Network Physiology Approach to the Cardiovascular System: Methodological Considerations

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Overview

- Technique to Study Cardiovascular Networks:
  - Vascular Structure vs. Function
  - Contrast vs. Label Free Methods
  - Local vs. Global Networks
- Label Free Imaging Technology
- Common Features of Vascular Networks
- Microvascular Networks
- Continuous Monitoring of Vascular Status

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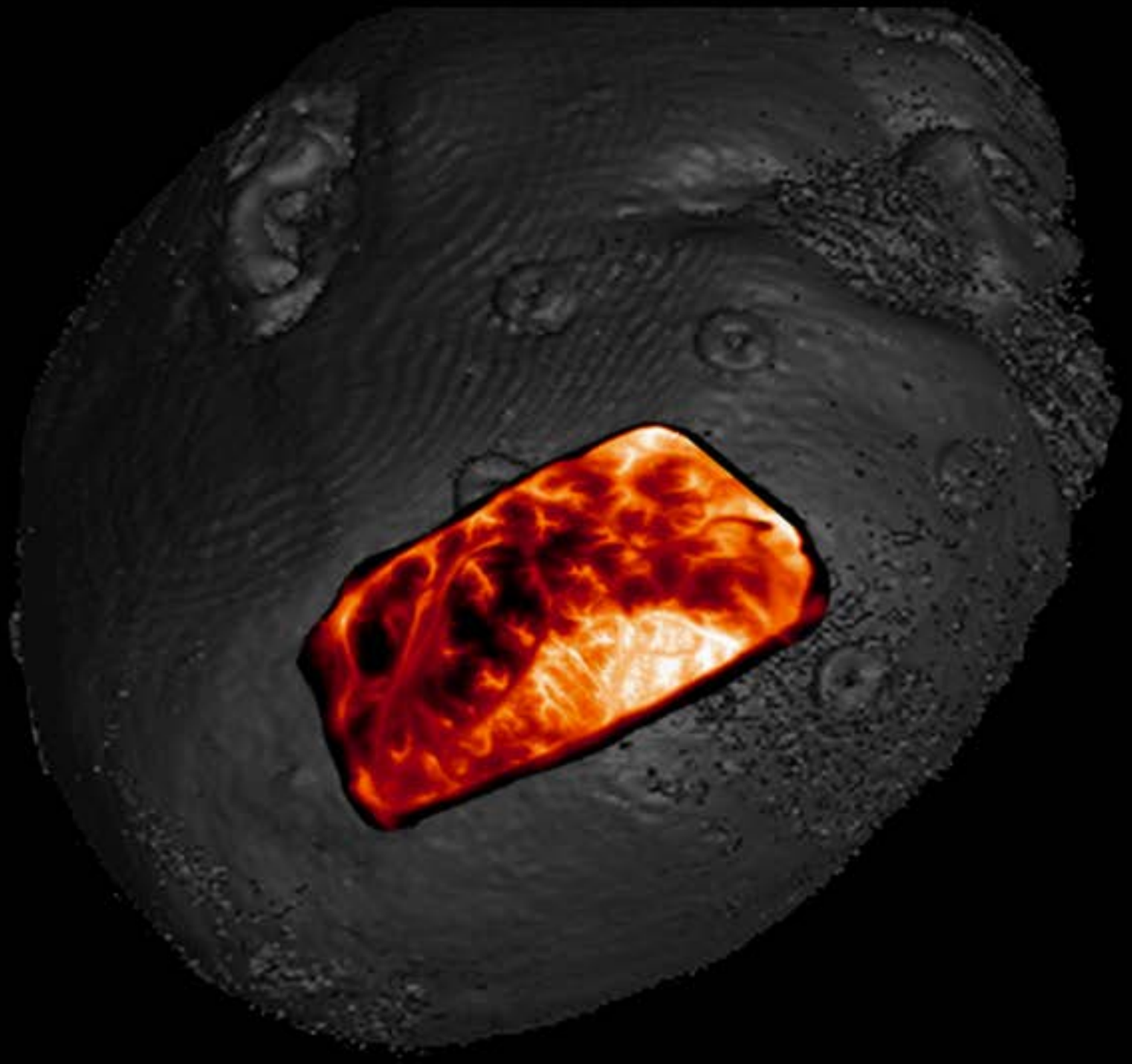
Label Free Technology
to Monitor Cardiovascular Networks.
NIH Experience

1. Infrared Imaging – *IR*
2. Laser Speckle Contrast Imaging – *LSCI*
3. Vein Imaging – *VEIN-VIEWER*
4. Laser Doppler Flow Probes – *LDF*
5. *- blood velocity*
6. *- local skin temperature*
7. *- tissue oxy- and de-oxygenation*
8. *- blood concentration*
9. Near-Infrared Tissue Oxygenation Probes – *StO_2*
10. Continuous Blood Pressure Monitoring

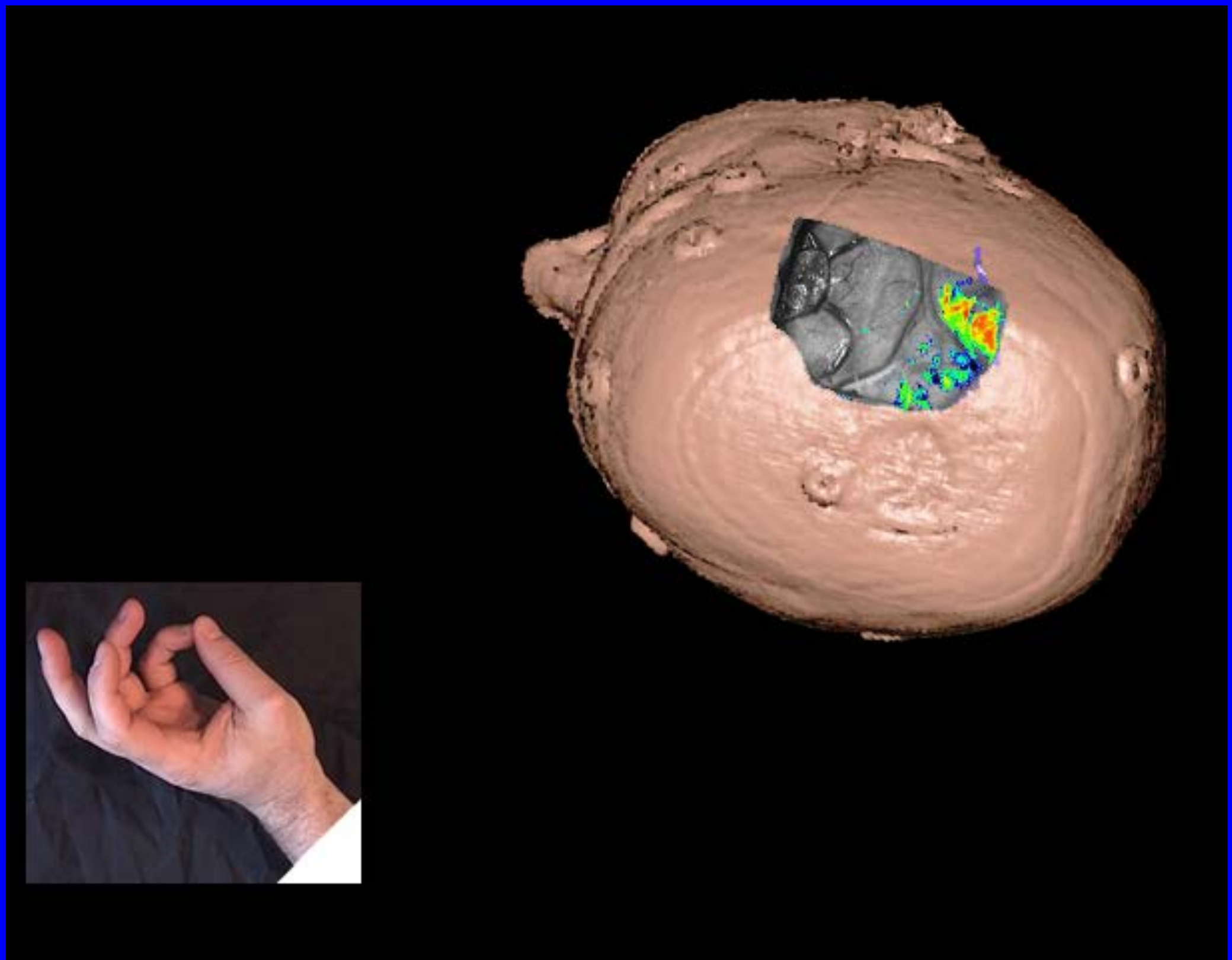
11. Wireless Skin Patches - *Electronic Tattoos*
12. Clinical Intravital Imaging – *Video capillaroscopy*

