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1 **Wireless, Skin-Interfaced Devices for Pediatric Critical Care: Application to**
2 **Continuous, Noninvasive Blood Pressure Monitoring**

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3
4 Indwelling arterial lines, the clinical gold standard for continuous blood pressure (BP)
5 monitoring in the pediatric intensive care unit (PICU), have significant drawbacks due to their
6 invasive nature, ischemic risk, and impediment to natural body movement. A noninvasive,
7 wireless, and accurate alternative would greatly improve the quality of patient care. Recently
8 introduced classes of wireless, skin-interfaced devices offer capabilities in continuous,
9 accurate monitoring of physiologic waveform and vital sign data in pediatric and neonatal
10 patients, but have not yet been employed for continuous tracking of both systolic and diastolic
11 BP, as part of a critical base of information for guiding clinical decision-making in the PICU.
12 The results presented here focus on materials and mechanical designs that optimize the
13 system-level properties of these devices to enhance their reliable use in this context, to
14 achieve full compatibility with the complete range of body sizes, skin types, and sterilization
15 schemes typically encountered in the PICU. Systematic analysis of the data collected using
16 these devices, over 82 hours of continuous recordings from 23 pediatric patients, yields
17 derived, noninvasive values of BP that can be quantitatively validated against direct, time-
18 synchronized recordings from arterial lines. The results from a diverse patient cohort,
19 including those under various pharmacological protocols, suggest that wireless, skin-
20 interfaced devices can, in certain circumstances of practical utility, accurately and
21 continuously monitor BP in the PICU patient population.

22 23 **1. Introduction**

24 Invasive arterial catheterization with an indwelling arterial line (a-line) forms the basis
25 for continuous blood pressure (BP) monitoring of patients in critical care. These data are
26 extremely important, as highly hypertensive or hypotensive events may indicate dramatic,
27 life-threatening changes in physiological well-being that require medical intervention.^[1-3]

1 Despite serving as the clinical gold standard for tracking such events, a-lines—received by
2 approximately 36% of all adult intensive care unit (ICU) patients in the United States—
3 involve multiple risks, notably limb ischemia and infection.^[2,4-8] The placement of an a-line
4 also poses its own challenges, including the need for procedural sedation and difficulties in
5 obtaining vascular access in small or very ill patients. These considerations are particularly
6 pronounced in infants admitted to the pediatric ICU (PICU), where intrusive a-lines are
7 disproportionately sized with respect to their small arteries.^[9-11] Managing such complications
8 requires various clinical interventions, such as ultrasound imaging to assist and guide
9 placement of the a-line, but with significant additional workload and, in the context of
10 COVID-19, increased risk of exposure of frontline health-care workers to the virus.^[12-15] A-
11 lines are also highly restrictive in nature, with many hospitals electing to use cumbersome—
12 albeit protective—accessories (e.g., padded splints, braces, tapes) to immobilize the puncture
13 site and prevent any disturbance to the a-line itself, inevitably restricting natural movements
14 of the patient.^[16-17] While discrete, oscillometric cuff-based BP measurements avoid the
15 ischemic, infectious, and procedural risks associated with a-lines, they do not offer
16 continuous, beat-to-beat information, they can be inaccurate in BP extremes or in certain
17 patients, and they can contribute to skin-related injuries (e.g., skin breakdown, pressure
18 ulcers) for infant PICU patients.^[18-20] With full consideration of these limitations, a clinical
19 tool that could provide continuous, accurate, and beat-to-beat BP measurements, in a manner
20 that is conducive to free body movement and is safe for sensitive pediatric skin, with minimal
21 practitioner management and/or intervention, would be invaluable.

22 As described recently by our group, a simple pair of time-synchronized wireless, skin-
23 interfaced devices, built according to the principles of soft hybrid electronics, can non-
24 invasively capture continuous waveform and vital sign data (e.g., electrocardiography (ECG),
25 photoplethysmography (PPG), heart rate (HR)) for neonatal and pediatric patients in ICUs.^[21]
26 Initial exploratory results suggest the use of pulse arrival time (PAT), defined as the time for a

1 pulse to travel from the heart to a peripheral site (foot or hand), as a proxy for systolic BP
2 (SBP). While SBP measurements are important in hemodynamic monitoring, they are
3 inadequate for critically ill patients, for whom diastolic BP (DBP) provides valuable
4 information about the risk for coronary artery malperfusion. SBP does not reliably predict
5 DBP in critical illness and, therefore, requires its own independent measurements. A
6 combination of PAT and HR is of interest for its strong correlation with both SBP and DBP in
7 adult patients, and there currently exist FDA-approved, *wired* clinical BP monitors, based on
8 PAT and HR.^[22-25] This multivariate analysis approach, for both SBP and DBP prediction, has
9 not, however, been explored for patients in the PICU or neonatal ICU (NICU), nor has it been
10 accomplished using wireless technologies relevant to these vulnerable subjects.

11 Our previously reported system features a binodal pair of devices, one that mounts on
12 the chest and another that mounts on a limb, typically the hand or foot. This latter device
13 performs PPG, in a most recent design that doubly wraps around the limb, with an umbilical
14 interconnect that unites the two wrapping components.^[21] Such a configuration demands
15 extreme levels of bendability and, without optimized materials and layouts, it imposes
16 constraints on the patient's range of motion, and it is susceptible to motion artifacts that can
17 dramatically reduce the signal quality and reliability of the measurement.

18 This paper reports two sets of advances in this context. The first focuses on aspects of
19 materials science and mechanical design that support a stable, yet soft and comfortable,
20 interface between the limb unit and patients in the PICU, across a broad range of ages and
21 body sizes. This component of the work includes quantitative, system-level studies by digital
22 image correlation (DIC) methods, high-speed tracking techniques, and finite element analysis
23 (FEA) simulations. The results, together with comparative analysis of various, low-modulus
24 materials for device encapsulation and skin adhesion, yield devices optimized for pediatric
25 uses, including procedures for sterilization that do not alter the operational characteristics or
26 the properties of the constituent materials. Pilot studies based on 23 PICU patients and over

1 82 cumulative hours of recordings demonstrate reliable performance of these systems, without
2 adverse events. The second part of the paper examines empirical relationships that connect
3 key hemodynamic parameters associated with these recordings to both SBP and DBP.
4 Comparisons to corresponding measurements performed with a-lines establish the accuracy of
5 relationships that include both HR and PAT, across a diverse patient cohort and set of
6 pharmacological circumstances. The collective results suggest that wireless, soft electronics
7 have the potential to significantly improve the care of patients in the PICU.

9 **2. Results and Discussion**

10 **2.1. Wireless, Skin-Interfaced Devices in the PICU**

11 Recently introduced wireless, skin-interfaced devices can provide ICU-grade
12 monitoring of continuous waveform and vital sign data for neonatal and pediatric patients.^[21]
13 This noninvasive technology, comprised of flexible, stretchable electronic systems
14 encapsulated with thin, soft, medical-grade polyorganosiloxane materials, features two
15 separate devices that operate in a time-synchronized manner. The first device (“chest device”;
16 weight: ~12 g; dimensions: ~5 cm x 3 cm x 0.6 cm (length x width x height)) mounts on the
17 chest for measurements of: 1) 1-lead ECG through gold-plated electrodes interfaced to the
18 skin via a thin, conductive hydrogel adhesive (KM 40A, Katecho), 2) respiratory rate,
19 seismocardiography (SCG), body orientation, activity levels and vocal biomarkers (crying
20 patterns) through a triaxial, high-bandwidth accelerometer, and 3) central-skin temperature
21 via a clinical-grade temperature sensor. The second device (“limb device”; weight: ~9 g;
22 dimensions: ~9 cm x 3 cm x 0.6 cm (length x width x height)) mounts on a peripheral
23 extremity (foot or hand), secured with a soft wrap, for measurements of: 1) transmission
24 mode, dual-wavelength (red and infrared) PPG, from which blood oxygenation (SpO₂) can be
25 derived, and 2) peripheral-skin temperature via a clinical-grade temperature sensor. Images of
26 and schematic representations of the pair of devices (**Figure 1A**), as worn by a 37-week-old

1 PICU patient (Figure 1B-C), highlight the contrast between this system and the wired
2 collection of sensors that represent the current standard of care (Figure 1D-E).

3 Continuous and wireless device operation of up to 60 hours relies on embedded,
4 wirelessly rechargeable lithium-polymer batteries (60 mAh capacity) and Bluetooth low
5 energy communication protocols. Data can be stored onto memory modules (4 gigabyte
6 storage capacity) within the devices themselves and/or live-streamed to a nearby connected
7 Bluetooth-enabled device (e.g., iPad Pro), allowing for uninterrupted recording and
8 acquisition of physiological waveforms and vital signs (Figure 1F).

9 **2.2. Optimized System-Level Mechanics and Materials of the Peripheral Limb Device**

10 The system-level layout, mechanics, and materials of the chest device remain
11 relatively unchanged compared to those reported previously.^[21] The focus here is on several
12 advances in encapsulation design and material choices (unoptimized design (UD) vs.
13 optimized design (OD)) for the peripheral limb device (**Figure 2A-B**, Figure S1), to improve
14 their interfaces to peripheral limbs of pediatric patients (Figure 1C, Figure S2). Here, an inner
15 filler layer of OO-30 polyorganosiloxane elastomer (Ecoflex OO-30, Smooth-On) and an
16 outer shell of A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) encapsulate
17 the device. This design proves to be a critical component for high signal quality data
18 collection from transmission-mode PPG, as the dual-wavelength light-emitting diodes (LEDs)
19 must maintain alignment with the photodetector upon wrapping around the small limbs of
20 these patients. In particular, this configuration reduces the strain magnitude (Figure 2C-D;
21 Supplementary Video 1) and shear strain (Figure 2E-F; Supplementary Video 2) distributions
22 upon uniaxial stretching deformations of the serpentine wiring that connects the LEDs to the
23 photodetector on the main body of the device. Experimental confirmation of the effects relies
24 on digital image correlation (DIC) approaches that quantify the axial displacement of
25 speckled surface patterns (Figure S3-S4), for accurate measurement of surface
26 deformations.^[26] Results show that the strain magnitude and shear strain profiles for the

1 regions in between the LED unit and the photodetector ($x = 18$ mm) at the edge regions of the
2 OD decrease by $\sim 33\%$ and $\sim 96\%$, respectively, compared to those of the UD devices (Figure
3 2G-H). Validated finite element analysis (FEA) simulations (Figure S5-S8) complement these
4 experimental results, illustrating the high strain concentration in the UD, compared to the
5 minimal strains in the OD, as the device undergoes bending deformations (Figure 2I-J) that
6 occur as the device wraps the hand or foot of a PICU patient. Figure 2K further highlights the
7 differences in structural mechanics between the UD and OD, and importantly, the influence of
8 the choice of soft materials for encapsulation. The OD, with an outer encapsulation shell of
9 A-20 polyorganosiloxane elastomer and inner filler layer of OO-30 polyorganosiloxane
10 elastomer, decreases the effective modulus by $\sim 83\%$ and $\sim 96\%$, compared to that of the UD
11 with the same materials and of the UD with the A-20 polyorganosiloxane as both the shell and
12 filler, respectively (Figure S9).

13 Another method to characterize the stiffness of the system is to compute the natural
14 frequency and damping ratios of key structural components. The oscillatory behaviors for the
15 LED units of the UD and OD can be captured by the high-speed tracking method.^[27] As
16 expected, both devices exhibit damped harmonic oscillations (Figure 2L; Supplementary
17 Video 3), from which the natural (resonant) frequency and damping ratios are characterized
18 (Figure 2M-N). The OD shows $\sim 49\%$ and $\sim 38\%$ decreases in natural frequency and damping
19 ratio, respectively, compared to those of the UD. Fundamentally, experimental
20 characterizations via DIC and the high-speed tracking method, complemented by FEA
21 analyses, confirm that the OD, with its two-part polyorganosiloxane elastomer encapsulation
22 and space-efficient encapsulation design, enhance the soft mechanical properties of the
23 system, of critical importance for wrapping small peripheral limbs of pediatric patients. To
24 adhere and secure the limb device with the OD in place, the soft fabric wrap utilizes a velcro
25 hook and loop dot to complete full wrapping of the device around the peripheral limb.

1 Hydrogel pieces can also be integrated with the bottom surface of the device (Figure S20) to
2 enable adhesion to the skin.
3

4 **2.3. Characterization of Soft Materials Used for Device Encapsulation and Skin**

5 **Adhesion**

6 As FEA simulations indicate (Figure 2K, Figure S9), soft materials are important
7 factors in determining the effective mechanical properties of the overall system. Thus, the
8 compatibility of these devices with the sensitive, fragile skin of PICU patients relate directly
9 to the use of such materials (e.g., polyorganosiloxane elastomers and gels), for both device
10 encapsulation/packaging and direct skin contact. The layered soft materials stack on the skin,
11 for both the chest and limb device, is shown in **Figure 3A**. In the case of the chest device, a
12 soft hydrogel (KM 40A, Katecho), based on the 2-acrylamido-2-methylpropane sulfonic
13 acid/acrylic acid (AMPS/AA) copolymer, forms the conductive interface between the bottom
14 layer (A-20 polyorganosiloxane elastomer)/gold-plated ECG electrodes of the device and the
15 skin.

16 *2.2.1. Stability of the A-20 Polyorganosiloxane Elastomer*

17 Continuous and safe use of these devices in the ICU environment fundamentally
18 requires the long-term stability and robustness of the outer encapsulation shell material (A-20
19 polyorganosiloxane elastomer). Although many studies focus on the mechanical stability of
20 polydimethylsiloxane (PDMS),^[28-30] as a function of long shelf aging time periods at ambient
21 conditions, limited data are available for other polyorganosiloxane elastomeric materials.
22 Some studies suggest that certain commercial variants undergo softening and loss of
23 compression strength over time, perhaps due to fillers, such as iron oxide, that induce
24 cleavage of the siloxane backbone.^[31-32] Additionally, residual fragments from organo-tin
25 catalysts (e.g., tin dicarboxylates, dialkyltin dicarboxylates) typically used for condensation
26 curing of these materials, together with ambient humidity, can significantly affect load-
bearing properties, due to bond cleavage of the siloxane backbone and associated reduction of

1 load-bearing polymer chains.^[33-34] Here, analysis of Shore hardness yields information on the
2 mechanical stability of dyed A-20 polyorganosiloxane elastomer over a time period spanning
3 more than two months (Figure 3B, top). Additional such measurements upon repeated
4 exposure to high temperature (121°C), humidity, and pressure conditions in an autoclave
5 steam sterilizer, further confirm the mechanical stability of the material (Figure 3B, bottom).
6 Both experiments in Figure 3B indicate that no significant changes occur under these
7 conditions. The observations are particularly relevant for emerging uses of these devices in
8 tropical or humid climates, such as those typically encountered in South America, Africa, and
9 Asia. Battery-free devices^[21,35] and designs that use removable batteries^[21] can be sterilized
10 within the autoclave, according to standard protocols.

11 In the ICU environment, UV germicidal irradiation (UVGI) is another common
12 sterilization approach.^[36] Here, light in the UVC region of the spectrum (200-280 nm)
13 deactivates microorganisms and viruses that reside on common surfaces.^[37-38] This method is
14 increasingly popular in the context of the COVID-19 pandemic, as an energy-efficient,
15 chemical-free method that can be effective at low exposure doses (3.7 mJ/cm² and 16.9
16 mJ/cm² result in a 3-log reduction and full deactivation of SARS-CoV-2, respectively).^[39]
17 Studies of the stability of the A-20 polyorganosiloxane elastomer upon exposure to UVC are
18 relevant in this context. Figure 3C shows FTIR transmission spectra of A-20
19 polyorganosiloxane elastomer, at a thickness of ~30 μm, as a function of cycles of exposure
20 to UVC at a dose (31.8 mJ/cm²; narrow-band UVC, λ = 254 nm) that exceeds reported
21 thresholds for significant log reduction and full deactivation of SARS-CoV-2 and other
22 similar SARS-family viruses.^[37-39] All spectra display the same stretching bands (e.g., the
23 strong, broad peak (ν = 1008 cm⁻¹) representative of the siloxane backbone (Si-O-Si)
24 stretching, the strong, sharp peak (ν = 786 cm⁻¹) representative of Si-C stretching), indicating
25 no observable chemical change. Despite the small wavelengths of UVC, some studies have
26 shown that UVC penetrates into the stratum corneum (~30 μm thickness)—the outermost

1 layer of the skin—inducing chemical damage.^[40] Similarly, other studies have shown that
2 UVC can overcome the thermodynamic energy barrier required to decompose both the Si-C
3 (~301 kJ/mol) and Si-O-Si (~447 kJ/mol) bonds of certain polyorganosiloxane rubbers.^[41]
4 Photons in the UVC wavelength range (254 nm) exceeds the energies of these bonds, leading
5 to chain scission of the main backbone and associated side chains, eventually forming new
6 radicals. The penetration depth at which UVC induces such chemical changes in
7 polyorganosiloxanes, such as PDMS, is still under debate,^[42] with some studies suggesting
8 depths ranging from ~20-30 nm^[43] to ~8-14 μm .^[44] While FTIR is valuable for discerning
9 specific functional groups in the bulk, any possible chemical changes induced in the ultrathin,
10 near-surface region of these materials should be further investigated with more surface-
11 sensitive techniques, such as near edge x-ray absorption fine structure (NEXAFS).^[45]
12 Regardless, radical fragments produced by photoirradiation are known to recombine,^[45-46] and
13 furthermore, polyorganosiloxane materials feature constant diffusion of residual oligomers to
14 the surface (“recovery”).^[46] Therefore, sufficiently thick layers of A-20, as the outer
15 encapsulation shell for the chest and limb devices, should maintain compatibility with UVC
16 sterilization techniques.

17 *2.2.2. Surface Energy Modulation of A-20 as a Route for Improving Adhesion to Hydrogels*

18 Pristine polyorganosiloxanes are intrinsically hydrophobic, and they have low surface
19 energies with poor wettability. In contrast, hydrogels consist of a hydrophilic macromolecular
20 polymer network structure, and typically possess high surface energy. As the de Bruyne
21 empirical rule of adhesion postulates, the incompatibility and weak matching of surface
22 polarities between these two classes of materials leads to poor adhesive bonding properties
23 between them.^[47-48] Thus, the integration of such dual opposing surface energy materials into
24 a singular device system, such as in the case of the interfacial contact between the A-20
25 bottom layer of the chest device and the conductive AMPS/AA hydrogel, may benefit from
26 increases in the surface energy of the A-20 polyorganosiloxane elastomer. Here, changes in

1 the water contact angle between pristine A-20 ($111 \pm 3^\circ$) and A-20 modified with a
 2 trisiloxane ethoxylate (Silwet L-77, Bioworld) surfactant ($83 \pm 4^\circ$) indicate an increase in the
 3 hydrophilicity and surface energy of the surfactant-modified A-20 (Figure 3D), approaching
 4 values close to that of the AMPS/AA hydrogel ($49 \pm 3^\circ$).

