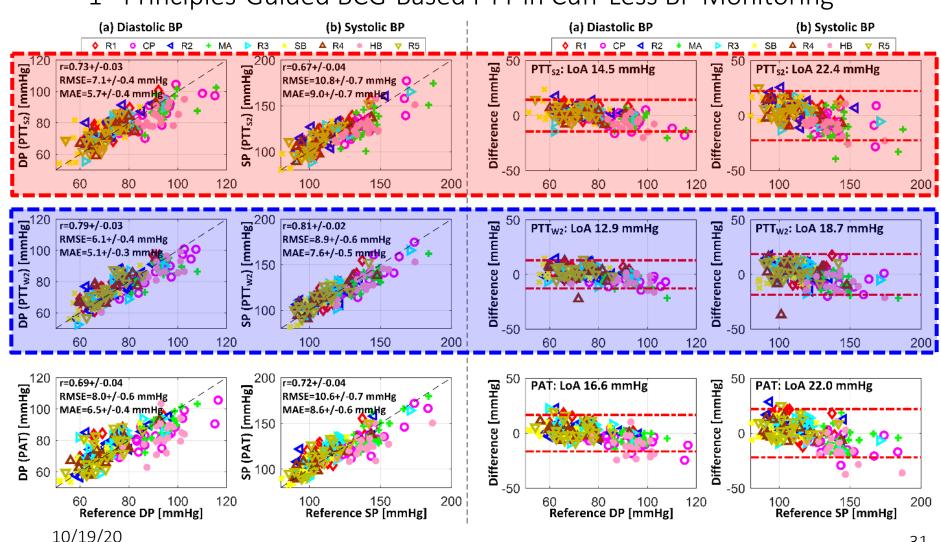
Ultra-Convenient Cuff-Less BP Monitoring via

BCG



Ultra-Convenient Cuff-Less BP Monitoring via

1st Principles-Guided BCG-Based PTT in Cuff-Less BP Monitoring



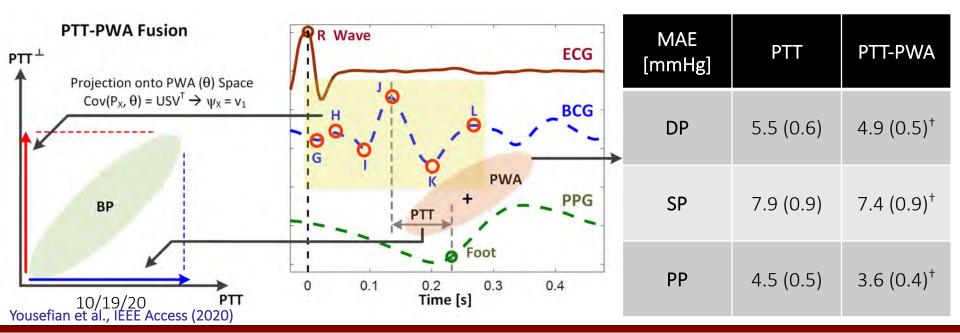
Utra-Convenient Cuff-Less BP Monitoring via

BCG:

PTT-Pulse Waye Analysis (PWA) Fusion in BCG and PPG supplementary to PTT

$$P_X = k_{X,1} \tau + K_{X,2} \psi_X(\theta) + k_{X,3}$$

- 1) X = S (systolic), D (diastolic), P (pulse)
- 2) The predictor τ is PTT based on the BCG
- 3) The predictor $\psi_X(\theta)$ is a a function of fiducial points θ in BCG and PPG