Real-time Intraoperative Imaging of Human Brain with Infrared Camera

Gorbach A. et al., Annals of Neurology, 2003

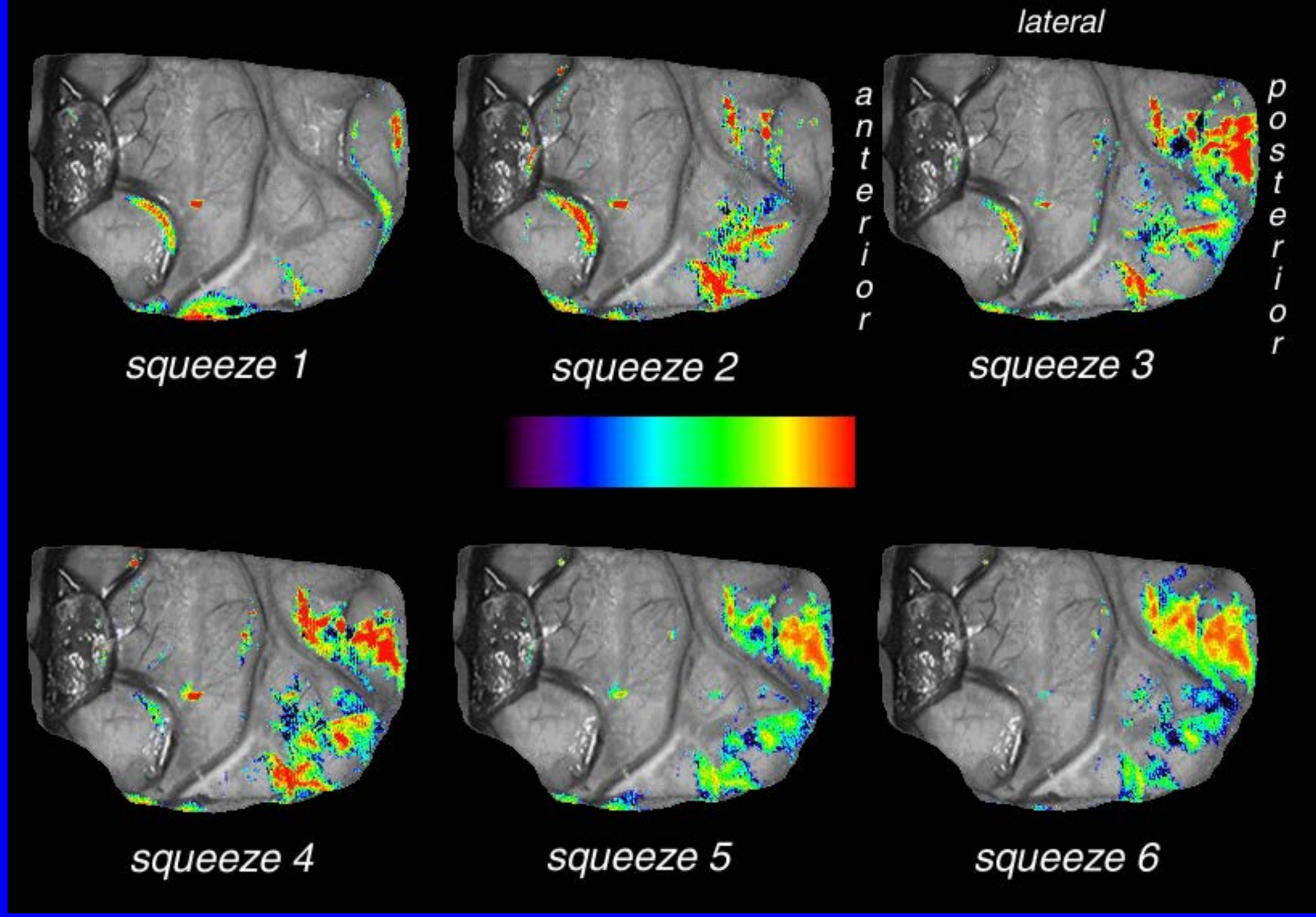


Gorbach A. et al., Annals of Neurology, 2003



Gorbach A. et al., Annals of Neurology, 2003