5 The surface energy properties appear in the Young-Dupre equation,^[49] which states
 6 that the thermodynamic work (work of adhesion) required to separate two different interfacial
 7 phases (e.g., liquid and solid) to an infinite distance is related to the contact angle:

$$W = \gamma(1 + \cos(\theta)) \quad (1)$$

8 where W is the work of adhesion (mJ/m^2), γ is the surface tension of the liquid ($\gamma_{\text{water/air}, 25^\circ\text{C}} =$
 9 $71.99 \text{ mJ}/\text{m}^2$), and θ is the contact angle. Figure 3E illustrates the work of adhesion between
 10 polar liquid water droplets and pristine A-20 ($44 \pm 9 \text{ mJ}/\text{m}^2$), surfactant-modified A-20 ($77 \pm$
 11 $18 \text{ mJ}/\text{m}^2$), and the AMPS/AA hydrogel ($104 \pm 12 \text{ mJ}/\text{m}^2$). As expected, the surfactant-
 12 modified A-20 increases ($\sim 77\%$) the work of adhesion, confirming the effectiveness of this
 13 surfactant modification approach.

14 Figure 3F demonstrates results from 90° peel force testing of AMPS/AA hydrogel on
 15 pristine A-20 and surfactant-modified A-20 substrates. While the surfactant-modified A-20
 16 exhibits a substantial increase ($\sim 52\%$) in peel force compared to pristine A-20, consistent with
 17 increased adhesion with the hydrogel, the values are relatively small. Many factors, in
 18 addition to surface polarity/wettability, influence adhesion, including the specific nature of
 19 the chemical interactions (covalent, hydrogen, ionic, dispersion forces, etc.) between the
 20 materials, mechanical dissipation, and the topology of the adherend connections.^[50-51]
 21 Additional investigations of these effects may lead to strategies for further improvements.

22 Figure 3G illustrates comparative results from similar peel testing of three commercial
 23 hydrogel adhesives on an adult with sensitive skin, including: 1) individually packaged
 24 neonatal tape strips (“Covidien Hydrogel”), 2) an acrylate/acrylamide (“Acrylate/AAm”)
 25 copolymer-based hydrogel (KM 30 E, Katecho), and 3) the AMPS/AA hydrogel. The
 26

1 measurements indicate that all three adhesives remain on the skin both immediately after
 2 application and after 20 h of wear, including during overnight sleep. The Acrylate/AAm and
 3 AMPS/AA hydrogel adhesives both require significantly less (~81%) peel force compared to
 4 the Covidien hydrogel tape when immediately adhered to the skin. After 20 h of wear,
 5 however, the AMPS/AA hydrogel adhesive exhibits the smallest peel force (~83% and ~25%
 6 less than Covidien hydrogel and Acrylate/AAm hydrogel, respectively). These characteristics
 7 are attractive for applications on fragile skin in the PICU setting, as the material optimally
 8 balances gentleness on the skin with long-term adherence for continuous ECG measurements.

9 **2.3. Continuous BP Monitoring in the PICU with Wireless, Skin-Interfaced Devices, via** 10 **PAT and HR**

11 Time-synchronized ECG and PPG waveforms (**Figure 4A**) captured using these
 12 devices allow for calculations of the PAT, as defined by the time delay between the ECG
 13 waveform R-wave peak and the onset of the PPG waveform at the peripheral limb device.

14 Also, HR, defined by the time interval between successive R-wave peaks can be derived.^[21-25]

15 Values of PAT and/or HR can be connected to BP through empirical relationships defined by
 16 model equations and calibration procedures (Figure 4B-C). The four model equations
 17 examined here range from a multivariate linear form,^[22-25]

$$18 \quad BP = a(PAT) + b(HR) + c \quad (2)$$

19 to a univariate linear form,^[21-25,52-53]

$$20 \quad BP = a(PAT) + b \quad (3)$$

$$21 \quad BP = a(HR) + b \quad (4)$$

22 to a nonlinear inverse square relation,^[54]

$$23 \quad BP = a\left(\frac{1}{PAT^2}\right) + b \quad (5)$$

24 in which BP can represent SBP or DBP. Figure 4D-E illustrates representative examples of
 25 continuous SBP and DBP recordings for: 1) a 127-week-old female patient with acute

1 hypoxemic respiratory failure, Trisomy 21, and multiple organ dysfunction, and 2) a 47-
2 week-old female patient with biliary atresia, status post liver transplant, and hypertension
3 secondary to liver condition, respectively. In both cases, multivariate linear regression
4 (Equation 2) of the initial ten minutes of PAT and HR data to the corresponding a-line BP
5 data yield model coefficients (e.g., a, b, c) from which to estimate BP at subsequent times.
6 These results highlight the agreement of BP determined in this manner with direct
7 measurements using indwelling a-lines. This correspondence persists even through periods of
8 significant fluctuations in BP.

9 **2.3. Evaluation of BP Prediction Model Performance**

10 The studies include data collected from 23 PICU patients, corresponding to a total of
11 290,108 paired comparisons of SBP (**Figure 5**) and DBP (**Figure 6**) determined using data
12 collected with the devices described in Figure 1 and measurements performed with indwelling
13 a-lines. Bland-Altman plots (Figure 5A-D, Figure 6A-D) describe the quantitative agreement
14 between values determined using each of the four prediction models and the corresponding a-
15 line results. For SBP prediction (Figure 5A-D), the mean and SD of the difference in BP is 1.7
16 ± 8.7 mmHg, 0.3 ± 12.2 mmHg, -1.9 ± 11.4 mmHg, and -1.1 ± 76.1 mmHg, corresponding to
17 prediction models in Equation 2-5, respectively. The correlation matrix in Figure 5E
18 summarizes the Pearson's product-moment correlation coefficient ("r") between each of the
19 different models and the a-line SBP. The results indicate that the model with the strongest
20 linear relationship ($r = 0.85$) with the a-line is, as expected, the multivariate PAT/HR model
21 (Figure 5F). For DBP prediction (Figure 6A-D), the mean and SD of the difference in BP is
22 1.8 ± 6.2 mmHg, 0.7 ± 9.0 mmHg, -1.1 ± 9.0 mmHg, and 0.5 ± 9.7 mmHg, respectively. The
23 correlation matrix in Figure 6E also suggests that the multivariate PAT/HR model for DBP
24 has the greatest linear correlation (Figure 6F) with the a-line ($r = 0.77$).

25 The Food and Drug Administration (FDA) recognizes consensus standards for
26 evaluation of noninvasive BP measurements (ANSI/AAMI/ISO 81060-2:2013) that require

1 that the mean and SD of the BP difference between the test device and the reference (e.g.,
2 indwelling a-line or cuff/stethoscope BP auscultation) is less than or equal to 5 mmHg and 8
3 mmHg, respectively, for adults.^[55] The Bland-Altman results in our study (Figure 5A-D,
4 Figure 6A-D) indicate that the devices and analysis approaches (Equation 2-5) meet these
5 adult FDA specifications for measurements of DBP. For SBP, the mean difference, across all
6 four models, is well within the 5 mmHg limit, the SD—of which the smallest value is 8.7
7 mmHg with the multivariate PAT/HR model—slightly eclipses the 8 mmHg criterion. Despite
8 this marginal discrepancy, the results suggest that optimized wireless, skin-interfaced devices,
9 when calibrated with the multivariate PAT/HR model, can yield acceptable quantitative
10 equivalence to the clinical gold standard a-line for BP measurements in the PICU, as further
11 evidenced by the strong statistical correlation between the comparative measurements (Figure
12 5E-F, Figure 6E-F). An important fact is that, although the indwelling a-line is considered to
13 be the clinical gold standard for BP measurements, the results can be subject to both over- and
14 underestimation, due to improper dampening of waveforms.^[56]

15 The aforementioned FDA consensus standard typically requires a sample size of at
16 least 85 patients, determined from a power t-test with a 5% probability that a working device
17 was rejected ($\alpha = 0.05$) and a 2% probability ($\beta = 0.02$) that an inaccurate device would be
18 approved.^[55, 57] This criterion is specifically set for studies that utilize manual
19 cuff/stethoscope auscultation as the BP reference. Due to challenges associated with
20 recruitment of patients with indwelling a-line reference measurements, the FDA recommends
21 that validation studies using invasive BP references to have a minimum sample size of 15
22 patients.^[55, 57] Therefore, the sample size ($n = 23$ patients) used for the analyses presented here
23 not only *exceeds* the required minimum, but the large amount of within-subject data (e.g.,
24 290,108 total observations from 23 patients = an average of 12,613 observations per patient)
25 provides sufficient statistical power for high confidence conclusions. Previous work suggests

1 >99% power to detect significant associations with only 2,400 nested observations, which this
2 study exceeds.^[58]

3 **2.4. Changes in BP During and After Pharmacologic Interventions**

4 Pharmacologic interventions are common in the PICU. Certain drugs can induce
5 hemodynamic changes, as observed in measures of BP, HR, and PAT.^[59-61] **Figure 7** displays
6 various examples of the ability of measurements using the wireless, skin-interfaced devices,
7 with the multivariate PAT/HR model (Equation 1), to capture such changes. Figure 7A shows
8 the effects of enteral lorazepam, administered to a 75-week-old patient with a history of
9 bronchopulmonary dysplasia, due to extreme prematurity, and hospitalized for acute
10 hypoxemic respiratory failure. Note the gradual increase in PAT (Figure 7A, first row), along
11 with gradual decrease in HR (Figure 7A, second row) and both SBP and DBP (Figure 7A,
12 third and fourth rows, respectively). The a-line SBP and DBP data also reflect these
13 decreasing trends. All observed patterns are consistent with known sedative effects of
14 lorazepam, a benzodiazepine.^[62-63] Figure 7B shows the effects of methadone, a synthetic
15 opioid analgesic, administered to an 8-week-old patient with seizures, severe anoxic brain
16 injury, and multiple fractures. Note similar hemodynamic trends in PAT, HR, and BP,
17 consistent with the known sedating narcotic effects of methadone.^[64-65] Figure 7C shows the
18 effects of an intravenous dose of hydromorphone, a semisynthetic opioid analgesic and
19 morphine derivative, administered to a 101-week-old patient with Trisomy 21 and
20 hospitalized for respiratory failure, due to respiratory syncytial virus bronchiolitis. Here, after
21 administration, more frequent and dramatic oscillations appear in PAT, HR, SBP and DBP,
22 all of which the devices capture, and BP by the a-line. Such oscillatory hemodynamic patterns
23 can occur after administration of opioid analgesics, notably morphine, and particularly in
24 premature infants, but the physiological mechanism behind such oscillations is still
25 unknown.^[66-68] Figure 7D shows the response to an intravenous injection of dexamethasone,
26 given to a 31-week-old patient hospitalized with seizures and acute hypoxemic respiratory

1 failure. Dexamethasone, a corticosteroid, is known to elevate HR and BP, with hypertension
2 as a common side effect of the treatment.^[69-71] Upon administration, a large rise in HR (Figure
3 7D, second row) appears, along with moderate increases in SBP and DBP (Figure 7D, third
4 and fourth rows, respectively), all of which then return to a stable baseline. Measurements
5 with the devices maintain reliable correlation with the a-line during these dramatic changes in
6 HR. In all four cases, which feature distinct pharmacologic interventions and patients of
7 differing ages and medical conditions, the devices, using the multivariate PAT/HR model,
8 provide consistent performance with the a-line for BP measurements.

10 3. Conclusion

11 The collective results from this study suggest that wireless, skin-interfaced devices can
12 be optimized, through careful selection of materials and mechanics designs, for use in the
13 PICU environment. The results support continuous, noninvasive measurements of vital signs
14 and, through empirical models, SBP and DBP for patients with an accuracy comparable to the
15 clinical gold standards, including those determined with indwelling a-lines. Importantly, these
16 devices can capture immediate hemodynamic changes that occur after pharmacologic
17 interventions, which may be useful in guiding further clinical management. The 23 PICU
18 patients included in this study represent a pragmatic cohort of infants with a-line monitoring,
19 most with respiratory failure for varying reasons, and a few with liver failure and airway
20 abnormalities. The soft, flexible, and “pediatric-sized” design of the wireless, skin-interfaced
21 devices described here are not only applicable, but also highly compatible with these PICU
22 patients. These systems remove the restrictive burden of wired-based systems and mitigate the
23 potential for skin-based issues or injuries that typically arise from use of these conventional
24 physiologic monitoring systems. The noninvasive, wireless operation of these devices also
25 minimizes the risks of ischemia, infection, and procedural difficulties typically associated
26 with usage of a-lines.

1 The analyses presented here required an initial calibration period, when the indwelling
2 a-line's reference BP measurements are needed to convert the PAT and HR data into BP
3 values. However, it would be more ideal to completely bypass the usage of the indwelling a-
4 line for any initial calibrations or recalibrations due to its invasive nature. Thus, an alternative
5 clinical case scenario would be to simply use a noninvasive BP reference for calibration, such
6 as the oscillometric cuff, which has been similarly implemented by the FDA-approved, wired
7 Sotera Visi system, thereby eliminating any need for the a-line.²⁴⁻²⁵

8 Naturally, the application of these wireless, skin-interfaced devices can be extended
9 outside of the ICU environment for use in both the outpatient ambulatory setting and the in-
10 home setting, as means for continuous monitoring and tracking of patients discharged from
11 the ICU. To enable real-time monitoring of BP for the user, the desired calibration algorithm,
12 such as the multivariate PAT/HR model, can be implemented within the software of the tablet
13 application. Any potential recurrences of health emergencies or vital sign abnormalities could
14 then quickly be transmitted to clinicians to guide further therapeutic decision-making.

15 Long-term, continuous monitoring of the devices is enabled by robust adhesion of the
16 devices to the skin. In the case of the chest device, a soft AMPS/AA-based hydrogel
17 maintains the conductive, adhesive interface between the device and skin (Figure 3G). For the
18 limb device, a soft fabric velcro wrap and optional use of the hydrogel (Figure S20) adheres
19 and maintains the alignment and positioning of the LED and photodetector components
20 required for PPG measurements. Additional methods for securing the limb device in place is
21 to utilize socks or mittens, depending on the location of device placement.

22 To our knowledge, this study is the first systematic inquiry that explores the
23 correlation between continuous noninvasive and invasive BP measurements in the PICU. The
24 results are highly promising, but they also underscore the need for further clinical
25 investigations with larger cohort sizes and of different ICU patient populations (e.g., neonatal
26 critical care, neurocritical care, cardiac critical care, across a broader age range). Future

1 directions, including examination of the potential causes for observed interpatient variability
2 (Figure S16-S17), such as disrupted autonomic regulation of hemodynamics^[72], will yield
3 further insights that may improve the overall monitoring accuracy.

4 **4. Experimental Section/Methods**

5 *Encapsulation of the chest and limb devices:* General details on the assembly and
6 encapsulation of the chest device can be found elsewhere.^[21] To provide strain isolation of the
7 center island of the flexible printed circuit board (fPCB) of the chest device, a low-modulus
8 (~4 kPa) polyorganosiloxane gel (“OOO-35”; Ecoflex Gel, Smooth-On) is used to completely
9 enclose the island. Additionally, due to the sticky nature of the OOO-35 gel, the center island
10 of the fPCB can then be adhered and secured onto the center position of the bottom
11 encapsulation layer, consisting of a thin (~500 μm) polyorganosiloxane elastomer (“A-20”)
12 film (1:1 w:w Silbione RTV 4420, Elkem, mixed with 5 wt% silicone opaque dye (Silc Pig,
13 Smooth-On)). The rest of the inner space of the chest device is filled with another
14 polyorganosiloxane elastomer (“OO-30”; Ecoflex OO-30, Smooth-On). For the limb device,
15 the assembly and encapsulation process start with folding the flexible printed circuit board
16 (fPCB) to reduce the overall size of the device. To completely enclose the folded device, top
17 (white) and bottom (blue) encapsulation shell layers are designed for each device. These
18 encapsulation layers are thin (~500 μm) A-20 films (1:1 w:w Silbione RTV 4420, Elkem,
19 mixed with 5 wt% silicone opaque dye (Silc-Pig, Smooth-On)), formed by using a pair of
20 concave and convex aluminum molds and thermal curing at 100°C for 20 minutes. The folded
21 device is placed in between these cured A-20 top and bottom encapsulation layers. To avoid
22 tearing of the A-20 encapsulation layers from the fPCB or from mechanical deformations,
23 such as bending or twisting, the empty space in between the A-20 encapsulation layers and
24 the device is filled with OO-30. This material, with low modulus (0.069 MPa), provides
25 improved softness. The molds with these materials were overlaid and bonded from thermal
26 curing (100°C for 20 minutes), finishing the encapsulation process.

1 *Digital image correlation (2D-DIC) experiments:* The experiments involved recording
2 uniaxial-stretched devices using a high-speed camera (2048 × 1088 resolution, HT-2000M,
3 Emergent) with 35 mm imaging lenses (F1.4 manual focus, Kowa) at the frame rate of 100
4 fps. The devices were uniformly coated with black speckles (Figure S3), size of ~200-500
5 μm, by the spray-painting method. The open-source 2D-DIC software, Ncorr, was used to
6 measure material deformation of the devices.^[26] To achieve high resolution and accurate
7 deformation characteristics, DIC subset radius and spacing were set as 700 μm and spacing of
8 140 μm, resolving over 30,000 displacement grids. Strain magnitude and shear strain were
9 computed based on the Triangular Cosserat Point Theory.^[73]

10 *High-speed tracking experiments:* The same set of hardware, as the DIC experiments, was
11 used to record the oscillations of the devices. The sides of the LED units were painted black,
12 and the image set was recorded at 500 Hz to accurately track their fast oscillations. Both
13 devices were fixed vertically, and their LED units were initially bent 90° before the release.
14 Both systems were recorded until the oscillations were completely damped to capture the full
15 dynamics (>4,000 frames). The centers of the LED units were detected in a sub-pixel level,
16 tracked using the Hungarian algorithm, and linked by performing a five-frame gap closing to
17 produce a single, long, oscillating trajectory for each system. More details on the tracking
18 method can be found elsewhere.^[27]

19 *Finite element analysis (FEA) simulations:* The commercial FEA software, ABAQUS, was
20 utilized to determine the mechanical performance of the metal serpentine interconnects and
21 the encapsulation design of the devices. The objectives of the analysis were to ensure no
22 plastic deformation (i.e., $\epsilon < 0.3\%$) occurs in 1) the copper (Cu) layer interconnects when the
23 device undergoes different types of external loads (e.g., stretching, bending, twisting, and
24 wrapping around the foot), and 2) reduce the magnitude of the strain in the optimized soft
25 encapsulation. The effective modulus of the design types was calculated from the slopes in
26 Figure S9 and approximate cross-sectional area in the stretching region (UD ~ 45 mm² and

1 OD $\sim 9 \text{ mm}^2$), based on the uniaxial stretching results in Figure S8. The thin Cu ($\sim 18 \mu\text{m}$
2 thick) layers were modeled by composite shell elements (S4R), and the soft encapsulation was
3 modeled by hexahedron elements (C3D8R). The element size was tested to ensure the
4 convergence and the accuracy of the simulation results. The elastic modulus (E) and Poisson's
5 ratio (ν) were $E_{\text{PI}} = 2.5 \text{ GPa}$ and $\nu_{\text{PI}} = 0.34$ for polyimide (PI); $E_{\text{Cu}} = 119 \text{ GPa}$ and $\nu_{\text{Cu}} = 0.34$
6 for copper; $E_{\text{A-20}} = 0.8 \text{ MPa}$ and $\nu_{\text{A-20}} = 0.5$ for A-20 polyorganosiloxane elastomer (Silbione
7 RTV 4420, Elkem); $E_{\text{OO-30}} = 60 \text{ kPa}$ and $\nu_{\text{OO-30}} = 0.5$ for OO-30 polyorganosiloxane elastomer
8 (Ecoflex OO-30, Smooth-On).