Oscillometric BP Measurement: Low Accuracy Issue



Oscillometry is the most widely used method for cuff BP measurement

Classical fixed-ratio method is population-based & prone to errors

Even high-end oscillometric BP monitors exhibit poor accuracy

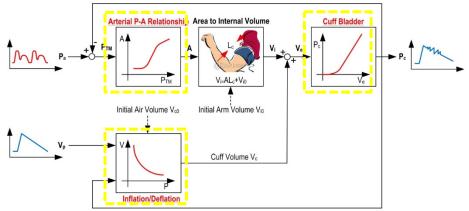
[gHmr 120	-	SP			
u] a		MAP	may 0	lefla	tion
sur		DP		Mary	m.
Cuff Pressure [mmHg]	- /i	nflation			
()	10 2	0	30	40 50
- <u>20</u>			0 Time (a)	[s]	1 1 1 1 1 1 1 1
Oscillation Amplitude [mmHg]	-		,		As/A _m = 0.61 A _D /A _m = 0.74
plitu 1		٨.	Am		A d
Amp		As			
tion 0	J	I W			
cilla					
Oscil)	10 2	0	30	40 50
			Time (b)	[s]	
	10	0/19/20	(6)		

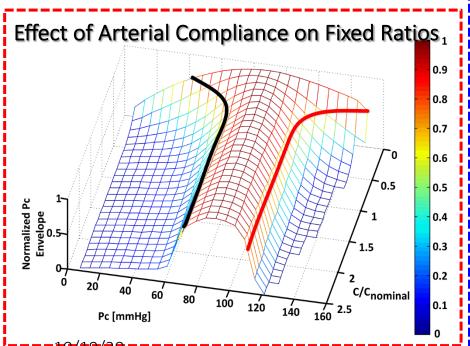
Device	Patient Type	BHS Grade	
SpaceLabs 90207	Droodamasia	SP	D
Natarajan et al., 1999	Preeclampsia	DP	D
IVAC Model 4200	l lagoital	SP	D
Shuler et al., 1998	Hospital	DP	С
Philips MP90	Name	SP	D
Mireles et al., 2009	Neurosurgery	DP	С
Microlife	Cardiac	SP	С
Shih et al., 2013	Catheterization	DP	С
Omron	Cardiac	SP	D
Shih et al., 2013	Catheterization	DP	D
Dinamap 1846 XT		SP	С
Beaubien et al., 2002	Hypertension	DP	С