IR IMAGES OF THE BRAIN DURING SEQUENTIAL MOTOR TASKS



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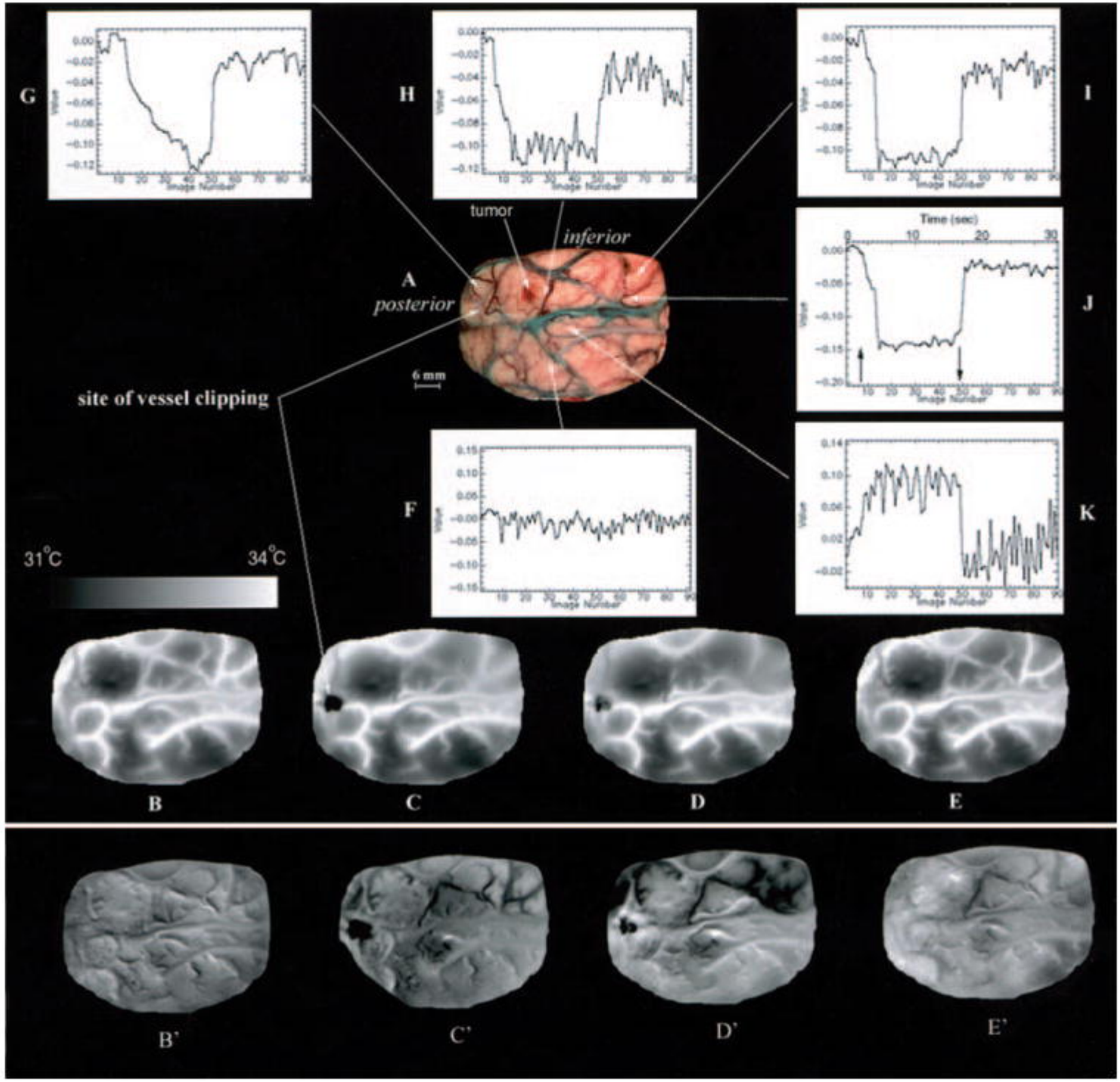
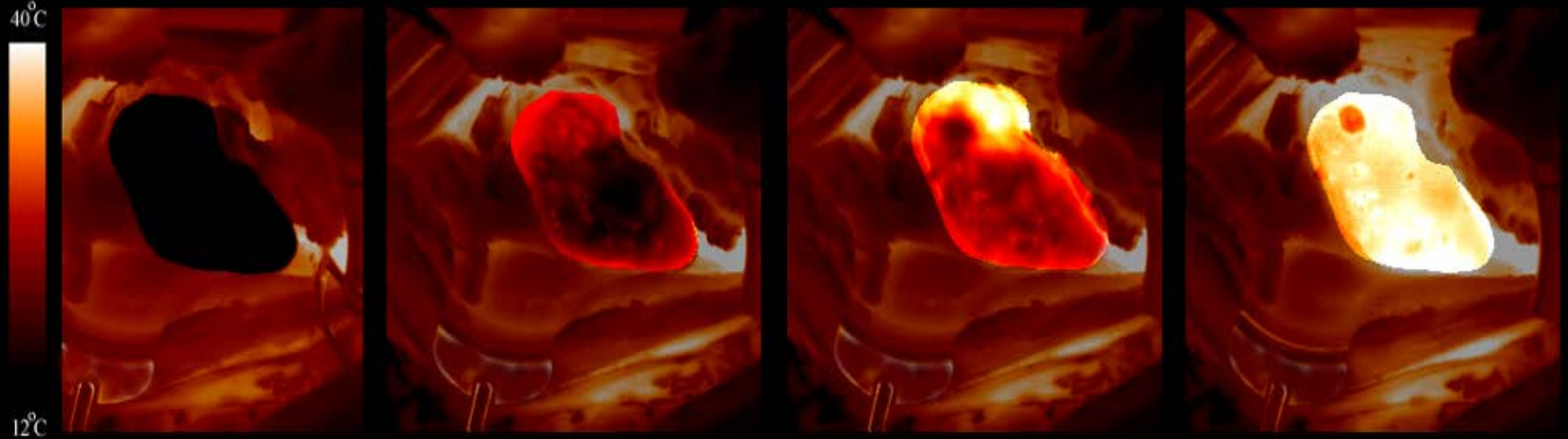
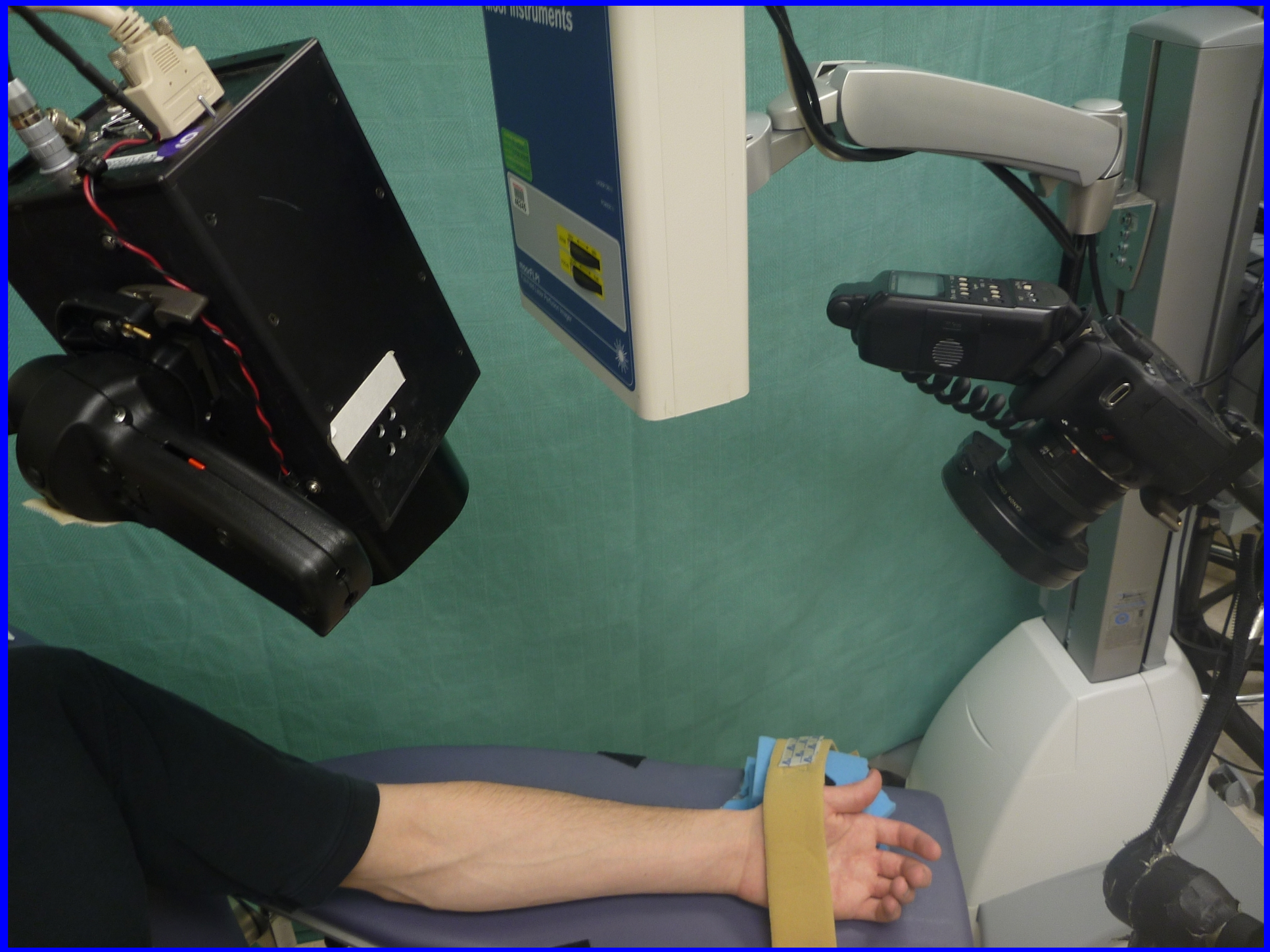