9 *Shelf aging:* A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) was prepared
10 by mixing part A and B (1:1 w:w ratio) and 5 wt% silicone opaque dye (Silc-Pig, Smooth-On)
11 in a two-step process in a planetary centrifugal mixer (Thinky ARE-310): 1) for 30 seconds at
12 2000 RPM, 2) 30 seconds at 2200 RPM, degassed for 3 minutes in a 90-mm petri dish, and
13 cured in a 70°C oven for 2 hours. Shore hardness measurements were taken with a Type OO
14 Shore durometer (Model 1600, Rex Gauge Company Inc.), mounted on an operating stand
15 (Model OS-4H, Rex Gauge Company Inc.). Presented results are the average of
16 measurements taken from 5 locations per sample, and propagated uncertainty (e.g., the square
17 root of the sum of the: 1) squared standard deviation of measurements taken from 5 locations
18 per sample, and the 2) squared instrument precision (0.5 OO scale)).

19 *Autoclave sterilization:* A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) was
20 prepared by mixing part A and B (1:1 w:w ratio) and 5 wt% silicone opaque dye (Silc-Pig,
21 Smooth-On) in a two-step process in a planetary centrifugal mixer (Thinky ARE-310): 1) for
22 30 seconds at 2000 RPM, 2) 30 seconds at 2200 RPM, degassed for 3 minutes in an
23 aluminum foil-lined 90-mm petri dish, and cured in a 70°C oven for 2 hours. Samples were
24 placed in the autoclave steam sterilizer (Heidolph Tuttnauer 3545E Autoclave Sterilizer,
25 Electronic Model AE-K), to undergo one exposure cycle, at a temperature of 121°C , for a
26 total of 75 minutes (15 minutes sterilization time, 60 minutes drying time). Shore hardness

1 measurements, taken 24 hours after each exposure cycle, were taken with a Type OO Shore
2 durometer (Model 1600, Rex Gauge Company Inc.), mounted on an operating stand (Model
3 OS-4H, Rex Gauge Company Inc.). Presented results are the average of measurements taken
4 from 5 locations per sample, and propagated uncertainty (e.g., the square root of the sum of
5 the: 1) squared standard deviation of measurements taken from 5 locations per sample, and
6 the 2) squared instrument precision (0.5 OO scale)).

7 *UVC exposure:* A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) was
8 prepared by mixing part A and B (1:1 w:w ratio) in a two-step process in a planetary
9 centrifugal mixer (Thinky ARE-310): 1) for 30 seconds at 2000 RPM, 2) 30 seconds at 2200
10 RPM, and degassed for three minutes afterwards. Samples were formed by spin-coating the
11 A-20 mixture on glass slides at 3000 RPM for 30 seconds and subsequent curing in a 70°C
12 oven for 15 minutes, yielding ~30 µm-thick substrates. The samples were placed in a dark,
13 enclosed chamber lined with aluminum foil, with a slit opening on top for direct exposure
14 from a continuous, constant intensity, and narrow-band ($\lambda = 254$ nm) 8-watt UV lamp
15 (UVLS-28, Analytik Jena). A digital UVC radiometer (Model 8.0 UVC, Solarmeter), placed
16 at the same point of exposure as the samples, measured UVC intensity ($\mu\text{W}/\text{cm}^2$), allowing
17 for determination of exposure dosage values.

18 *Fourier-transform infrared (FTIR) spectroscopy:* Solid state FTIR transmission spectra of the
19 prepared A-20 polyorganosiloxane elastomer (Silbione 4420, Elkem) samples were collected
20 with the use of a Thermo Scientific Nicolet iS50, over a range from 4000 to 400 cm^{-1} . FTIR
21 (cm^{-1}): $\nu = 2962$ (w; $\nu_{\text{as}}(\text{C-H})$), 1257 (m; $\nu_{\text{s}}(\text{C-H})$), 1008 (s; $\nu(\text{Si-O-Si})$), 786 (s; $\nu(\text{Si-C})$).

22 *Fabrication of Surfactant-Modified A-20 Polyorganosiloxane Elastomer:* Surfactant-modified
23 A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) was prepared by mixing
24 part A and B (1:1 w:w ratio) and 0.2 wt% trisiloxane ethoxylate surfactant (Silwet L-77,
25 Bioworld)^[74] in a two-step process in a planetary centrifugal mixer (Thinky ARE-310): 1) for
26 30 seconds at 2000 RPM, 2) 30 seconds at 2200 RPM. Samples were formed by spin-coating

1 the surfactant-modified A-20 mixture on glass slides at 250 RPM for 30 seconds and
2 subsequent curing in a 70°C oven for 15 minutes, yielding ~200 µm-thick substrates.

3 *Water contact angle (WCA) measurements:* Static WCA measurements were taken from 2 µL
4 deionized water droplets using a video contact angle system (VCA Optima XE, AST
5 Products). Presented results are the average and standard deviation of 5 WCA measurements
6 taken per sample.

7 *Peel force measurements on A-20 and surfactant-modified A-20 polyorganosiloxane*
8 *elastomer:* A-20 polyorganosiloxane elastomer (Silbione RTV 4420, Elkem) was prepared by
9 mixing part A and B (1:1 w:w ratio) in a two-step process in a planetary centrifugal mixer
10 (Thinky ARE-310): 1) for 30 seconds at 2000 RPM, 2) 30 seconds at 2200 RPM, and
11 degassed for three minutes afterwards. Samples were formed by spin-coating the A-20
12 mixture on glass slides at 250 RPM for 30 seconds and subsequent curing in a 70°C oven for
13 15 minutes. Surfactant-modified A-20 polyorganosiloxane elastomer (Silbione RTV 4420,
14 Elkem) was prepared by mixing part A and B (1:1 w:w ratio) and 0.2 wt% trisiloxane
15 ethoxylate surfactant (Silwet L-77, Bioworld) in a two-step process in a planetary centrifugal
16 mixer (Thinky ARE-310): 1) for 30 seconds at 2000 RPM, 2) 30 seconds at 2200 RPM.
17 Samples were formed by spin-coating the surfactant-modified A-20 mixture on glass slides at
18 250 RPM for 30 seconds and subsequent curing in a 70°C oven for 15 minutes.

19 AMPS/AA hydrogel (KM 40A, Katecho) strips of 20 mm width were adhered to these
20 samples, and a unit magnetic weight (#5862K23, McMaster-Carr) was attached, one-by-one,
21 to one end of the sample, such that the peel angle was 90°. The minimum weight required to
22 peel and detach the adhesive was recorded. Presented results are the average and standard
23 deviation of four trials.

24 *Peel force measurements on skin:* Covidien hydrogel (Argyle Hydrogel Adhesive Baby Tape
25 Strips, Covidien), Acrylate/AAm hydrogel (KM 30 E, Katecho), and AMPS/AA hydrogel
26 (KM 40A, Katecho) strips of 20 mm width were adhered to the pre-cleaned, left ventral

1 forearm of an adult female with sensitive skin, and a unit magnetic weight (#5862K23,
2 McMaster-Carr) was attached, one-by-one, to one end of the adhesive sample, such that the
3 peel angle was 90°. The minimum weight required to peel and detach the adhesive was
4 recorded, both immediately after application to the skin, and after 20 hours of wear (including
5 during overnight sleep).

6 *Clinical study design:* The Institutional Review Boards of Ann & Robert H. Lurie Children's
7 Hospital of Chicago (IRB 2018-1668) and Northwestern University (STU00208150)
8 approved the protocol for this prospective, single-center, observational pilot study. Eligible
9 patients included any patient under three years of age admitted to the PICU at the Ann &
10 Robert H. Lurie Children's Hospital of Chicago, who possessed an indwelling a-line for
11 continuous BP monitoring for clinical care. Informed consent for participation was obtained
12 from all patients' legal guardians.

13 *Device application and data collection.* After following a sterilization process approved by
14 the infection control committee of the Ann & Robert H. Lurie Children's Hospital of
15 Chicago^[21], the chest device was applied onto the chest, without interfering with existing
16 standard of care equipment and secured with AMPS/AA hydrogel adhesive (KM 40A,
17 Katecho). The limb device was wrapped around a peripheral extremity (foot or hand), free of
18 existing standard of care equipment, and secured with a soft velcro wrap. Both devices
19 wirelessly connect to an iPad Pro, enabling data transmission, collection, and storage.
20 Indwelling a-line recordings of SBP and DBP were extracted from the Philips Intellivue
21 MX800 patient monitor with the BedMaster™ software. Devices were removed to allow
22 certain procedures (e.g., MRI imaging, ultrasounds, surgery, baths) take place. A list of
23 clinically administered drugs and times of administration during the data collection period
24 was recorded in the Epic electronic medical record system.

25 *Data processing.* PAT and HR data were downloaded from the devices' internal memory and
26 subsequently time-synchronized to systolic and diastolic BP data from the indwelling a-line.

1 PAT, HR, SBP, and DBP data were removed during periods of data collection in which the
2 devices were either disturbed or removed (e.g., medical procedures). Likewise, the indwelling
3 a-line data were removed during periods when the BedMaster™ software malfunctioned or
4 the lines were disturbed (e.g., the line was being replaced or flushed).

5 *Calibration procedure.* For each patient, an initial ten-minute window of PAT and/or HR
6 data, measured by the wireless, skin-interfaced devices was calibrated to corresponding SBP
7 and DBP data from the indwelling a-line, using the relationships given by Equation 2-5.
8 Ordinary least squares regression, using the Python *statsmodel* module, defined the optimal
9 model coefficients (e.g., a, b, c). These coefficients were then applied to the remaining PAT
10 and/or HR data to estimate SBP and DBP. Recalibration was not performed for any patient.

11 *Post hoc statistical analysis.* Comparisons of BP measurements between the wireless, skin-
12 interfaced devices and the indwelling a-line were evaluated using the Python *Pandas* pairwise
13 correlation matrix function. Bland-Altman analysis was used to determine the level of
14 agreement between the two modalities, featuring 290,108 paired data points obtained from 23
15 subjects. Paired t-tests, using the Python *statannot* package were used to determine statistical
16 significance of the differences of the two modalities. Significance was applied to $p < 0.05$.

18 **Supporting Information**

19 Supporting Information is available from the Wiley Online Library or from the author.

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Sex (n)	
Male	13
Female	10
Race/Ethnicity (n)	
Caucasian	12
Hispanic/Latino	6
Black/African American	3
Asian	1
Other	1
At Time of Study (mean ± standard deviation)	
Age (weeks)	53 ± 47
Height (cm)	68 ± 15
Weight (kg)	8.2 ± 4.1
Arterial Line Location (n)	
Radial	17
Posterior tibial	4
Ulnar	1
Dorsalis pedis	1
Diagnoses (n)	
Acute respiratory failure	16
Respiratory syncytial virus	6
Seizures	3
Bronchopulmonary dysplasia from prematurity	2
Septic shock	2
Acute kidney injury	2
Metabolic crisis	1
Liver transplantation	4
Airway abnormality	2
Chronic respiratory failure	1

Table 1. Baseline demographics and clinical characteristics (n = 23 subjects)

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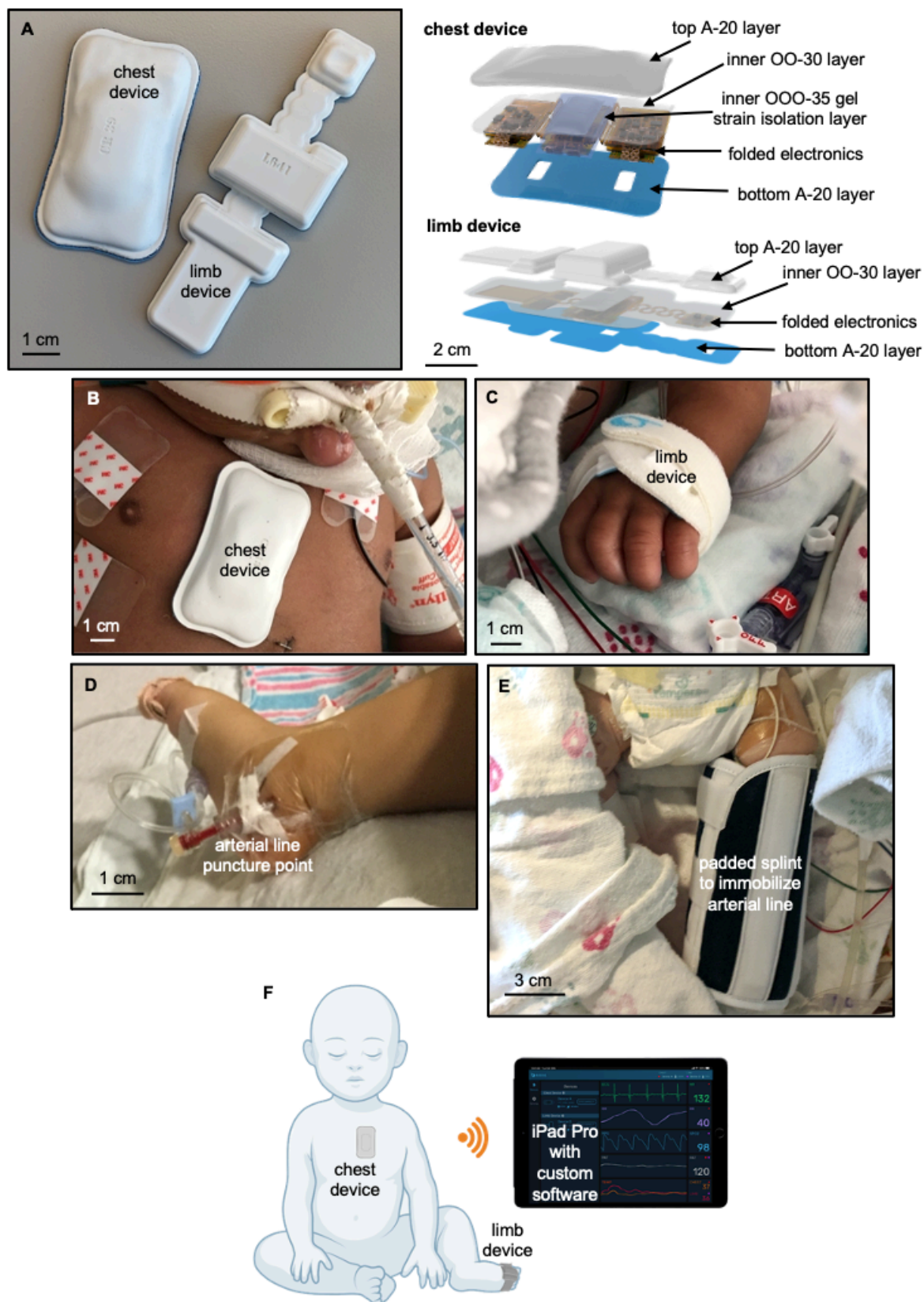


Figure 1. Soft, skin-interfaced devices for wireless measurements of blood pressure in pediatric intensive care unit (PICU) patients. (A) Photograph (left) depicting a top-down view of the devices, and schematic representation (right) of the configurations and materials