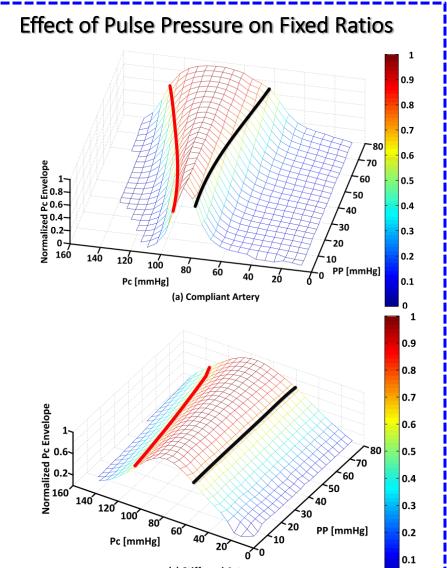


Elucidating Oscillometric BP Error Mechanisms



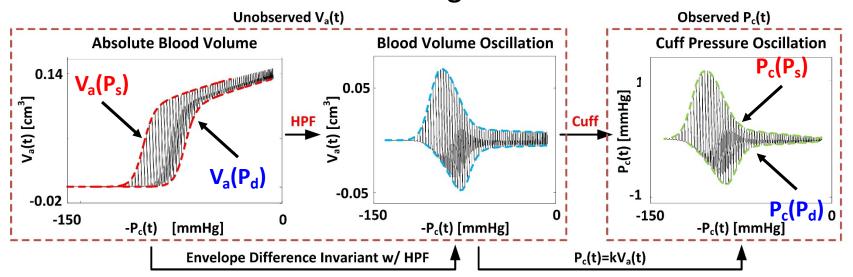






Patient-Specific Oscillometric BP Measurement

Oscillometric BP Measurement Algorithm: Model-Based SYSID



<u>Idea</u>

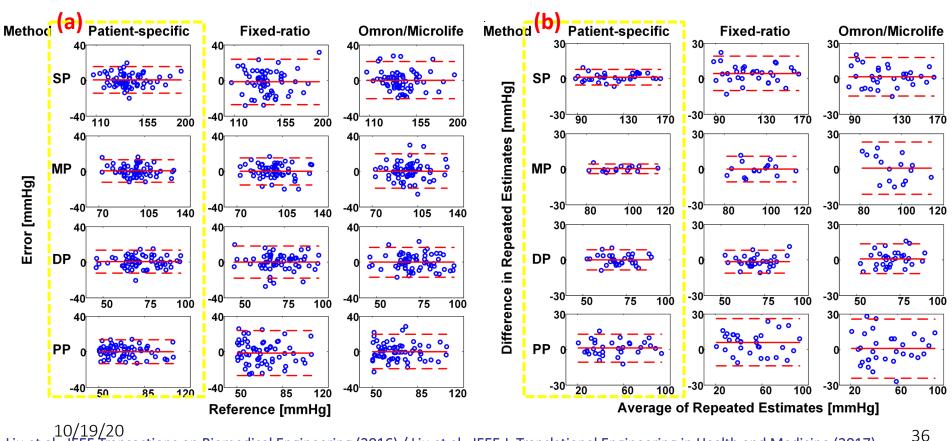
To estimate patient-specific BP and arterial compliance by fitting a patient's oscillogram signal to a mathematical model of oscillometry

$$\min_{\substack{a,b,c,k,P_s,P_d\\ \text{a,b,c,k,P_s,P_d}}} \left\| \underbrace{ \left(P_c(P_s) - P_c(P_d) \right) }_{\text{Measurements}} - k \underbrace{ \left(\widehat{V}_a(P_s) - \widehat{V}_a(P_d) \right) }_{\text{Model}} \right\|$$

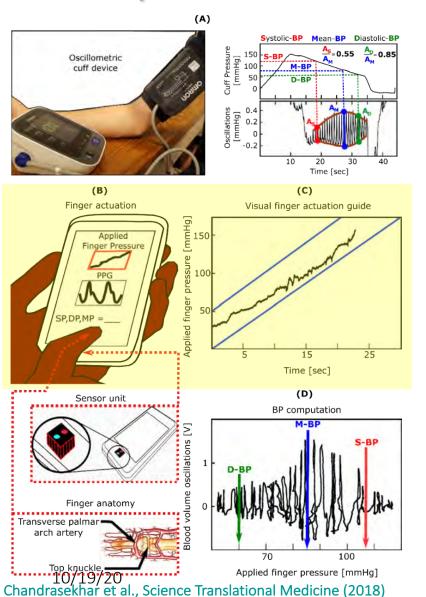
Patient-Specific Oscillometric BP Measurement

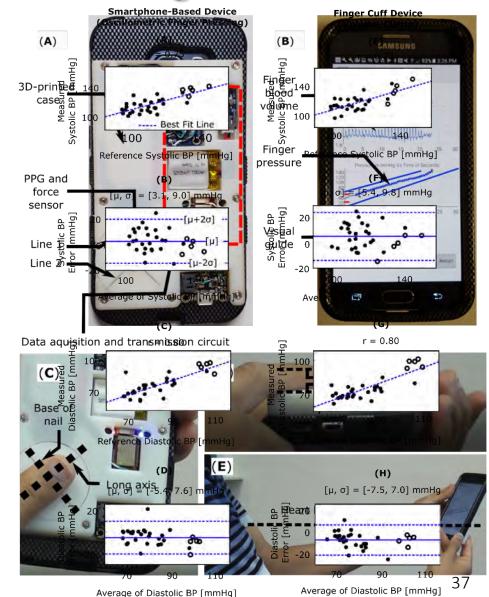
Blind Testing Results (145 Measurements from 88 Subjects): Precision & Repeatability

- 1) Comparable precision in normal PP group
- Significantly superior precision in high PP group (a)
- 3) Patient-specific method achieved repeatability within AHA recommended limits (b)