Gorbach A. et al., J. of Neurosurgery, 2004



A. Gorbach et al.,
Objective, Real-time, Intraoperative Assessment of
Renal Parenchymal Perfusion Using Infrared Imaging
American Journal of Transplantation 2003, 3: 988-993

Optical Imaging of Forearm Blood Flow



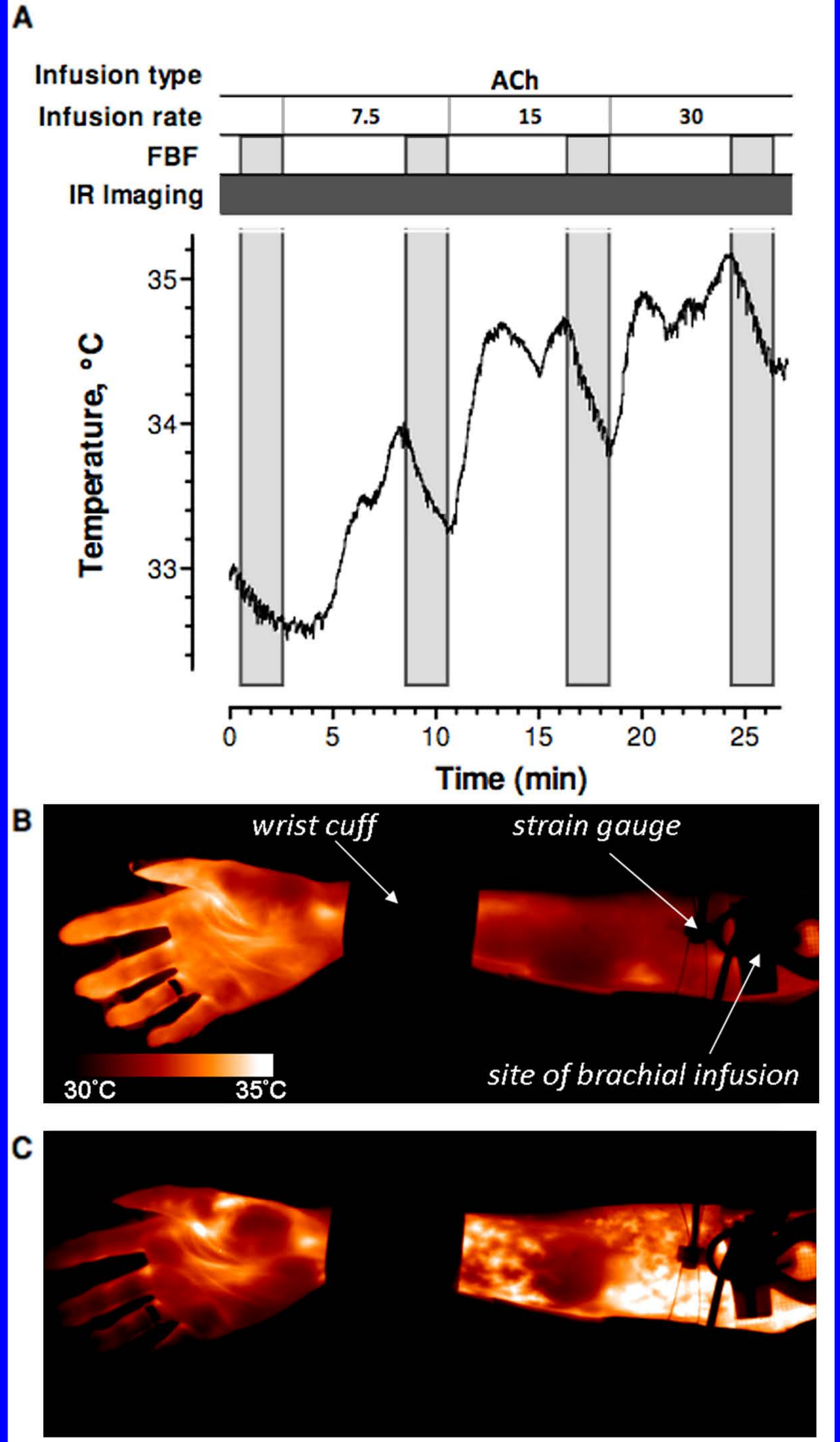
Recruitment of the Vessels during *Acetylcholine* Infusion