1 of the devices. The system consists of a chest device (capable of electrocardiography (ECG)
2 measurements) and a limb device (capable of photoplethysmography (PPG) measurements).
3 **(B)** Photograph of a 37-week-old female patient in the PICU, wearing a chest device, flanked
4 by conventional ECG adhesive electrodes and a blood pressure cuff. **(C)** Photograph of the
5 same patient in **(B)**, wearing a limb device, secured with a soft velcro wrap, around the left
6 hand. **(D)** Photograph of the indwelling arterial line puncture point at the right dorsalis pedis
7 artery of a 50-week-old male patient in the PICU. The invasive arterial line, which is
8 oversized relative to the infant's foot, poses risk for ischemia and infection. **(E)** Photograph of
9 a 5-week-old male patient in the PICU, wearing a restrictive padded splint to immobilize and
10 protect the indwelling arterial line puncture point at the left posterior tibial artery. In contrast
11 to the devices shown in **(A)**, **(B)**, and **(C)**, the arterial line and its associated accessories
12 heavily limit free, natural body movement. **(F)** Schematic representation of an infant with the
13 wireless, skin-interfaced devices, which transmits physiological waveform and vital sign data
14 to a nearby iPad Pro.
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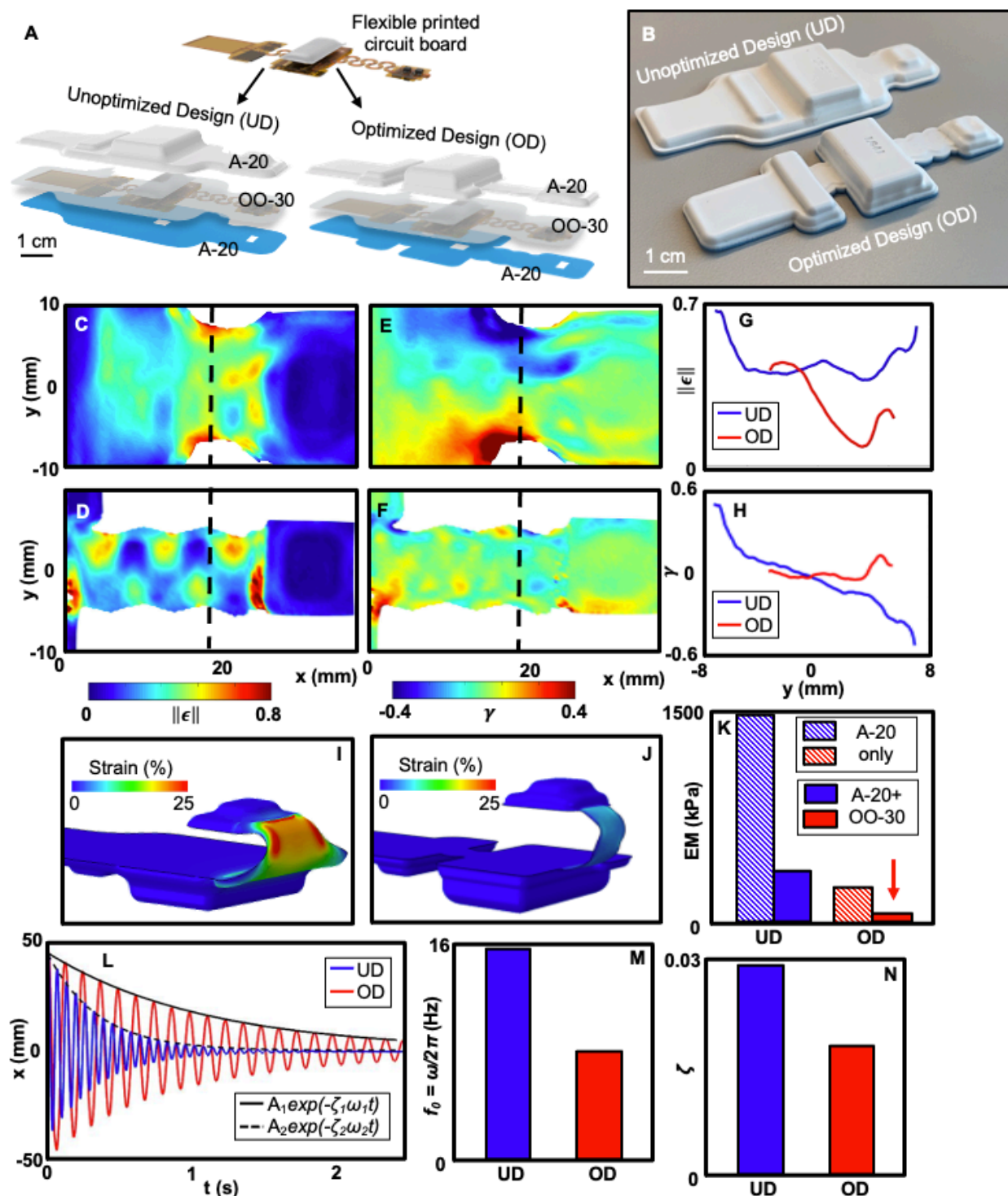


Figure 2. Optimized mechanics for robust wrapping around peripheral limbs. (A) 3-D rendering of the un-encapsulated, flexible printed circuit board for the limb device and the encapsulation schemes, featuring the unoptimized design (UD) and optimized design (OD). Polyorganosiloxane elastomers, denoted by the manufacturer's listed Shore hardness, are used for the outer encapsulation shell (A-20, white/blue) and inner filler layer (OO-30, transparent). (B) Photograph of the fully encapsulated limb devices. Experimental results via Digital Image Correlation of strain magnitude (C, D) and shear strain (E, F) for UD and OD, respectively, at 10% stretch. (G) Strain magnitude and (H) shear strain profiles at $x=18$ mm. FEA simulations of strain distribution in the encapsulation layer for bending deformations of

UD **(I)** and OD **(J)**. **(K)** Effective moduli (EM) of the device, computed via FEA, for UD (blue) and OD (red). Striped shading indicates that A-20 is used for both the outer encapsulation shell and inner filler layer, whereas solid shading indicates that A-20 is used for the outer encapsulation shell and OO-30 is used for the inner filler layer. **(L)** Experimental results of oscillation via the tracking method; initial release at 90°. **(M)** Natural frequencies and **(N)** damping ratios of UD and OD.

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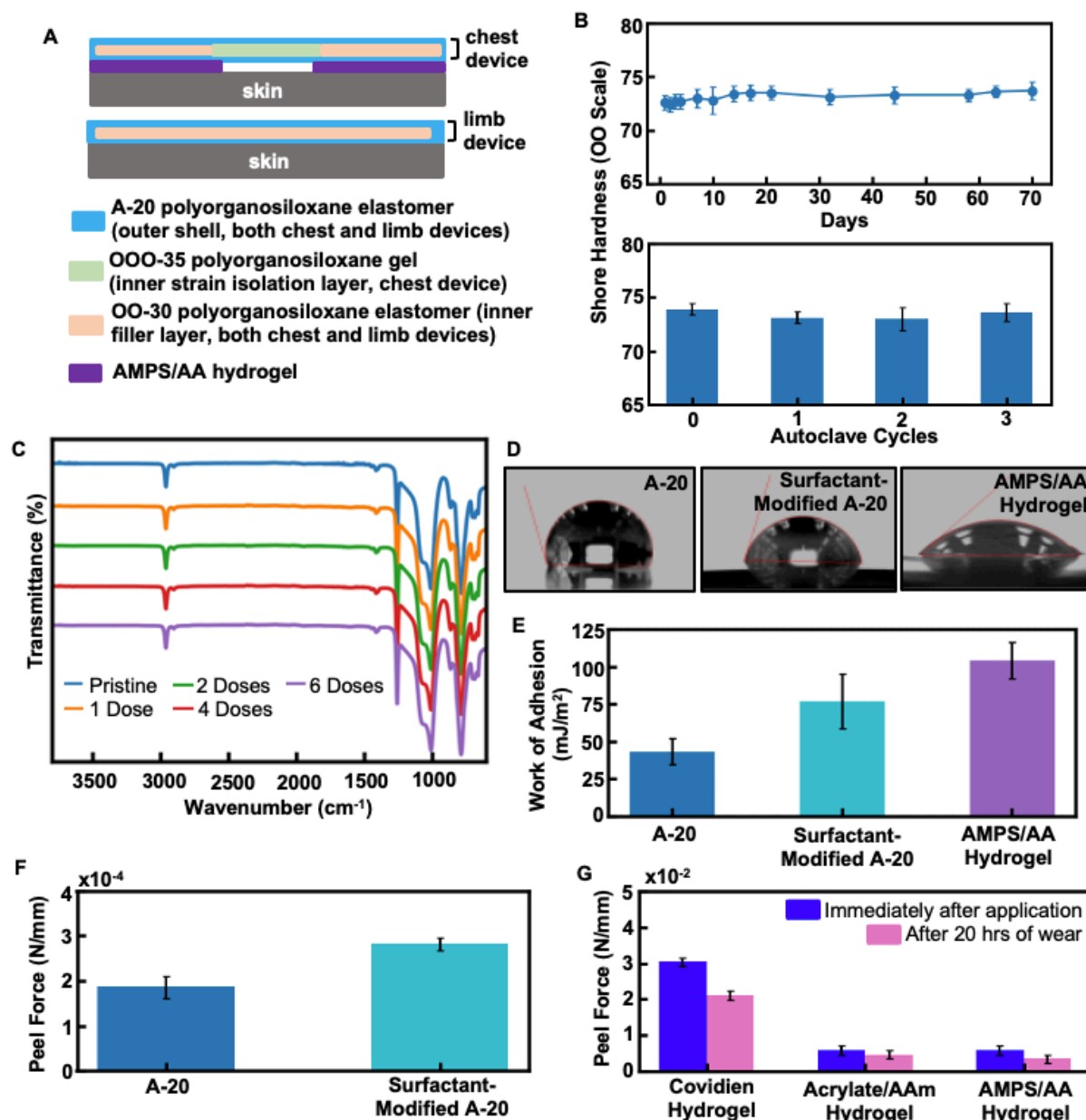


Figure 3. Characterization of soft materials used for wireless, skin-interfaced device encapsulation and skin adhesion. (A) Schematic representation of the cross-sectional, layer-by-layer soft materials stack for the chest device (top) and the limb device (bottom). Polyorganosiloxane elastomer and gel materials are denoted by the manufacturer's listed Shore hardness. (B) Mechanical stability of dyed A-20 polyorganosiloxane elastomer, as a function of the number of days of shelf aging (top) and the number of autoclave exposure cycles (bottom). (C) FTIR transmission spectra of A-20 polyorganosiloxane elastomer (~30 μm thickness), as a function of the number of UVC exposure doses. (D) Representative water contact angle images of A-20 polyorganosiloxane elastomer (left), surfactant-modified A-20 polyorganosiloxane elastomer (center), and AMPS/AA hydrogel (right). To improve hydrophilicity of the A-20 elastomer and compatibility with the AMPS/AA hydrogel, the surfactant (trisiloxane ethoxylate) modification can be employed. (E) Work of adhesion, as derived from the Young-Dupre equation and water contact angle measurements. (F) Peel force from 90° peel testing of AMPS/AA hydrogel on A-20 and surfactant-modified A-20 polyorganosiloxane elastomer substrates. (G) Peel force from 90° peel testing on an adult

with sensitive skin, for three hydrogel adhesives. Samples are immediately tested after application to the skin (blue) and after 20 hours of wear (pink).

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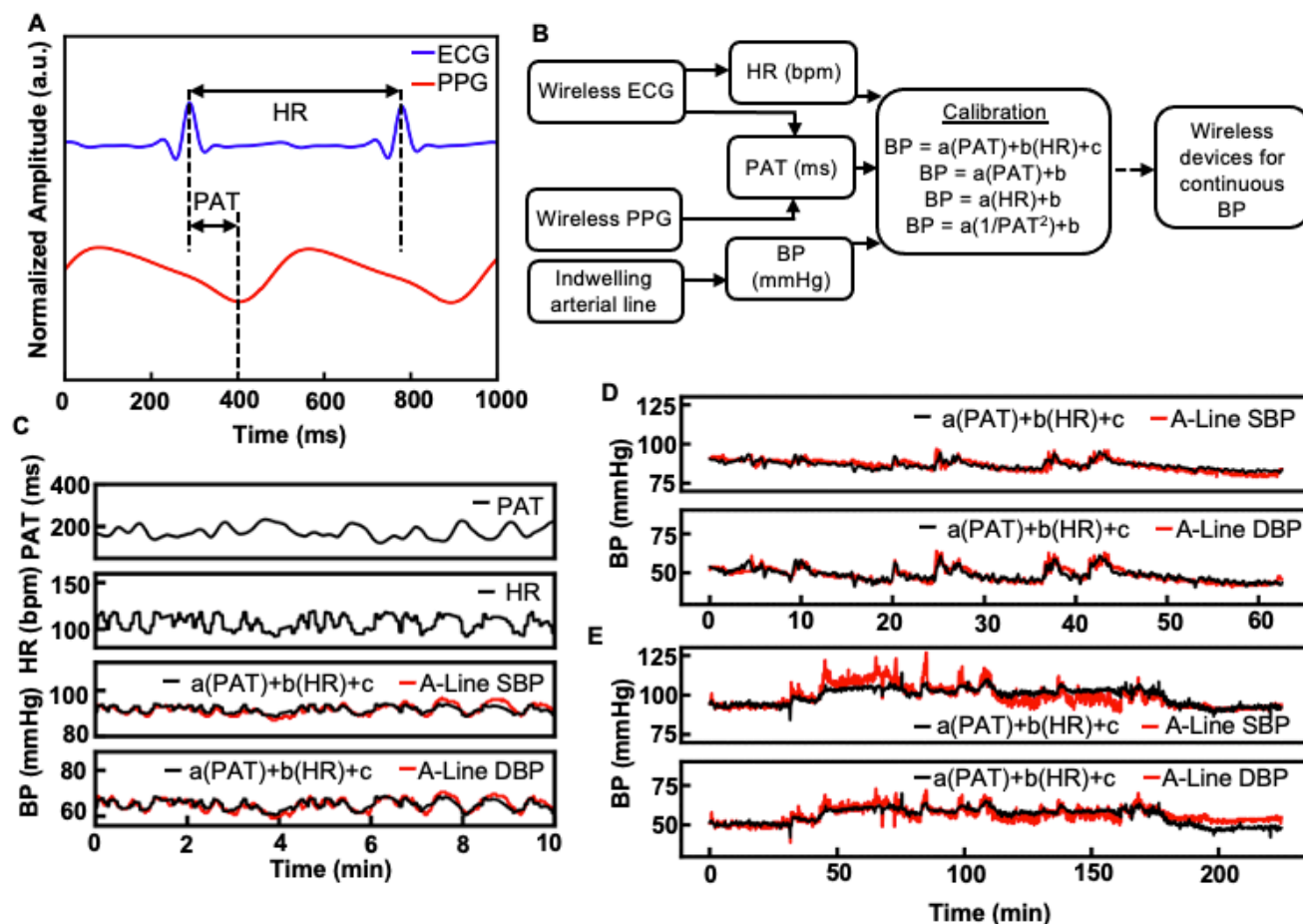


Figure 4. Pulse arrival time (PAT) and heart rate (HR), as measured by wireless, skin-interfaced devices, as a proxy for continuous BP monitoring. (A) Representative segments of time-synchronized and continuous electrocardiography (ECG) and photoplethysmography (PPG) recordings, as measured by the wireless, skin-interfaced chest and limb devices, respectively. From ECG and PPG, both PAT and HR can be derived. PAT is defined as the time delay between the ECG waveform R-peak and the onset of the PPG waveform at the peripheral limb device. HR is defined as the time interval between successive ECG waveform R-peaks. (B) Flow diagram illustrating steps for time-synchronized data collection and calibration of pulse arrival time (PAT) and (HR) to blood pressure (BP). (C) Representative example of an initial ten-minute window of PAT and HR, which are then calibrated and converted into systolic BP (SBP) and diastolic BP (DBP) via the equation $[a(PAT)+b(HR)+c]$. Here, the obtained model equations are: SBP (mmHg) = $[-0.02 \text{ ms}^{-1}(\text{PAT (ms)}) + 0.20 \text{ bpm}^{-1}(\text{HR (bpm)}) + 71.79 \text{ mmHg}]$, and DBP (mmHg) = $[-0.04 \text{ ms}^{-1}(\text{PAT (ms)}) + 0.24 \text{ bpm}^{-1}(\text{HR (bpm)}) + 38.42 \text{ mmHg}]$. (D) A 63-minute recording of a 127-week-old female patient with acute hypoxemic respiratory failure, Trisomy 21, and multiple organ dysfunction. Comparisons between the $[a(PAT)+b(HR)+c]$ model (black) and the arterial line (a-line) (red) are shown. (E) A 225-minute recording of a 47-week-old female patient with biliary atresia, status post liver transplant, and hypertension secondary to liver condition. Comparisons between the $[a(PAT)+b(HR)+c]$ model (black) and the a-line (red) are shown.

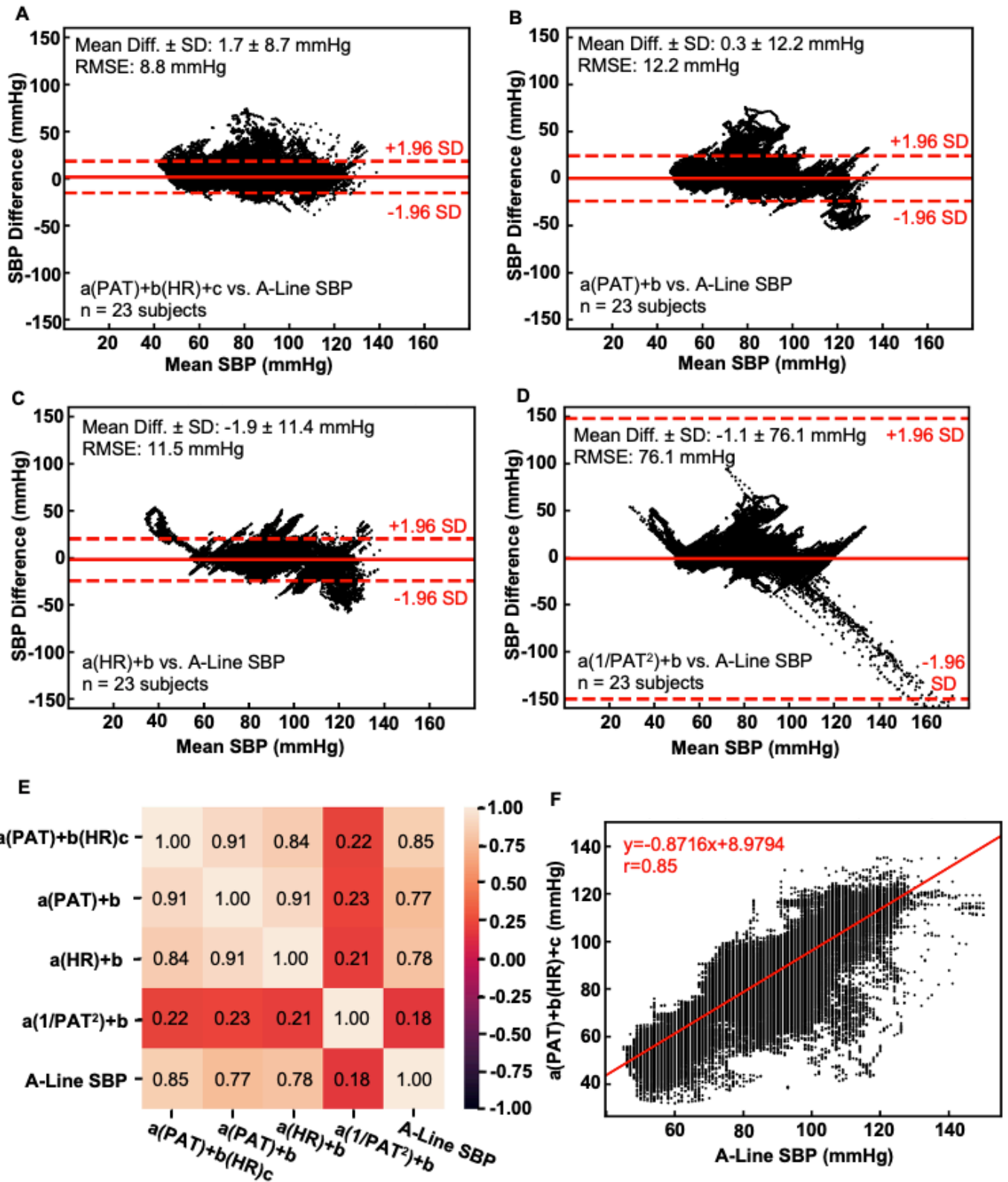


Figure 5. Comparisons of estimated systolic blood pressure (SBP) to arterial line (a-line) SBP (n = 23 subjects; 290,108 data points). (A) Bland-Altman plots describing the difference in SBP values between the a-line and the a(PAT)+b(HR)+c, (B) a(PAT)+b, (C) a(HR)+b, and (D) a(1/PAT²)+b calibration models. Solid red lines indicate the mean differences in SBP measurements between the two modalities, whereas red dashed lines indicate 1.96 standard deviations (SD) above and below the mean differences (e.g., 95% limits of agreement). (E) Correlation matrix describing the Pearson's product-moment

1 correlation factor (r) for SBP between the a-line and each calibration model. The
2 a(PAT)+b(HR)+c calibration model displays the highest correlation coefficient ($r = 0.85$)
3 from comparison with the a-line SBP measurements. (F) Scatterplot illustrating the linear
4 correlation between the a(PAT)+b(HR)+c and a-line SBP measurements. The corresponding
5 line of best fit ($x = \text{"A-Line SBP"}$, $y = \text{"a(PAT)+b(HR)+c"}$), with its equation and correlation
6 coefficient, is shown in red.