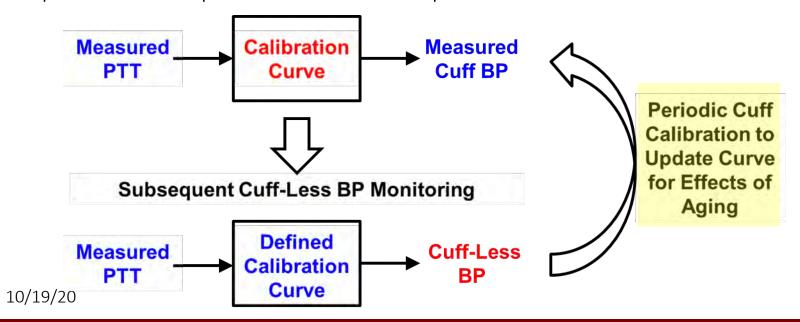
Smartphone-Based BP Monitoring





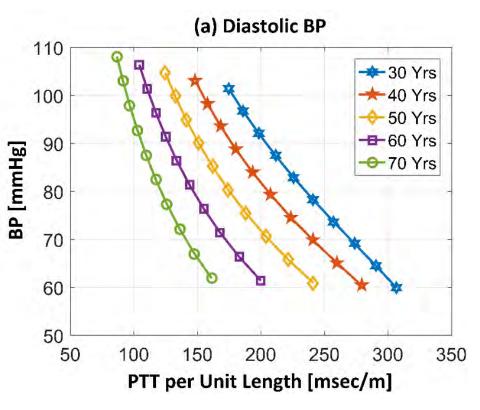
PTT-BP Relationship: Re-Calibration Period

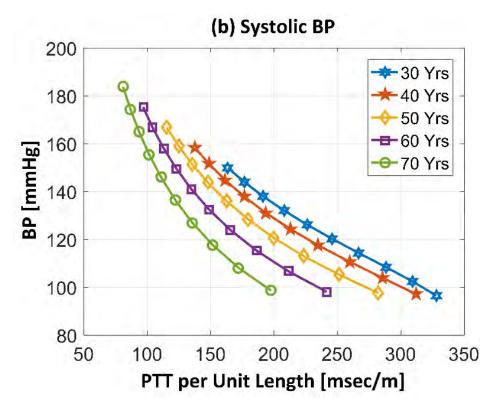
- How often the PTT-BP calibration relationship must be updated?
- Evolution of PTT-BP Relationship
 - Aging and disease → periodic update of PTT-BP model parameters.
 - 2) PEP and SMC → fast-acting; compensation not reasonable/ even feasible
- It is obviously desirable to perform the cuff initializations as infrequently as possible. The question is: how infrequent can it be?



Re-Initialization Period

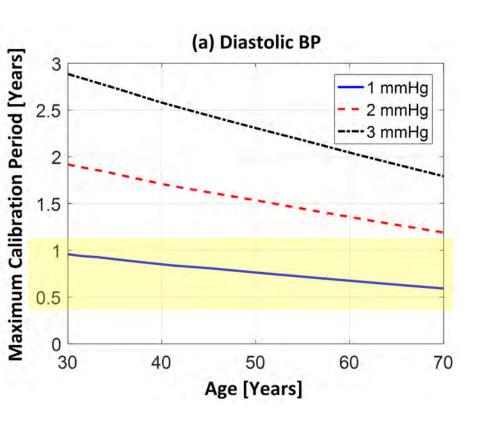
- One idea is to leverage mathematical models of PTT-BP relationship
- PTT-DP/SP relationship with age (B-H + Wesseling) → Theoretical prediction of re-calibration period

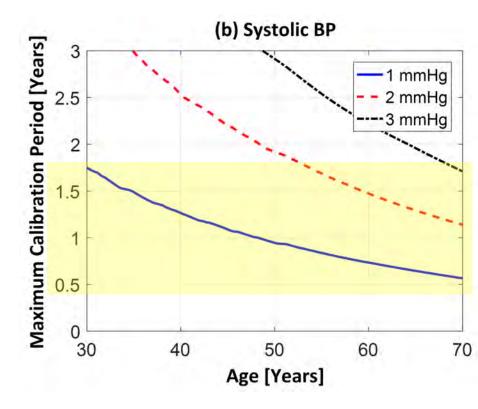




Re-Initialization Period

• The maximum calibration period to keep BP error < 1 mmHg is at least ~1 year for a 30 year old and declines linearly to ~6 months for a 70 year old.