7.5 *µg/min*

15 *µg/min*

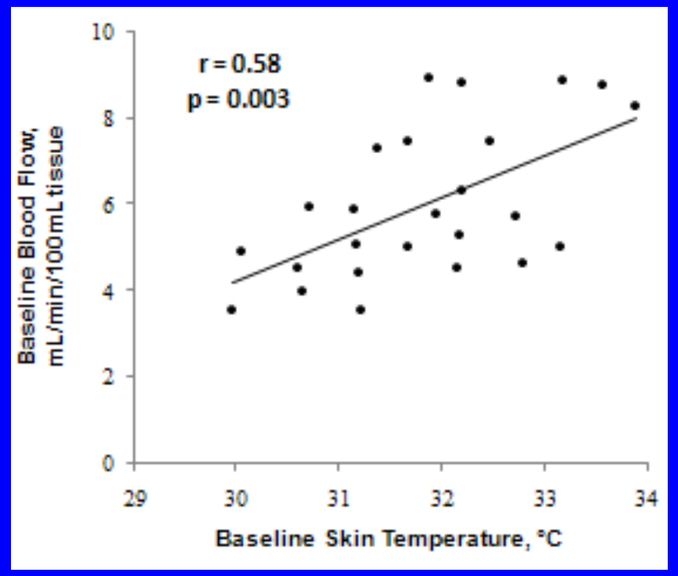
30 *µg/min*

Gorbach A. et al., Infrared Imaging of Nitric Oxide-mediated Blood Flow in Human Sickle Cell Disease. Microvascular Research, 2012



Gorbach A. et al., Infrared Imaging of Nitric Oxide-mediated Blood Flow in Human Sickle Cell Disease. Microvascular Research, 2012

Skin temperature as a Sensitive Biomarker of Vascular Function



- reflected agonist-induced changes in blood flow
- correlated with forearm blood flow
- predicted a blunted blood flow response to SNP
- may reflect subcutaneous blood flow via angiosomes

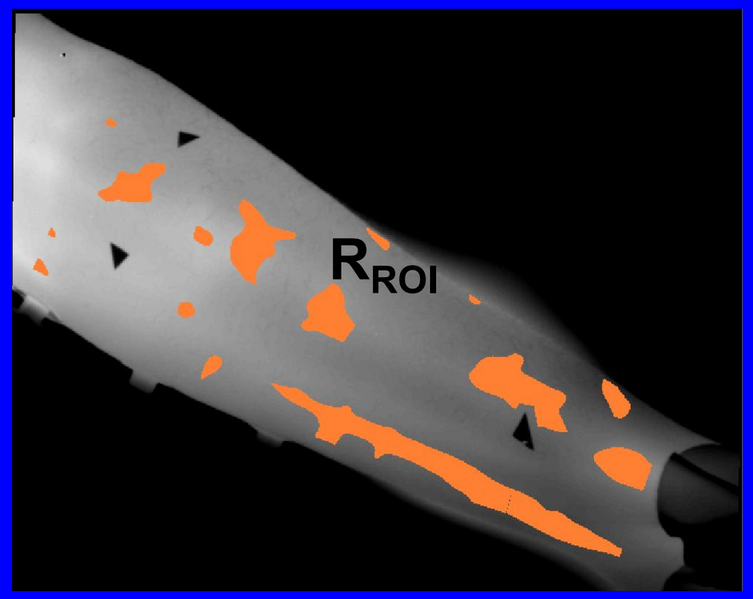
Gorbach A. et al., Infrared Imaging of Nitric Oxide-mediated Blood Flow in Human Sickle Cell Disease. Microvascular Research, 2012

Real-time Infrared Imaging Assessment of Blood Flow

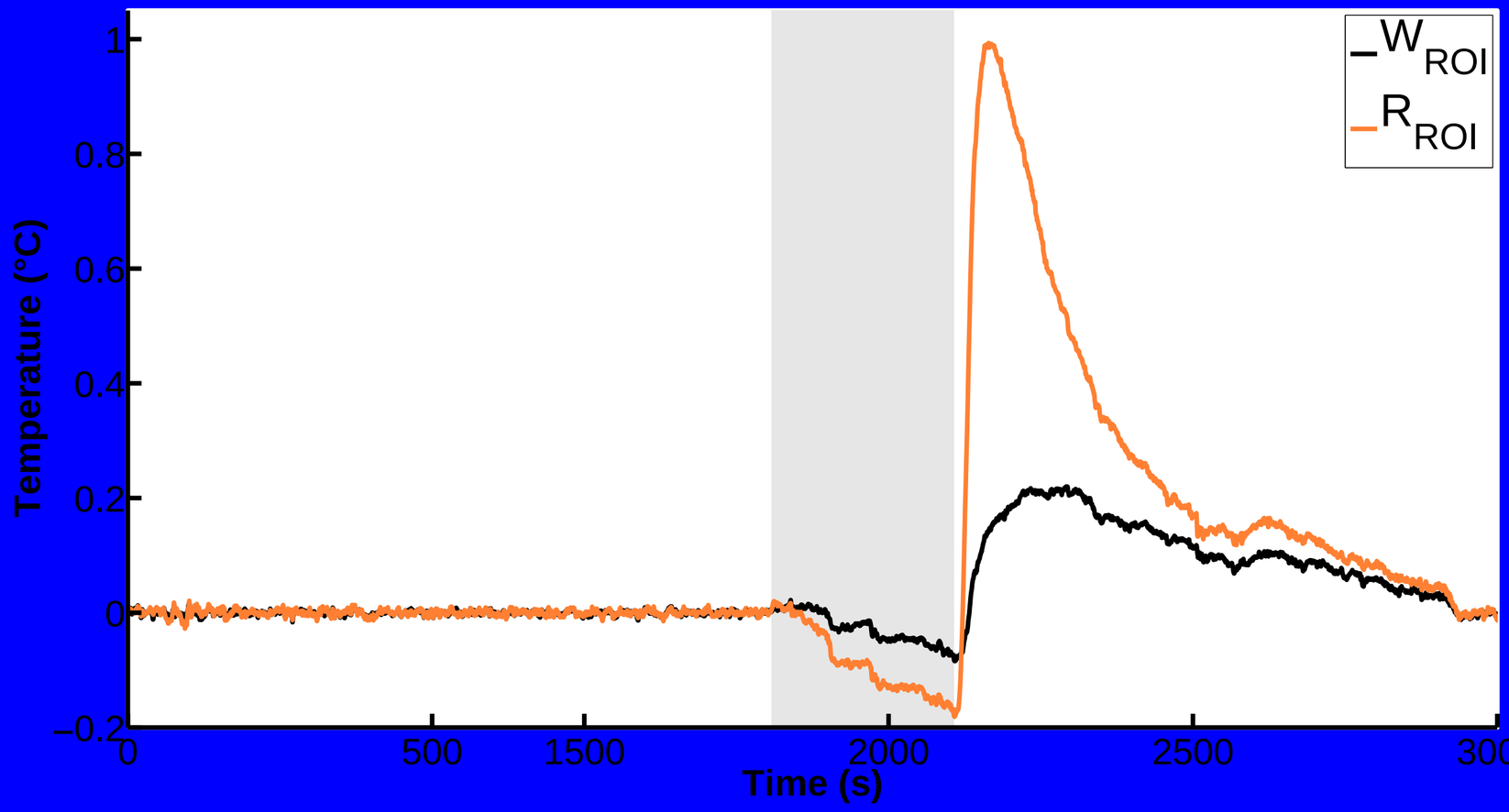
Difference in vasodilitation in *radial* artery supply vs. *ulnar* artery supply