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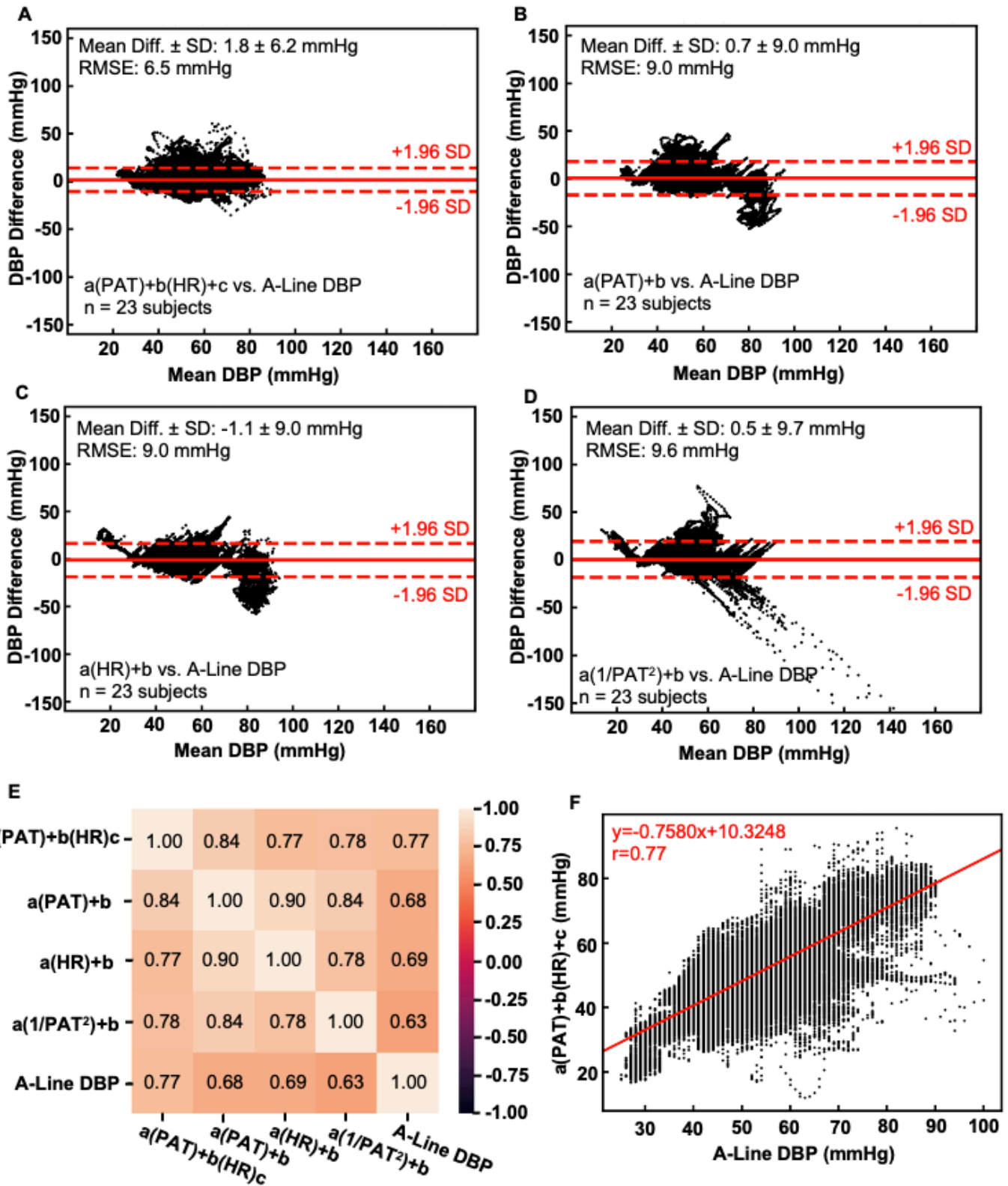


Figure 6. Comparisons of estimated diastolic blood pressure (DBP) to arterial line (a-line) DBP ($n = 23$ subjects; 290,108 data points). (A) Bland-Altman plots describing the difference in DBP values between the a-line and the $[a(\text{PAT})+b(\text{HR})+c]$, (B) $[a(\text{PAT})+b]$, (C) $[a(\text{HR})+b]$, and (D) $[a(1/\text{PAT}^2)+b]$ calibration models. Solid red lines indicate the mean differences in DBP measurements between the two modalities, whereas red dashed lines indicate 1.96 standard deviations (SD) above and below the mean differences (e.g., 95% limits of agreement). (E) Correlation matrix describing the Pearson's product-moment

1 correlation factor (r) for DBP between the a-line and each calibration model. The
2 [a(PAT)+b(HR)+c] calibration model displays the highest correlation coefficient ($r = 0.77$)
3 from comparison with the a-line DBP measurements. (F) Scatterplot illustrating the linear
4 correlation between the [a(PAT)+b(HR)+c] and a-line DBP measurements. The
5 corresponding line of best fit ($x = \text{"A-Line DBP"}$, $y = \text{"a(PAT)+b(HR)+c"}$), with its equation
6 and correlation coefficient, is shown in red.

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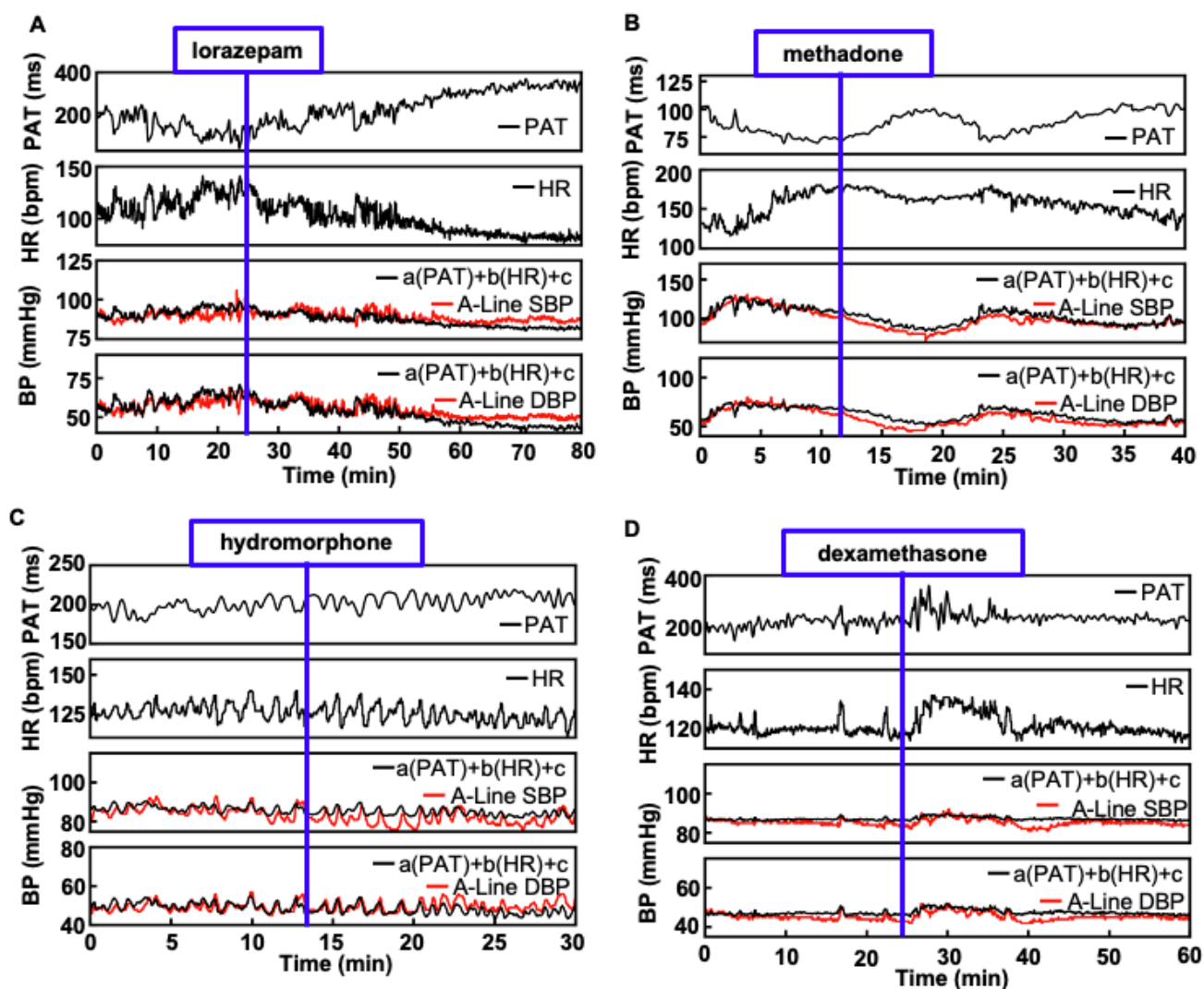


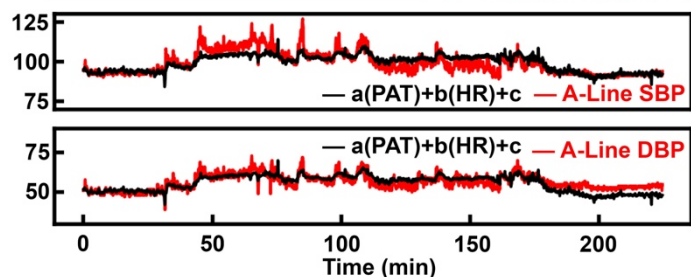
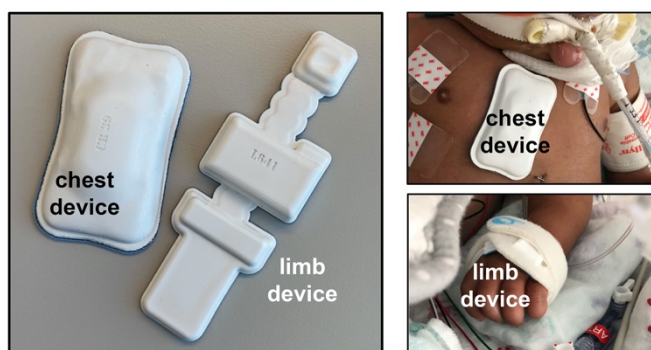
Figure 7. Performance of wireless, skin-interfaced devices, calibrated using $[a(\text{PAT})+b(\text{HR})+c]$, in capture of transient blood pressure and other hemodynamic changes after pharmacologic interventions. (A) An 80-minute recording of a 75-week-old male patient with bronchopulmonary dysplasia, history of extreme prematurity (gestational age of 23 weeks), and acute hypoxemic respiratory failure, featuring administration of enteral lorazepam at time = 24 minutes. **(B)** A 40-minute recording of an 8-week-old male with seizures, severe anoxic brain injury, and multiple fractures, featuring administration of methadone at time = 12 minutes. **(C)** A 30-minute recording of a 101-week-old male patient with respiratory syncytial virus bronchiolitis and Trisomy 21, featuring intravenous administration of hydromorphone at time = 13 minutes. **(D)** A 60-minute recording of a 31-week-old female patient with seizures and acute hypoxemic respiratory failure, featuring intravenous administration of dexamethasone at time = 23 minutes.

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Wireless, skin-interfaced devices, with optimized system-level mechanics and soft materials tailored to the pediatric intensive care unit (PICU) environment, offer a route for continuous, noninvasive blood pressure (BP) monitoring via measurements of pulse arrival time and heart rate. These devices continuously track short- and long-term BP trends, including during periods of pharmacological interventions.

Claire Liu[†], Jin-Tae Kim[†], Sung Soo Kwak[†], Aurelie Hourlier-Fargette[†], Raudel Avila, Jamie Vogl, Andreas Tzavelis, Ha Uk Chung, Jong Yoon Lee, Dong Hyun Kim, Dennis Ryu, Kelsey B. Fields, Joanna L. Ciatti, Shupeng Li, Masahiro Irie, Allison Bradley, Avani Shukla, Jairo Chavez, Emma C. Dunne, Seung Sik Kim, Jungwoo Kim, Jun Bin Park, Han Heul Jo, Joohee Kim, Michael C. Johnson, Jean Won Kwak, Surabhi R. Madhvapathy, Shuai Xu, Casey M. Rand, Lauren E. Marsillio, Sue J. Hong, Yonggang Huang, Debra E. Weese-Mayer*, John A. Rogers**

Wireless, Skin-Interfaced Devices for Pediatric Critical Care: Application to Continuous, Noninvasive Blood Pressure Monitoring



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9 **Wireless, Skin-Interfaced Devices for Pediatric Critical Care: Application to**
10 **Continuous, Noninvasive Blood Pressure Monitoring**
11

12 *Claire Liu[†], Jin-Tae Kim[†], Sung Soo Kwak[†], Aurelie Hourlier-Fargette[†], Raudel Avila, Jamie*
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14 *B. Fields, Joanna L. Ciatti, Shupeng Li, Masahiro Irie, Allison Bradley, Avani Shukla, Jairo*
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17 *Rand, Lauren E. Marsillio, Sue J. Hong, Yonggang Huang*, Debra E. Weese-Mayer*, John*
18 *A. Rogers**
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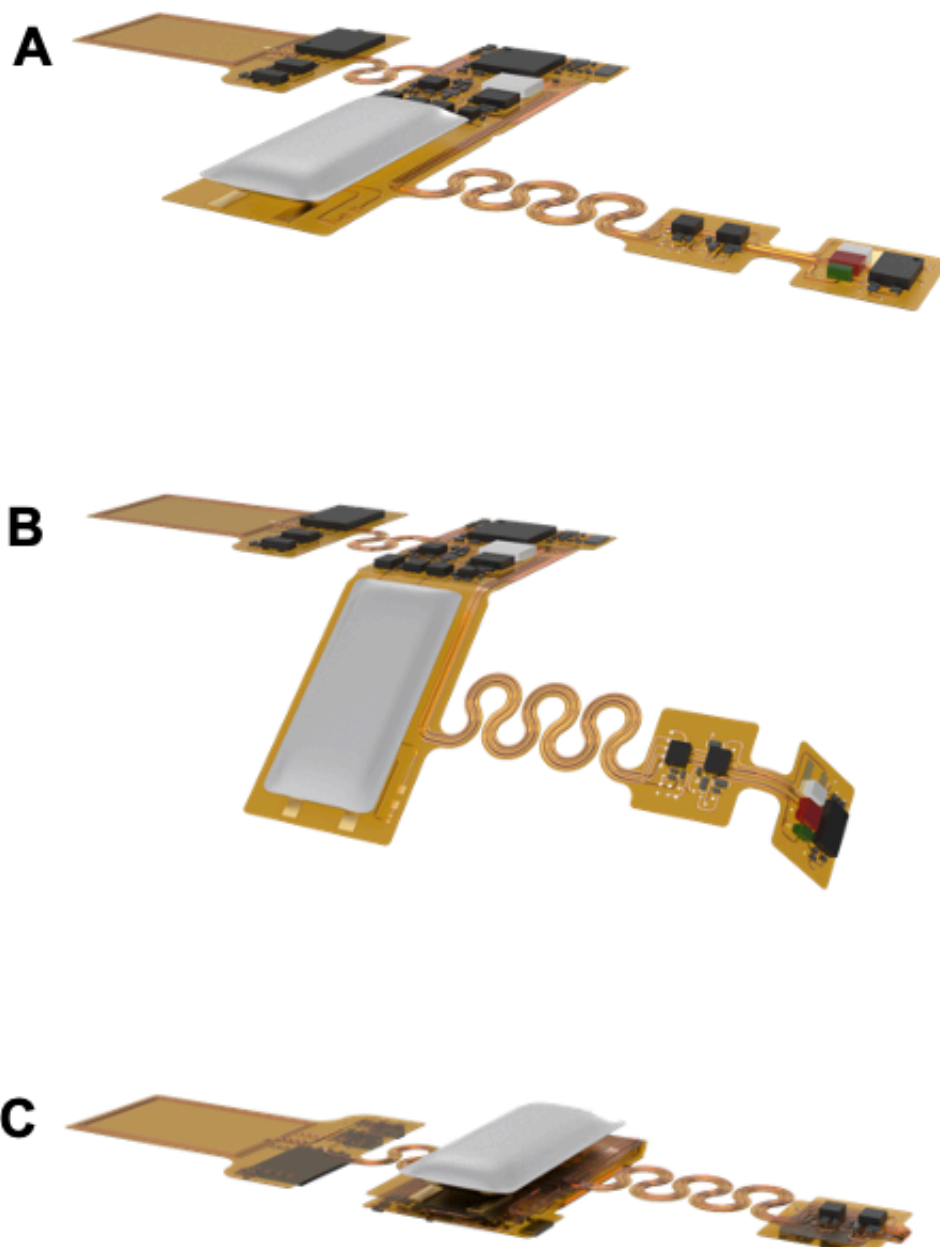


Figure S1. Folding of the full limb device flexible printed circuit board for preparation of encapsulation. 3D-rendering of (A) the unfolded, flexible printed circuit board layout of the limb device, (B) the folding of the circuit board, (C) the final folded flexible printed circuit board, ready for encapsulation within polyorganosiloxane elastomer materials.