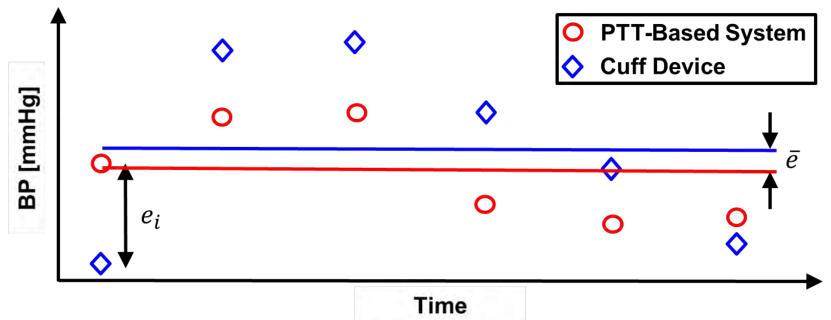






Acceptable Error Limits in Cuff-Less BP Devices

• Cuff-less BP may not be as accurate as cuff-based BP (due to the imperfect calibration and confounders (e.g., SMC)). But, by affording a large number of measurements that can be <u>averaged</u>, cuff-less BP may still be valuable in hypertension screening despite large errors in individual measurements.



→ What is the acceptable limit of individual cuff-less BP errors to achieve accurate hypertension detection comparable to auscultation and oscillometry?

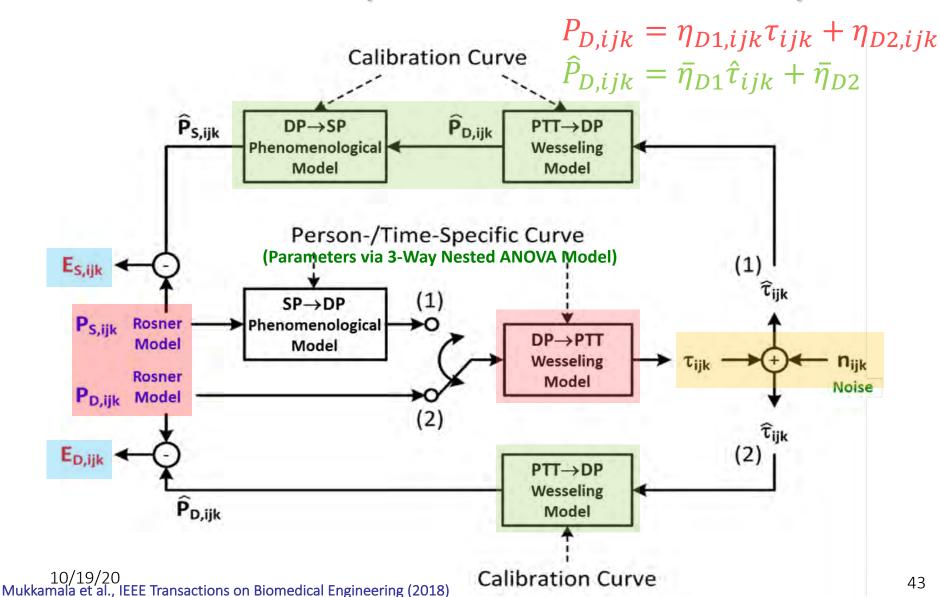
Within-Person BP Variability Model¹

3-Way Nested ANOVA Model

$$P_{X,ijk} = \overline{P}_X + \overline{P}_{X,i} + v_{P_X,ij} + e_{P_X,ijk}$$

- 1) \overline{P}_X : Population mean BP (X=S for SP and D for DP)
- 2) $\widetilde{P}_{X,i} \sim \mathcal{N}(0, \sigma_{P_X}^2)$: Between-person variability
- 3) $v_{P_X,ij} \sim \mathcal{N}\left(0,\sigma_{v_{P_X}}^2\right)$: Between-visit variability for a specific person
- 4) $e_{P_X,ijk} \sim \mathcal{N}\left(0,\sigma_{e_{P_X}}^2\right)$: Within-visit variability for a specific person and visit
- Systolic BP variability is greater than diastolic BP variability
- Between-visit period variability is greater than within-visit period variability
- Averaging single-visit cuff BP does not reduce between-visit period variability