Gorbach A. et al., Infrared Imaging of Nitric Oxide-mediated Blood Flow in Human Sickle Cell Disease. Microvascular Research, 2012

a)



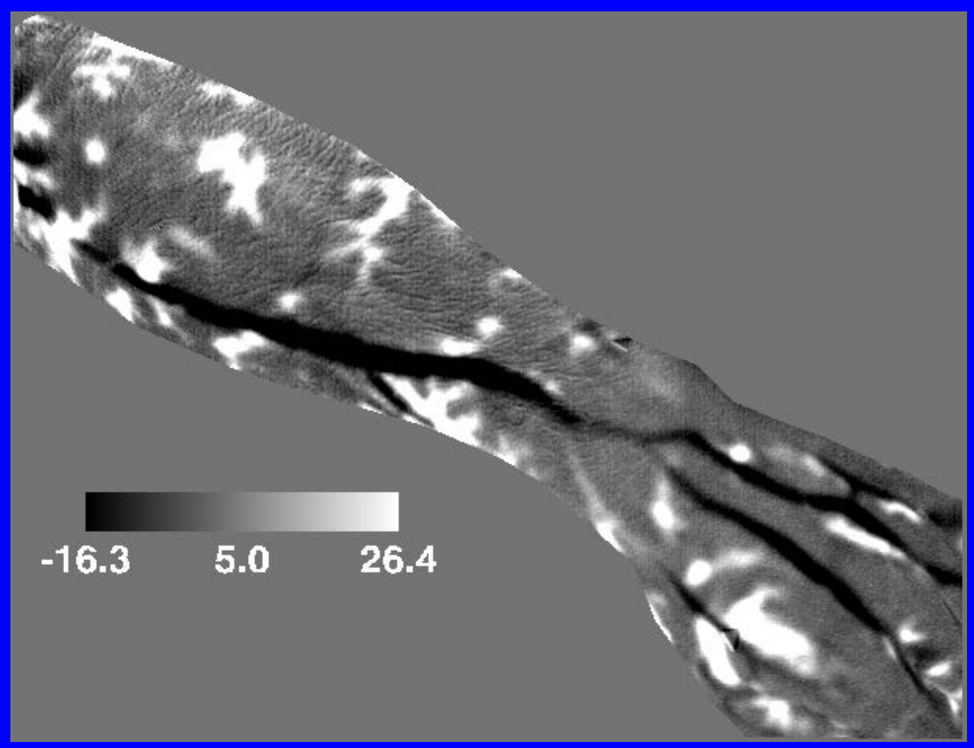
b)



(a) Computed R_{ROI} (clusters of orange pixels) overlying the raw IR image of a representative HV subject's forearm. (b) Time-temperature profiles of the W_{ROI} (black) and R_{ROI} (orange) for the same subject. Both profiles are baseline-corrected. The occlusion segment is highlighted in gray.

Chang K et al., Rapid vs. Delayed Infrared Responses After Ischemia Reveal Recruitment of Different Vascular Beds. Quantitative InfraRed Thermography. 12(2):173-183, 2015

IR image of the forearm (volar aspect) during 30 *µg/min brachial infusion of Acetylcholine*



IR image (processed) of forearm dorsal aspect, baseline condition

Balageas D., Roche J-M., Leroy F-H., Liu W.M, Gorbach A.M. Thermographic Signal Reconstruction Method: a Powerful Tool for Enhancement of Transient Thermographic Images. Biocybernetics and Biomedical Engineering J. 34(3):1-9, 2014

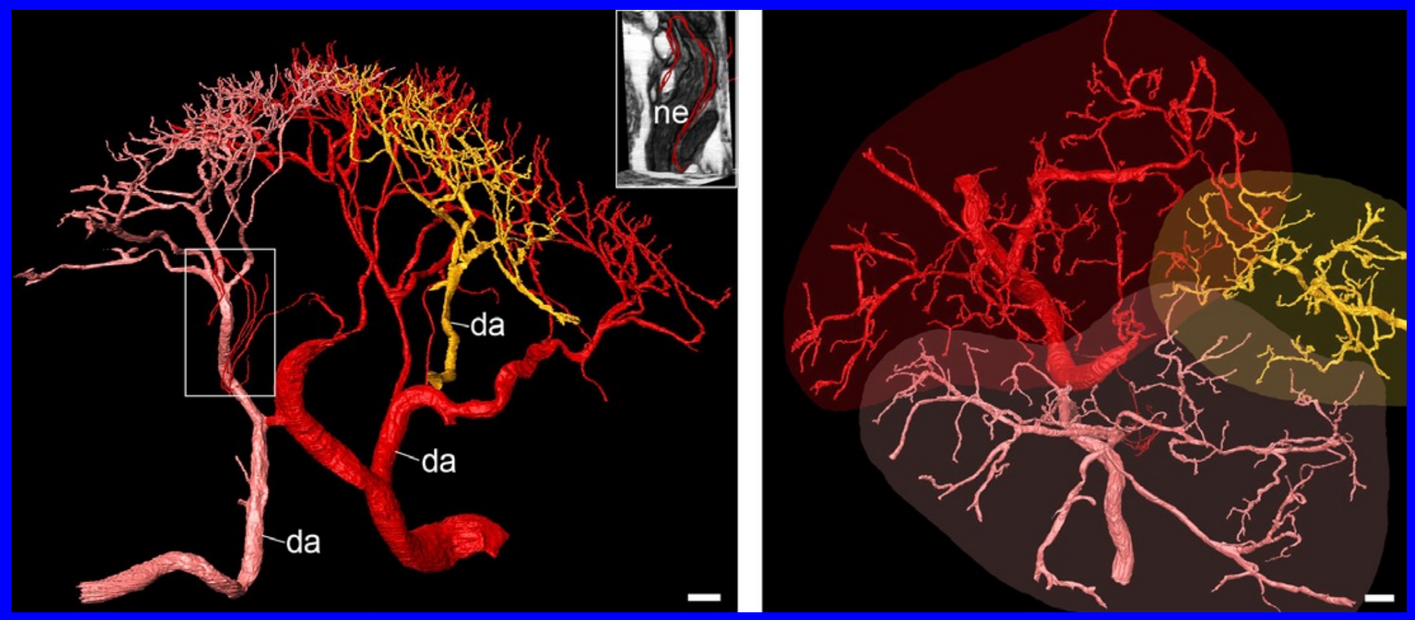
Arterial Units of the Dermal / Epidermal Junction

Lateral View

The boxed area is displayed in the insert in combination with two virtual resection planes. Note the capillaries, which supply a large nerve (ne) of the reticular dermis.