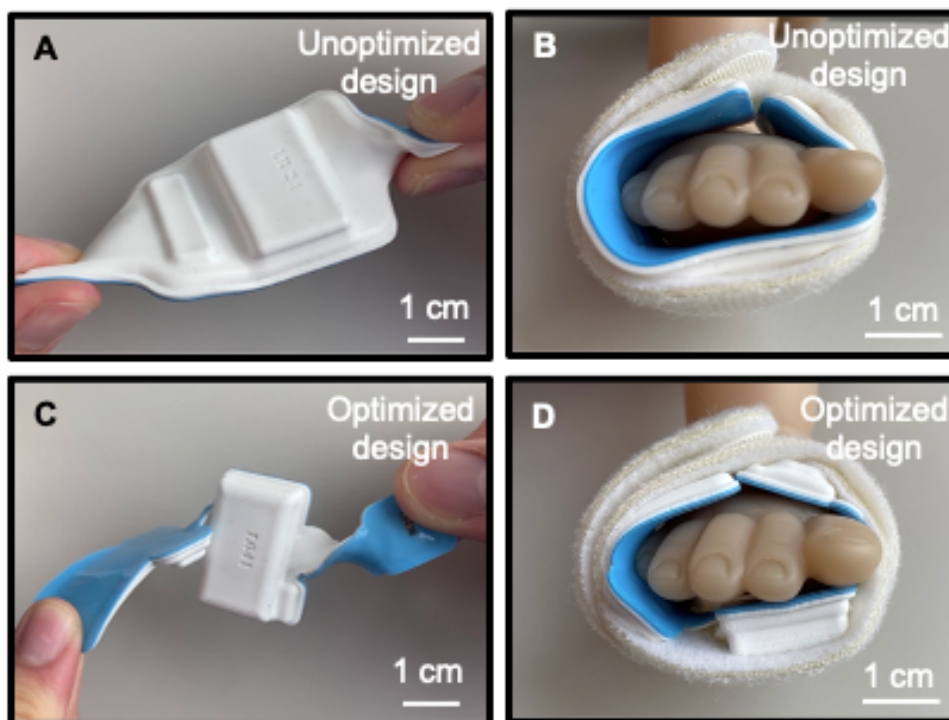
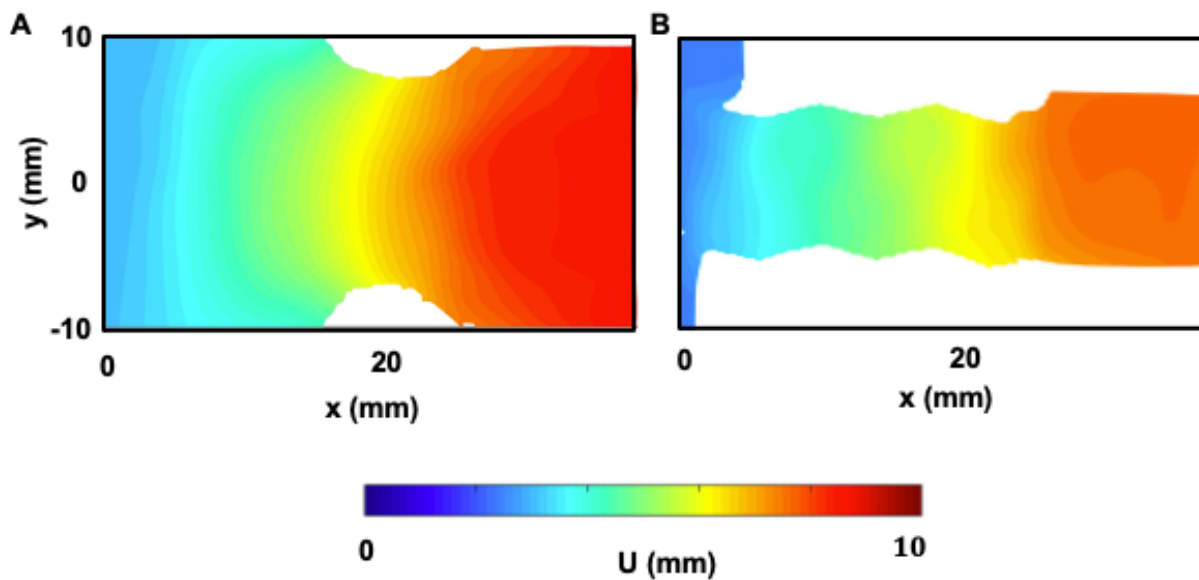


Figure S2. Optimized design of the limb device for improved mechanics and robust wrapping around peripheral limbs. Photographs of the unoptimized encapsulation design of the limb device in a (A) twisting deformation and for (B) wrapping around a model infant foot. Photographs of the optimized encapsulation design of the limb device in a (C) twisting deformation and for (D) wrapping around a model infant foot.



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29 3 **Figure S3.** Speckle patterns on unoptimized and optimized designs for DIC experiments. The 4
30 black speckles, size of $\sim 200\text{-}500\ \mu\text{m}$, were coated on the devices by the spray-painting
31 method.
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Figure S4. Experimental results via Digital Image Correlation that quantify axial displacement for UD (A) and OD(B), respectively at 10% stretch.

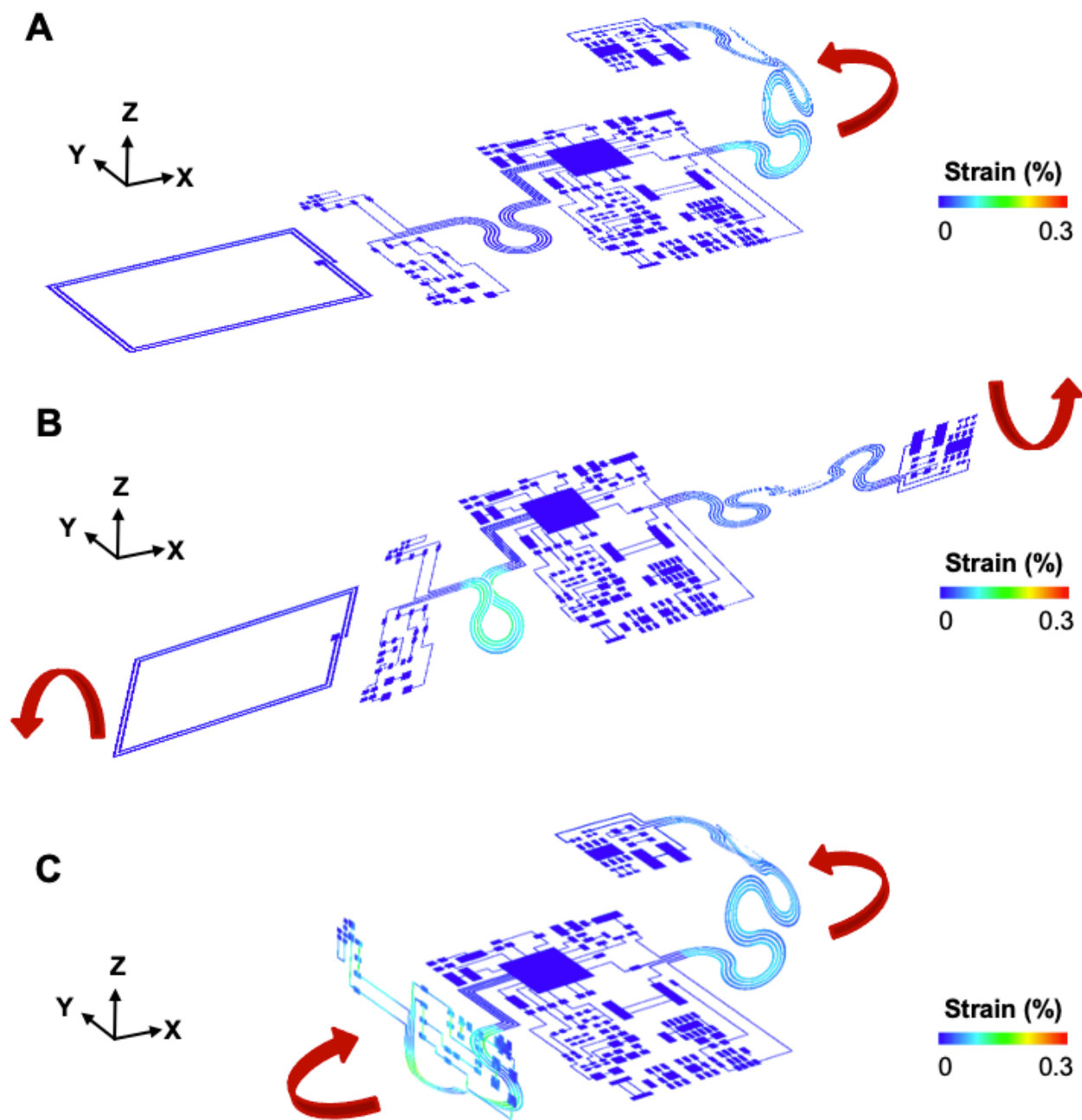


Figure S5. Strain Distribution in the top layer where the maximum strain occurs for A) bending radius of 5.5 mm, B) twisting angle 150°, and C) wrapping around the foot.

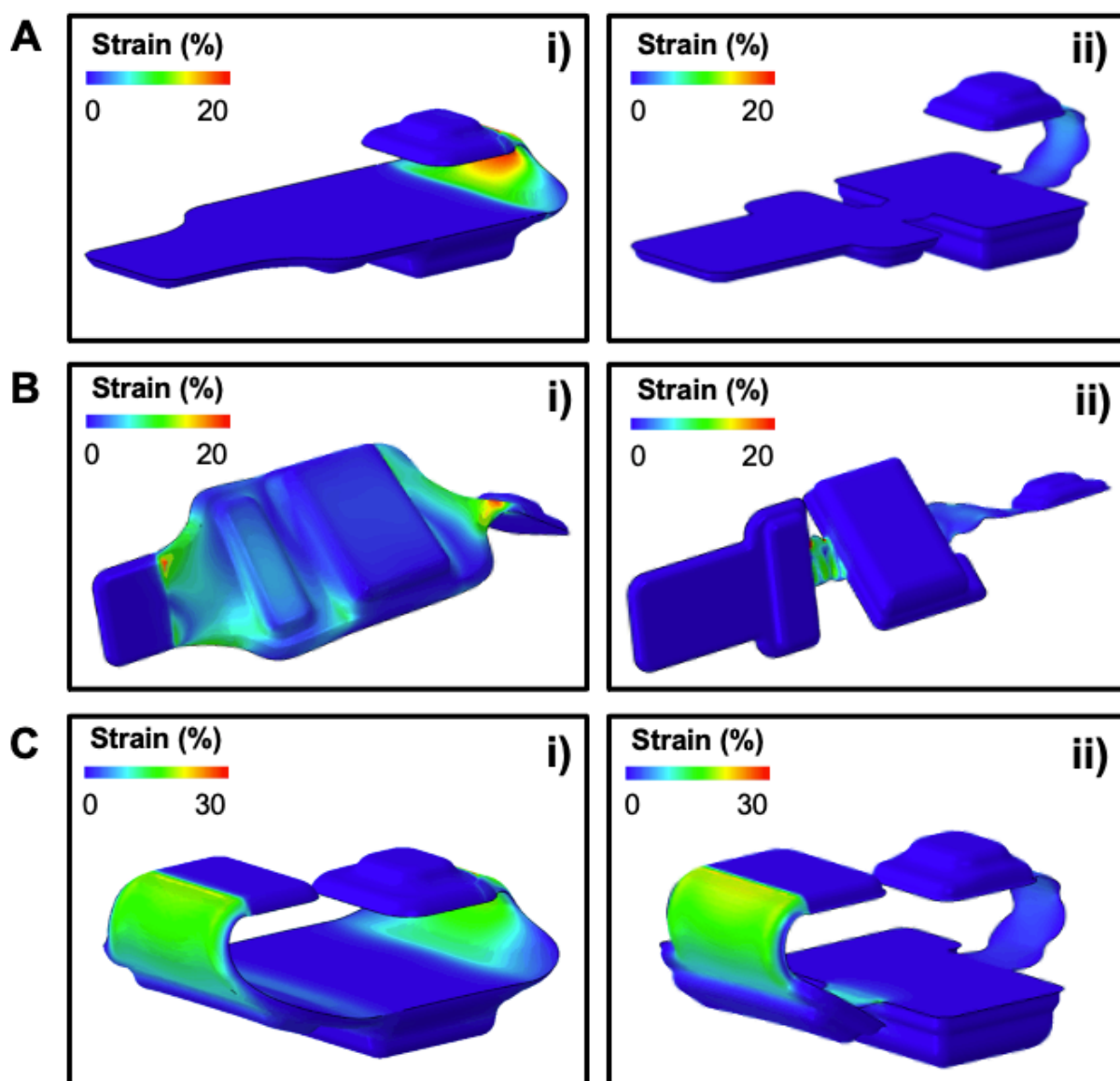


Figure S6. Strain distribution in the encapsulation layer for A) bending, B) twisting, and C) wrapping deformations of the i) unoptimized and ii) optimized designs.

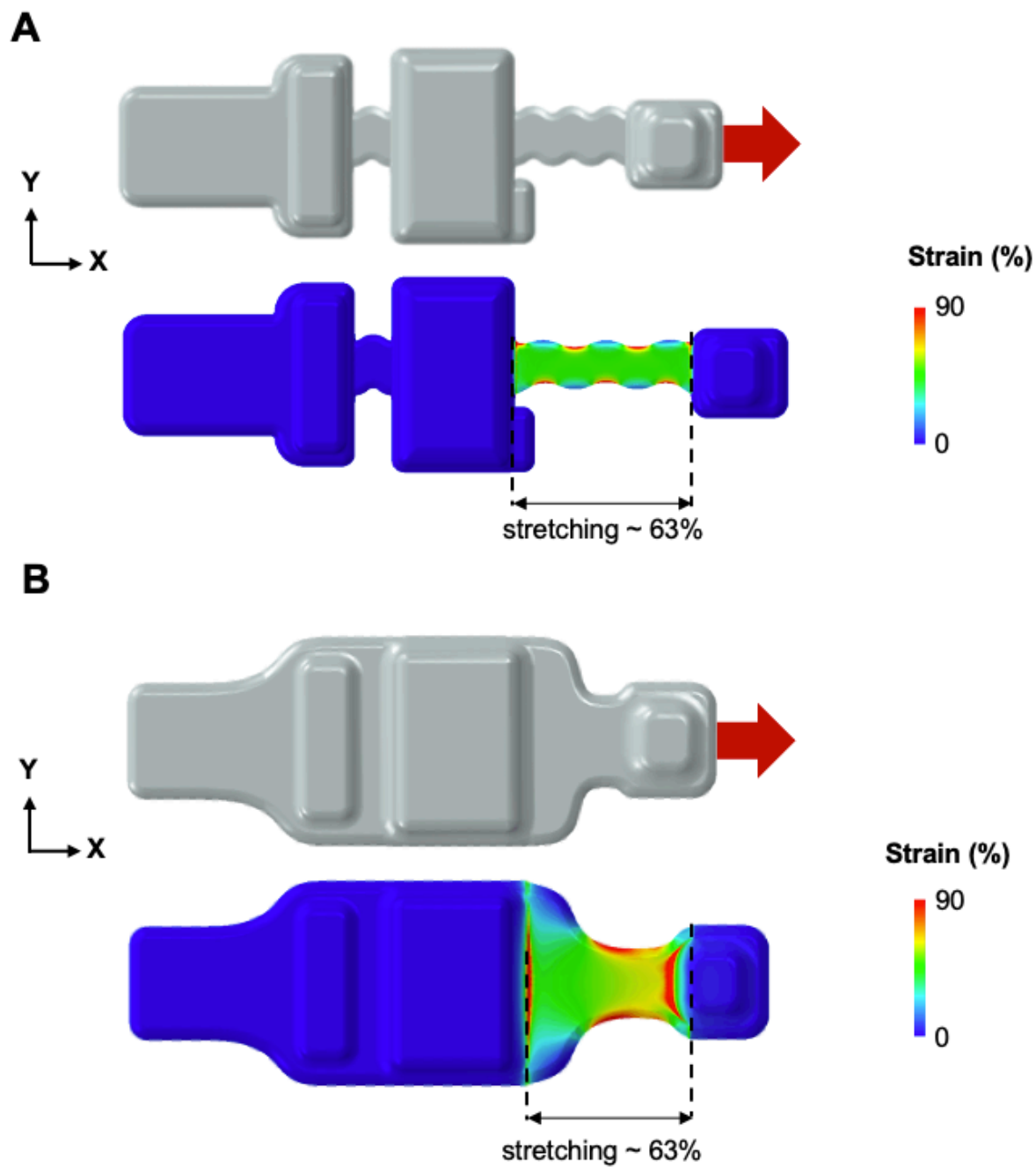


Figure S7. Strain distribution in the encapsulation for an applied uniaxial strain of 63% between A) unoptimized and B) optimized design.