Model-Based Acceptable Error Limits Analysis

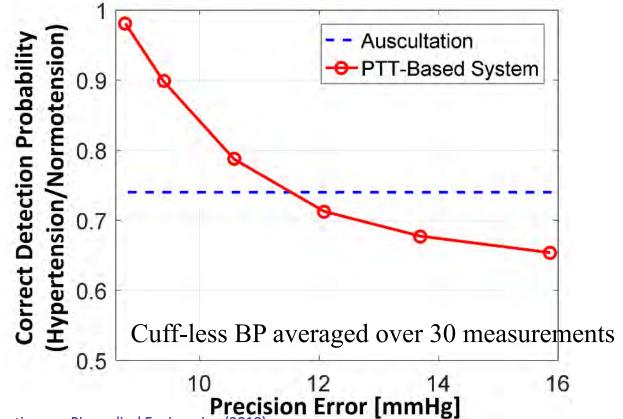




Acceptable Error Limits: Auscultation as

Reference

- SP precision limit: ~12 mmHg / DP precision limit: ~8 mmHg
- SP/DP bias: ~5 mmHg
- These predictions ignore auscultation error, white coat and masked effects, and nighttime measurements and may thus constitute lower bounds.





Acceptable Error Limits: Oscillometry as Reference

 The error in a PTT-based system w.r.t. an oscillometric device is expressed as the error in the PTT-based system w.r.t. auscultation minus the error in the oscillometric device w.r.t. auscultation:

$$\widehat{P}_{X} - \widehat{P}_{X,osc} = \underbrace{\left(\widehat{P}_{X} - P_{X}\right)}_{A} - \underbrace{\left(\widehat{P}_{X,osc} - P_{X}\right)}_{B}$$

- 1) A: Cuff-less BP error w.r.t. auscultation
- B: Oscillometric BP error w.r.t. auscultation
- 3) A and B may not be highly correlated b/c the error sources associated with A and B are distinct
- → SP precision error limit can be up to ~14 [= $\sqrt{(12^2+8^2)}$] mmHg; DP precision limit can be up to ~11 [= $\sqrt{(8^2+8^2)}$] mmHg; and bias error limits can be up to 10 mmHg in magnitude!

Acceptable Error Limits: Conclusions

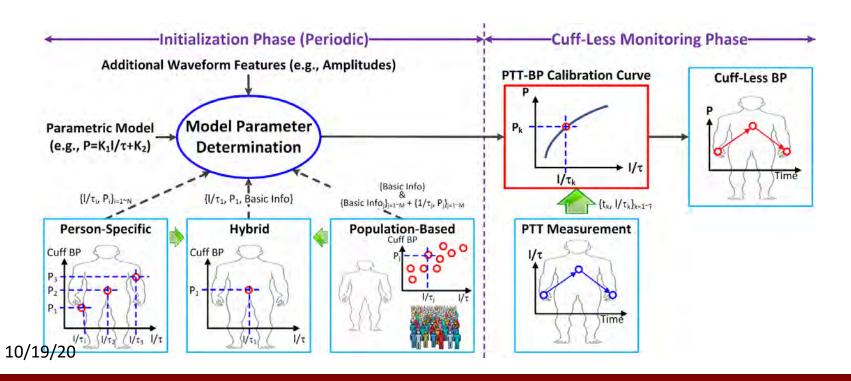
 PTT-based systems w/ bias and precision errors > 5 mmHg and > 8 mmHg, especially with respect to automatic cuffs, should not be readily dismissed.

• The evaluation should be on a hypertension screening accuracy test rather than a measurement accuracy test.

• A running average of many BP measurements should be reported to indicate the true underlying BP of the person.

Cuff-Less Blood Pressure (BP) Monitoring via PTT

- Key Components:
 - 1) PTT measurement methods
 - Parametric model relating PTT to BP
 - 3) Model parameter determination methods
 - 4) Re-calibration period & acceptable error limits





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