Top View

The capillaries supplying the nerve are outside the direct projection of the borders of the corresponding arterial unit..



Surface-rendered high-quality 3D models of three neighboring arterial trees (red, pink, yellow). Scale bars: 100 μ

S. H. Geyer et al., J. Anat. 223, pp.603—609, 2013

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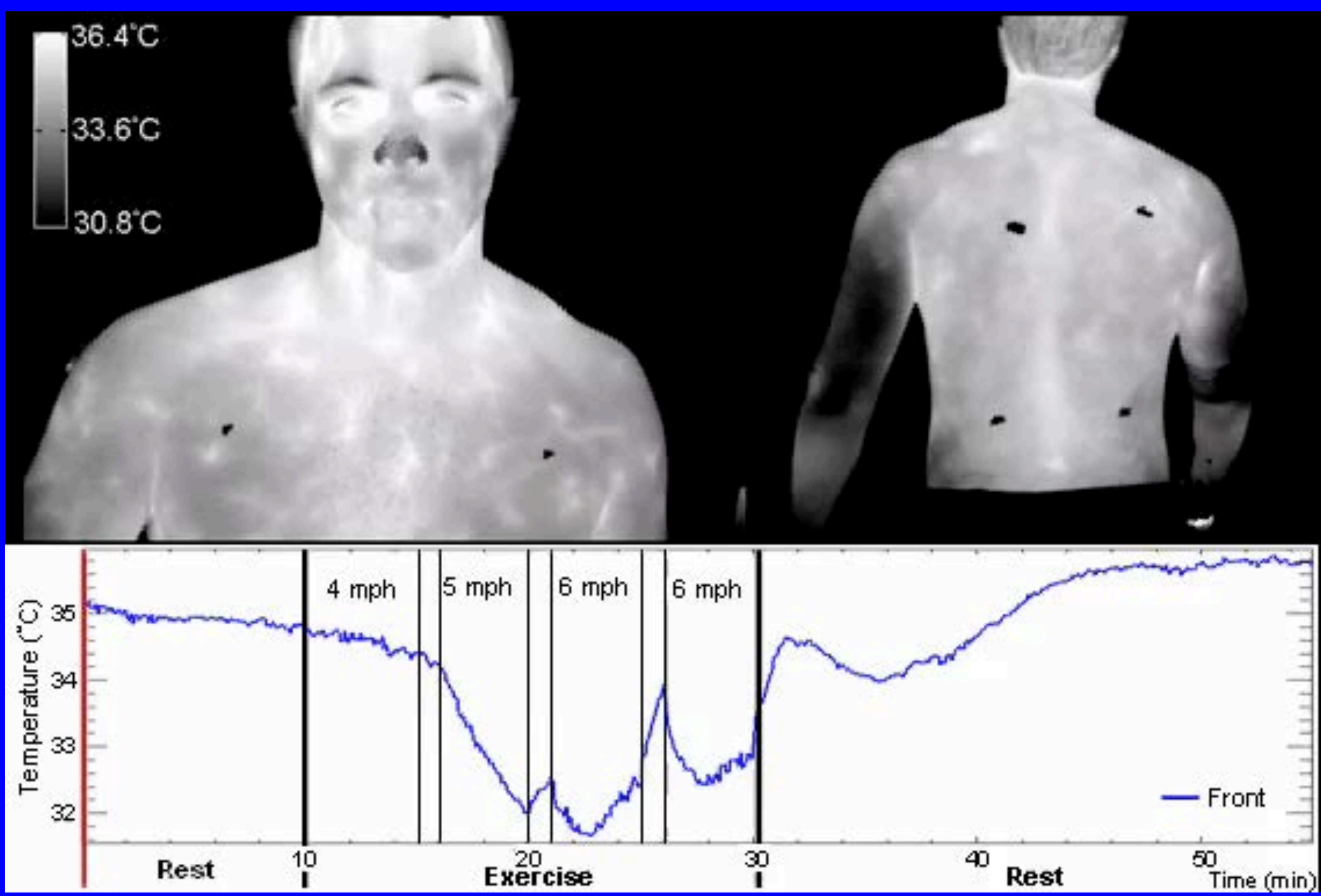
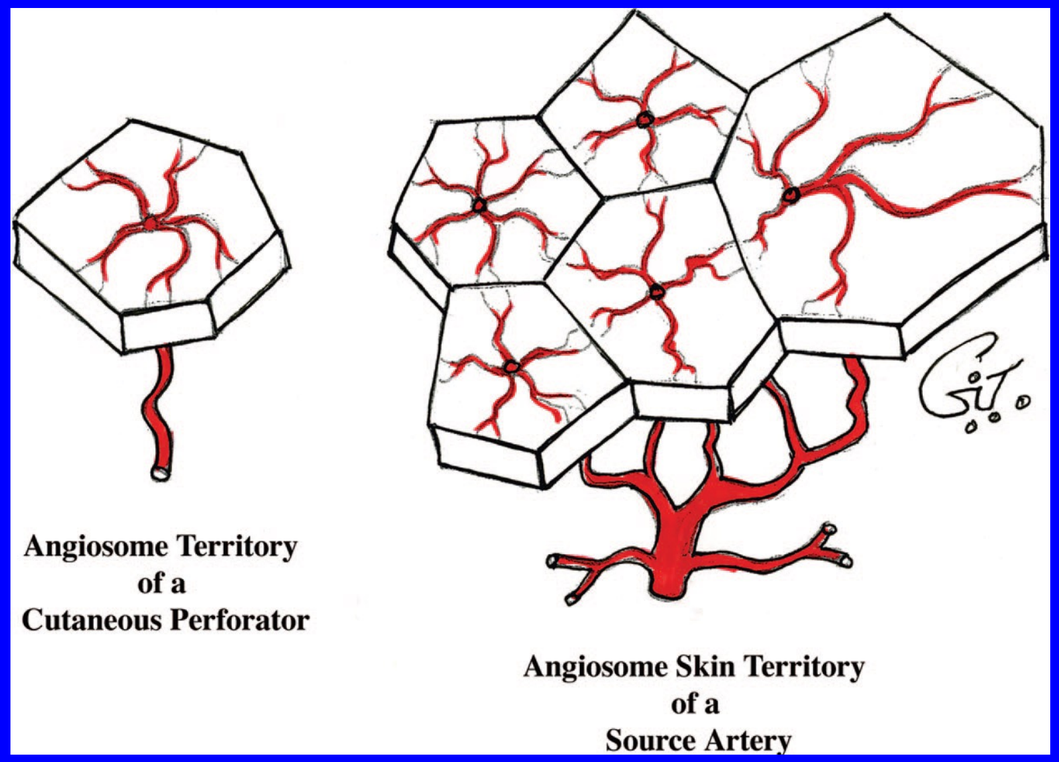
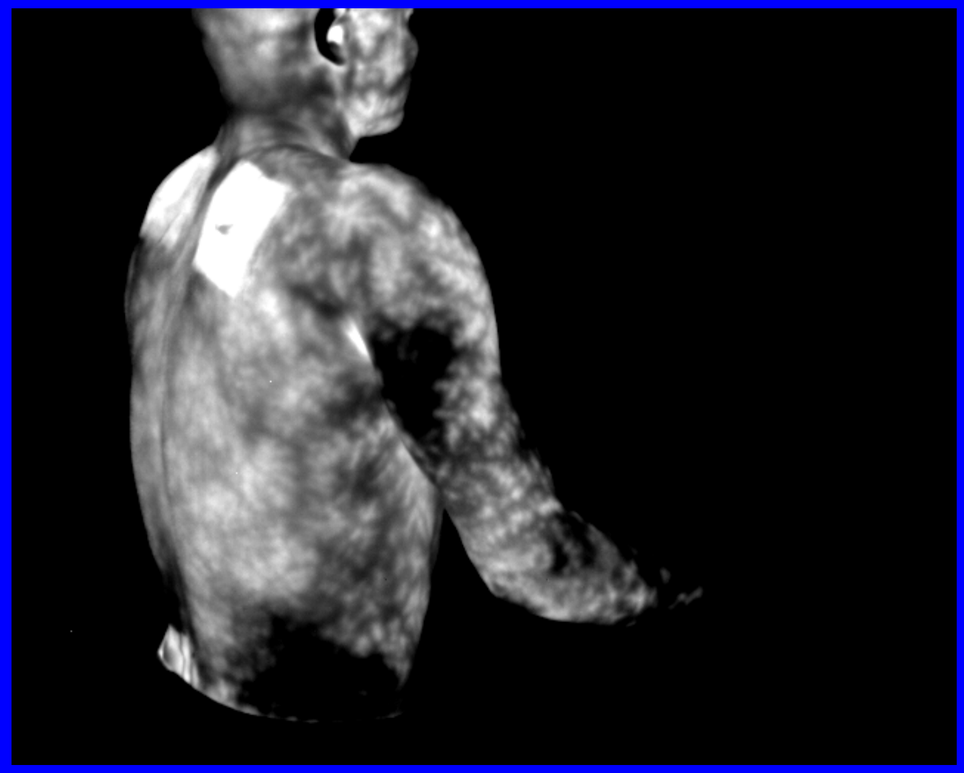