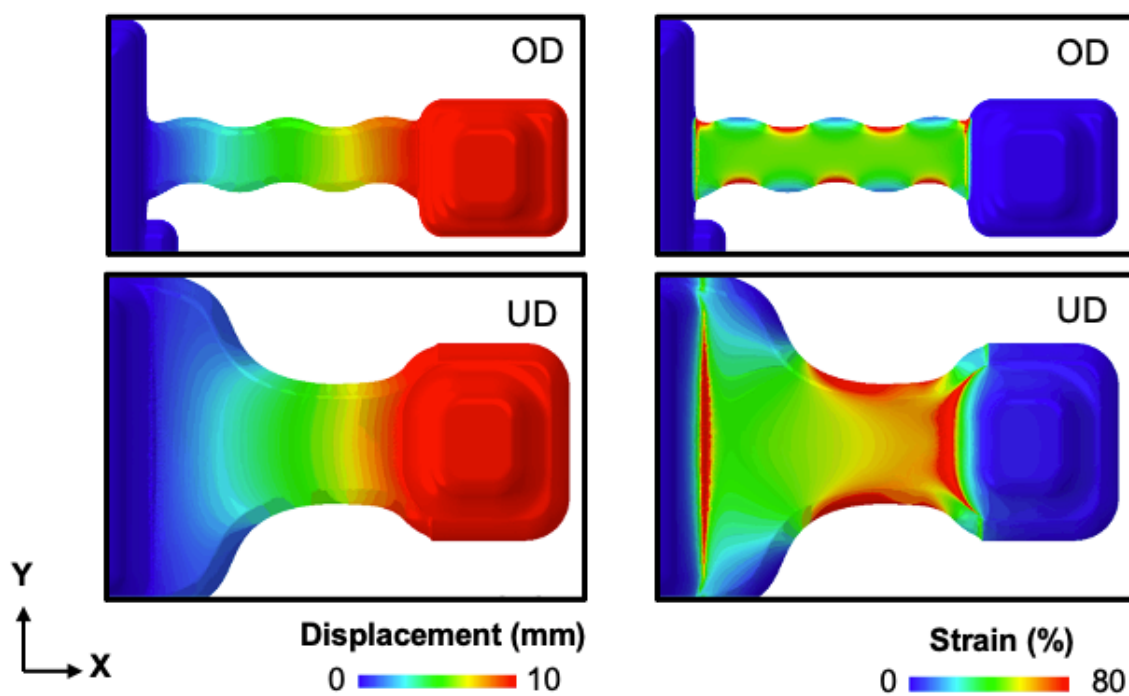
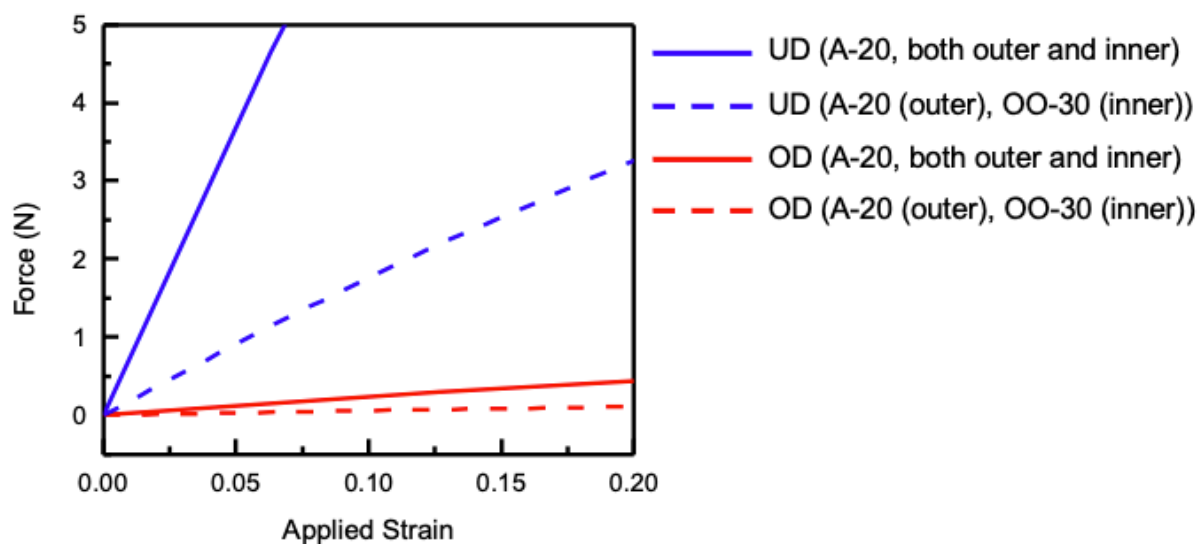
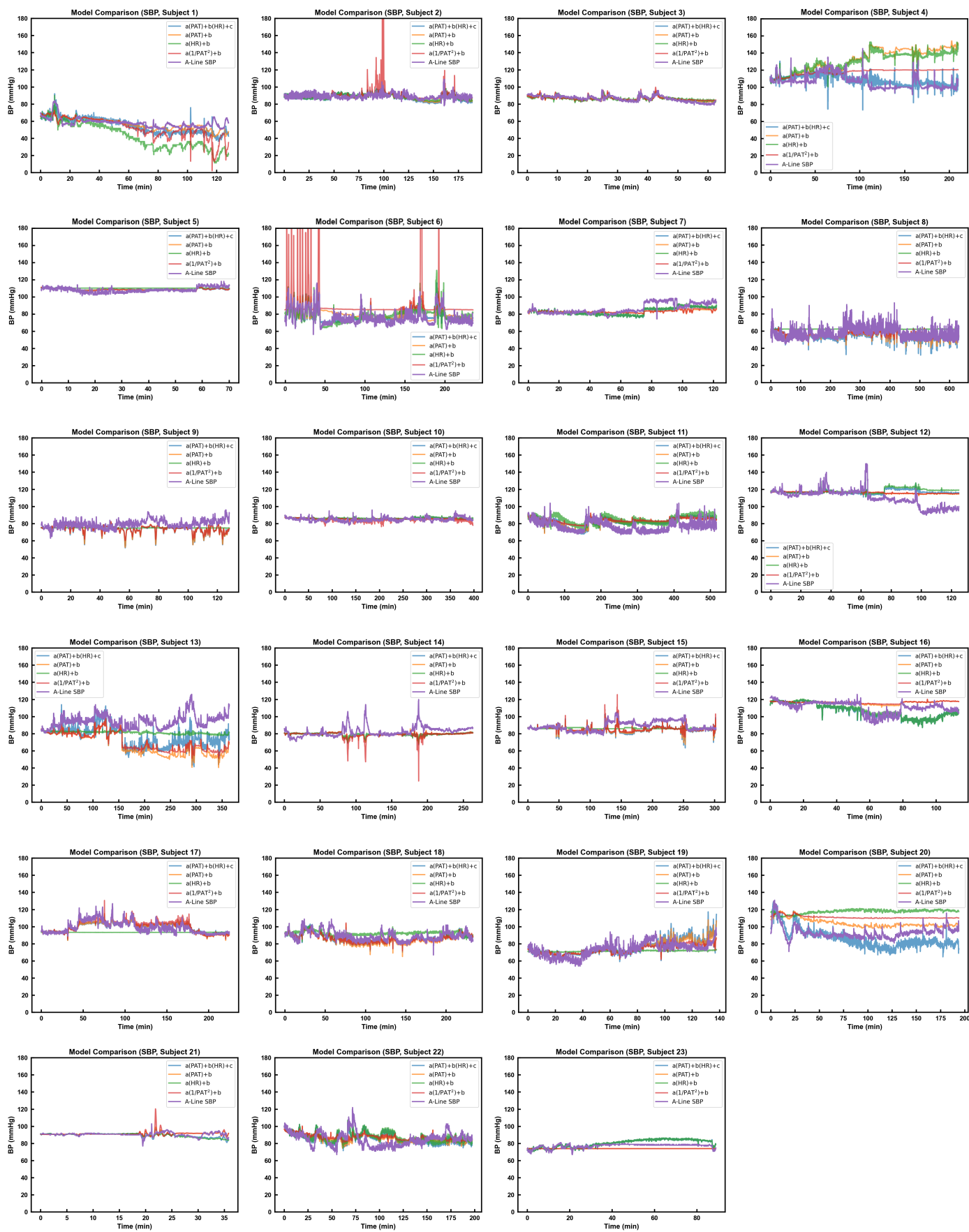


Figure S8. Displacement and corresponding strain distribution in the unoptimized (UD) and optimized (OD) encapsulation design for an applied uniaxial stretching of ~63%.

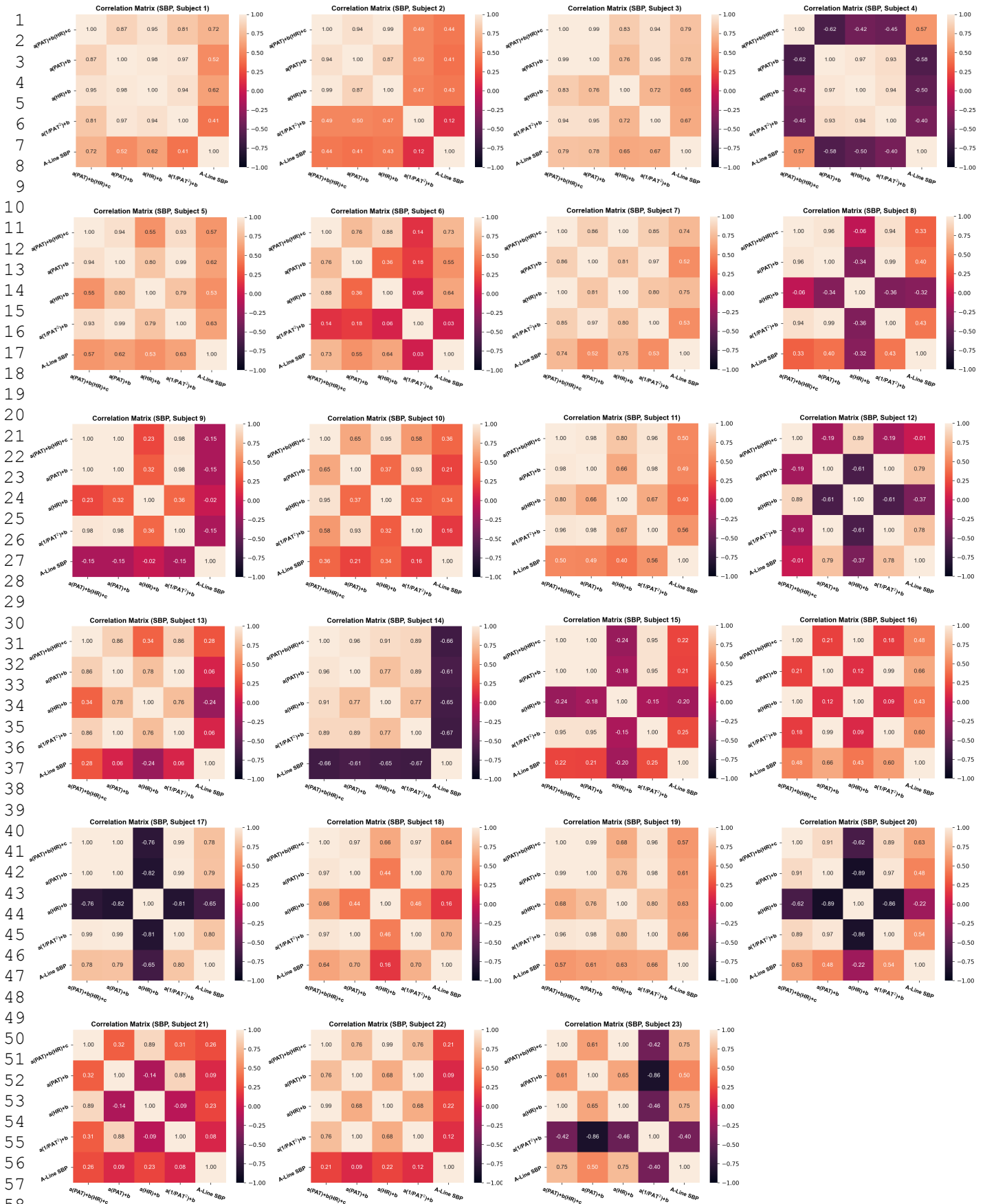


Design Type	Effective Modulus (kPa)
UD (A-20, both outer and inner)	~ 1475
UD (A-20 (outer), OO-30 (inner))	~ 365
OD (A-20, both outer and inner)	~ 252
OD (A-20 (outer), OO-30 (inner))	~ 62

Figure S9. Force vs. applied strain curve (top) and the effective modulus of each design (bottom), featuring different combinations of outer encapsulation shell and inner filler layer polyorganosiloxane materials.



1 **Figure S10.** Time-series comparisons between four calibration models and arterial line (a-
 2 line) systolic blood pressure (SBP), for all individual subjects ($n = 23$) in the study.



1 **Figure S11.** Correlation matrices illustrating the Pearson's product-moment correlation factor
 2 between four calibration models and arterial line (a-line) systolic blood pressure (SBP), for all
 3 individual subjects (n = 23) in the study.

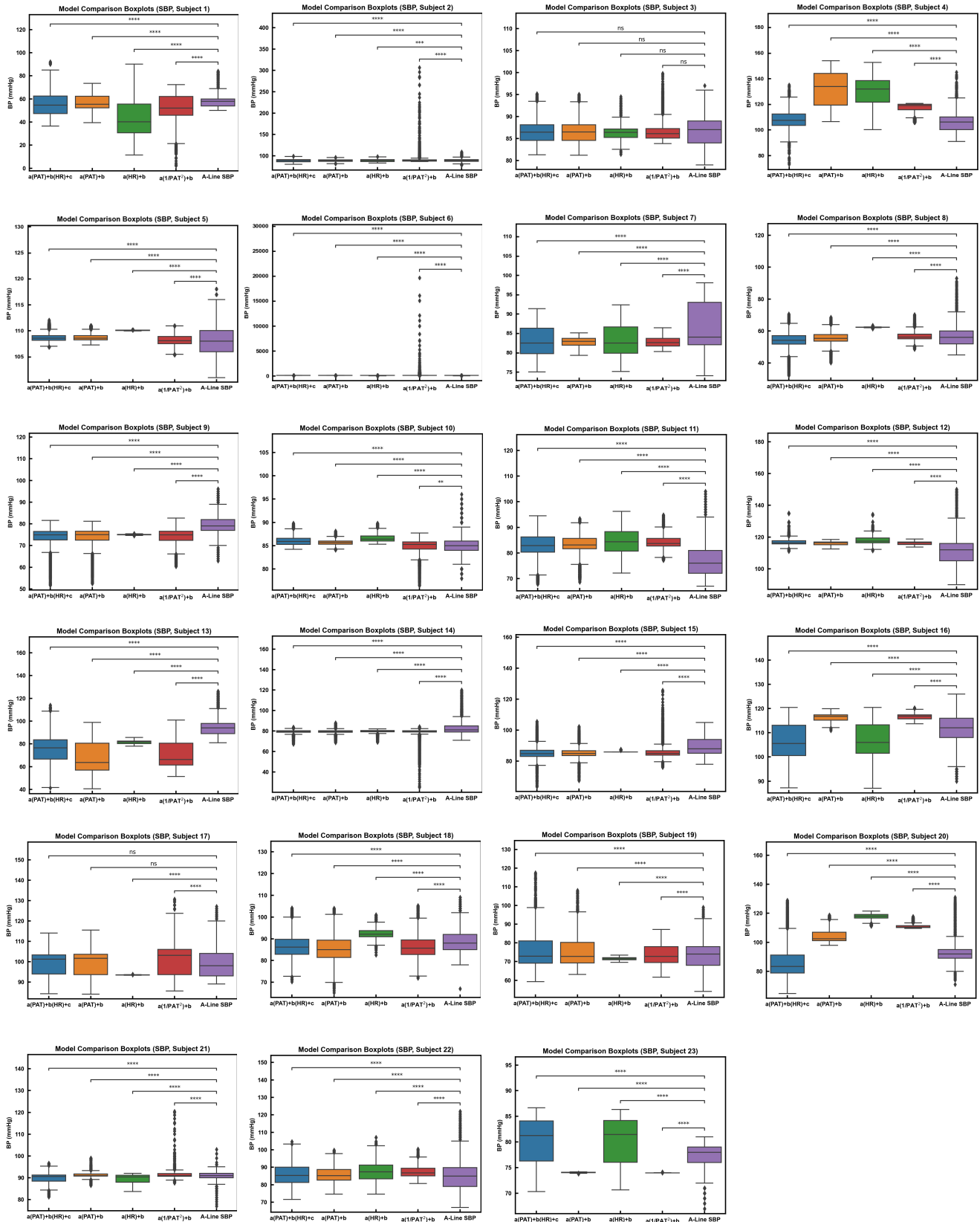


Figure S12. Boxplots describing systolic blood pressure (SBP) distributions derived from four calibration models and arterial line (a-line). A paired sample t-test, with Bonferroni correction, compares the mean difference between each calibration model and the a-line to determine if the true difference is zero (null hypothesis). Statistical annotation key: **** $p \leq 0.0001$, *** $p \leq 0.001$, ** $p \leq 0.01$, * $p \leq 0.05$, ns $p \leq 0.05$.

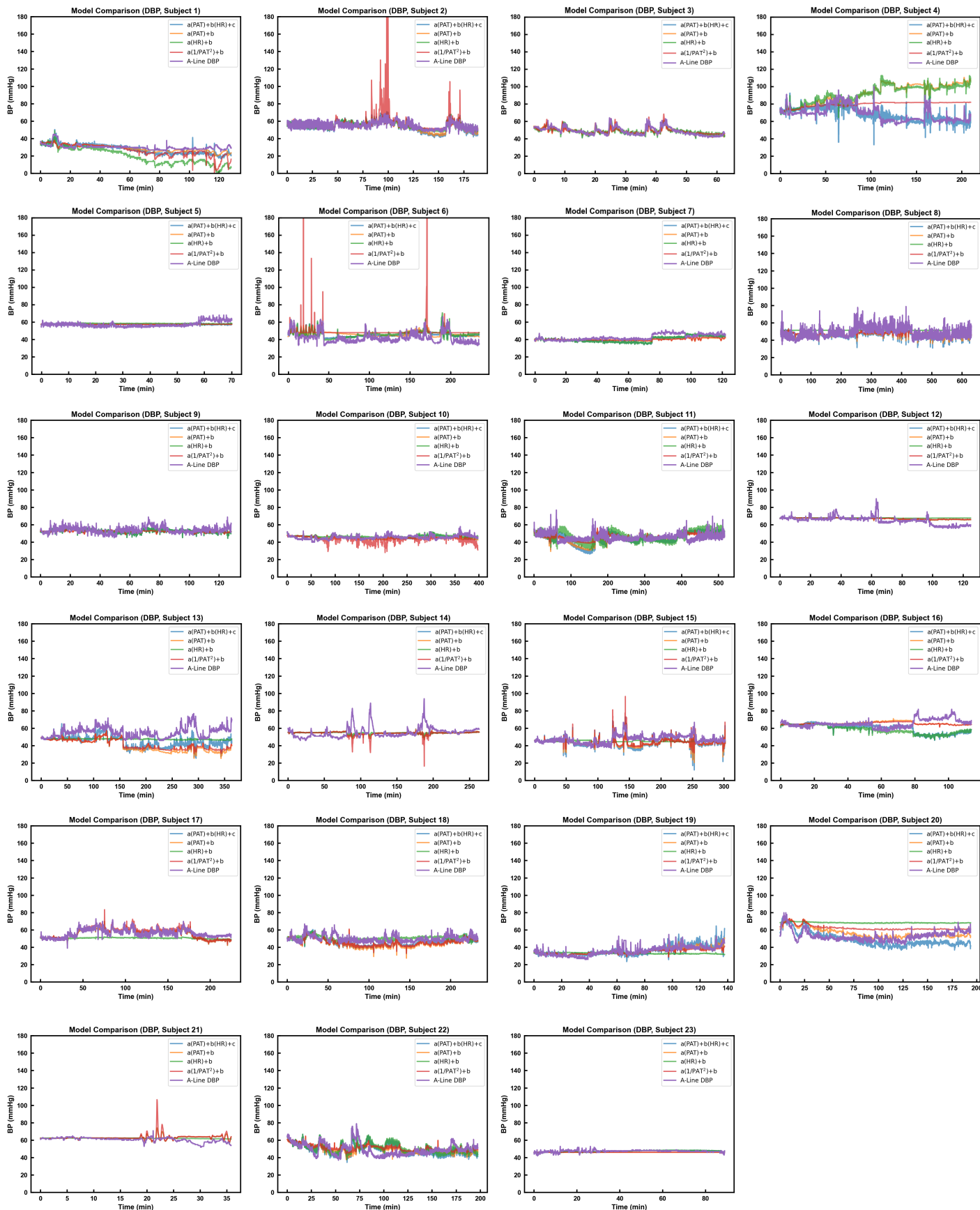
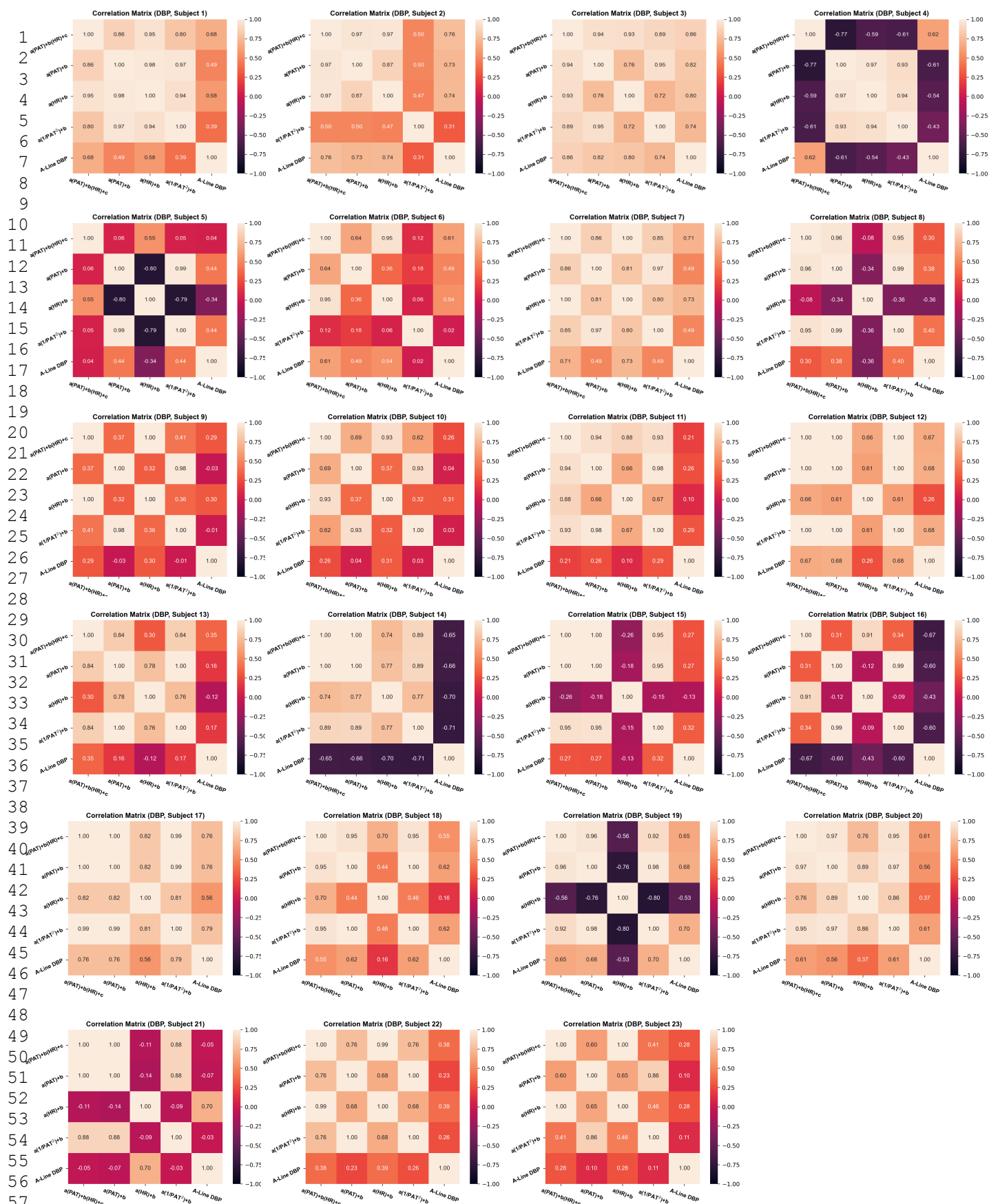


Figure S13. Time-series comparisons between four calibration models and arterial line (a-line) systolic blood pressure (DBP), for all individual subjects ($n = 23$) in the study.



1 **Figure S14.** Correlation matrices illustrating the Pearson's product-moment correlation factor
 2 between four calibration models and arterial line (a-line) diastolic blood pressure (DBP), for
 3 all individual subjects (n = 23) in the study.

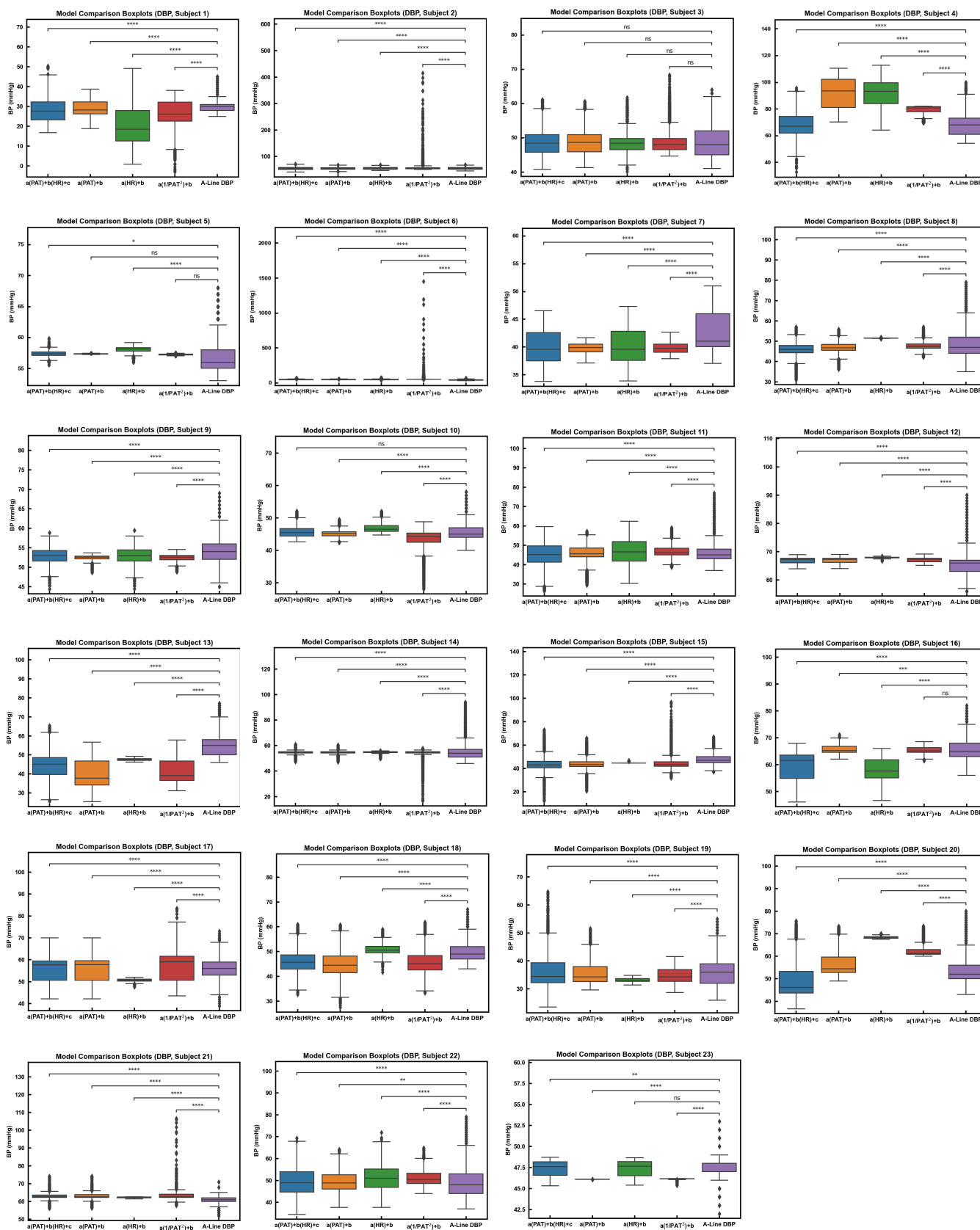


Figure S15. Boxplots describing diastolic blood pressure (DBP) distributions derived from four calibration models and arterial line (a-line). A paired sample t-test, with Bonferroni correction, compares the mean difference between each calibration model and the a-line to determine if the true difference is zero (null hypothesis). Statistical annotation key: **** $p \leq 0.0001$, *** $p \leq 0.001$, ** $p \leq 0.01$, * $p \leq 0.05$, ns $p > 0.05$.

Subject	Mean Difference (mmHg)	Standard Deviation (mmHg)
1	3.1	6.2
2	0.5	3.7
3	0.0	2.1
4	-1.8	6.6
5	-0.7	2.6
6	-1.4	6.1
7	3.3	4.1
8	2.5	6.2
9	5.6	6.7
10	-1.1	2.0
11	-5.4	5.5
12	-6.7	9.9
13	18.2	11.4
14	3.3	7.1
15	4.1	5.6
16	4.1	7.7
17	0.0	4.3
18	2.3	4.5
19	-2.4	7.7
20	6.9	8.6
21	0.8	2.6
22	-1.1	8.8
23	-3.1	3.1

Figure S16. Mean difference and standard deviation in systolic blood pressure between the [a(PAT)+b(HR)+c] calibration model and the arterial line for each subject.

Subject	Mean Difference (mmHg)	Standard Deviation (mmHg)
1	2.2	3.9
2	0.6	3.9
3	-0.0	2.3
4	0.7	7.0
5	-0.1	3.0
6	-4.2	4.4
7	2.5	2.4
8	2.1	5.5
9	1.2	3.5
10	0.0	2.4
11	1.2	6.7
12	-2.1	4.0
13	10.5	6.7
14	0.9	7.1
15	4.2	5.4
16	5.6	8.8
17	0.7	3.3
18	3.8	3.9
19	-0.5	4.4
20	4.2	6.5
21	-2.2	3.2
22	-0.4	7.1
23	0.1	1.3

Figure S17. Mean difference and standard deviation in diastolic blood pressure between the $[a(\text{PAT})+b(\text{HR})+c]$ calibration model and the arterial line for each subject.

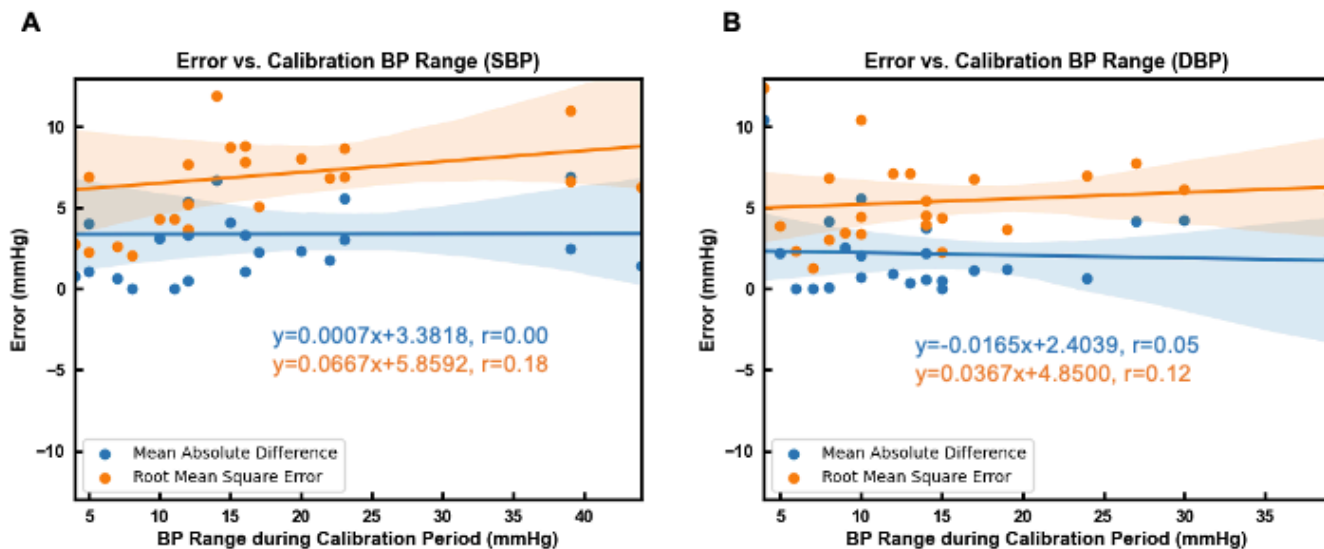


Figure S18. Scatterplots and corresponding lines of best fit relating (A) the range of systolic blood pressure (SBP) and (B) the range of diastolic blood pressure (DBP) during the ten-minute calibration period to the overall prediction error (e.g., mean absolute difference or root mean square error) between the [a(PAT)+b(HR)+c] calibration and the arterial line BP for each subject. Equations for the corresponding lines of best fit and the Pearson's product-moment correlation factor (y is either "Mean Absolute Difference" (blue) or "Root Mean Square Error" (orange) and x is the "BP Range during Calibration Period") are presented.

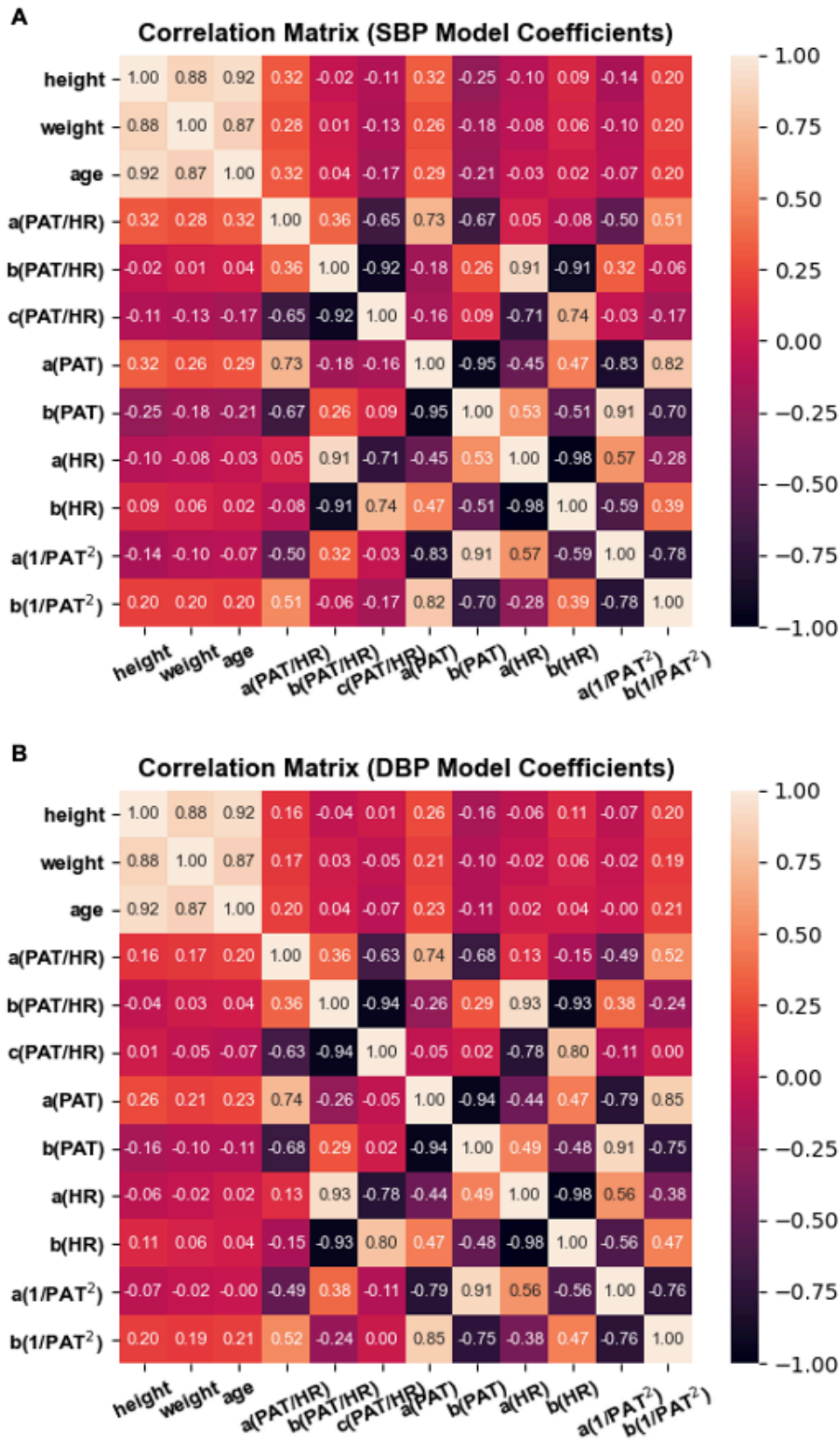


Figure S19. Correlation matrices illustrating the Pearson's product-moment correlation factor between each model coefficient from the four different calibration models and the height, weight, and age of each patient, for (A) systolic blood pressure (SBP) and (B) diastolic blood pressure (DBP).

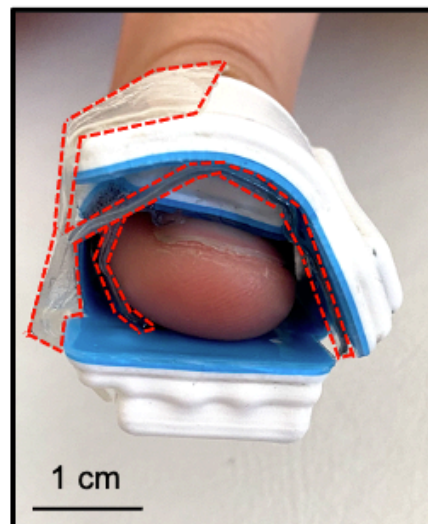
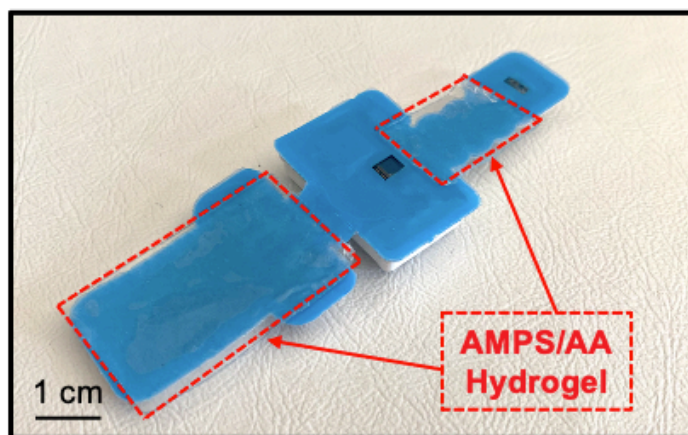


Figure S20. Adhesive approaches for securing the limb device to the skin. Photographs depicting the use of AMPS/AA hydrogel on the limb device (left) to facilitate adherence to the skin (of a 25-year-old female's right thumb) after wrapping of the device (right). Dashed red lines indicate pieces of AMPS/AA hydrogel.