https://www.nibib.nih.gov/labs-at-nibib/trans-nih-shared-resource-biomedical-engineering-and-physical-science-beps/infrared#quicktabs-intramural_tab_pane=3



Schematic representation of the cutaneous perforator angiosomes

the basic skin module (*left*) and several modules of different sizes
G. Ian Taylor, 2011



IR image of multiple angiosomes during subject's exercise
A. Gorbach, NIBIB

https://www.nibib.nih.gov/labs-at-nibib/trans-nih-shared-resource-biomedical-engineering-and-physical-science-beps/infrared#quicktabs-intramural_tab_pane=3

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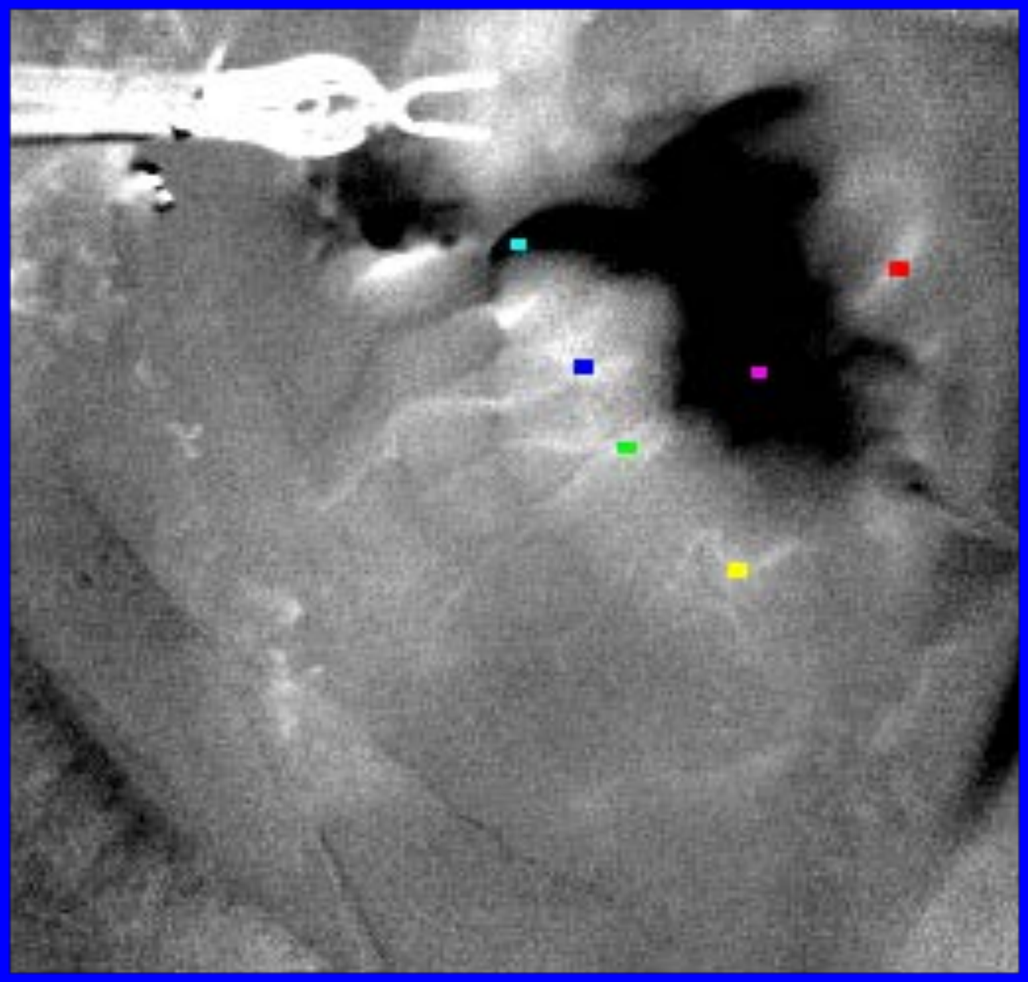
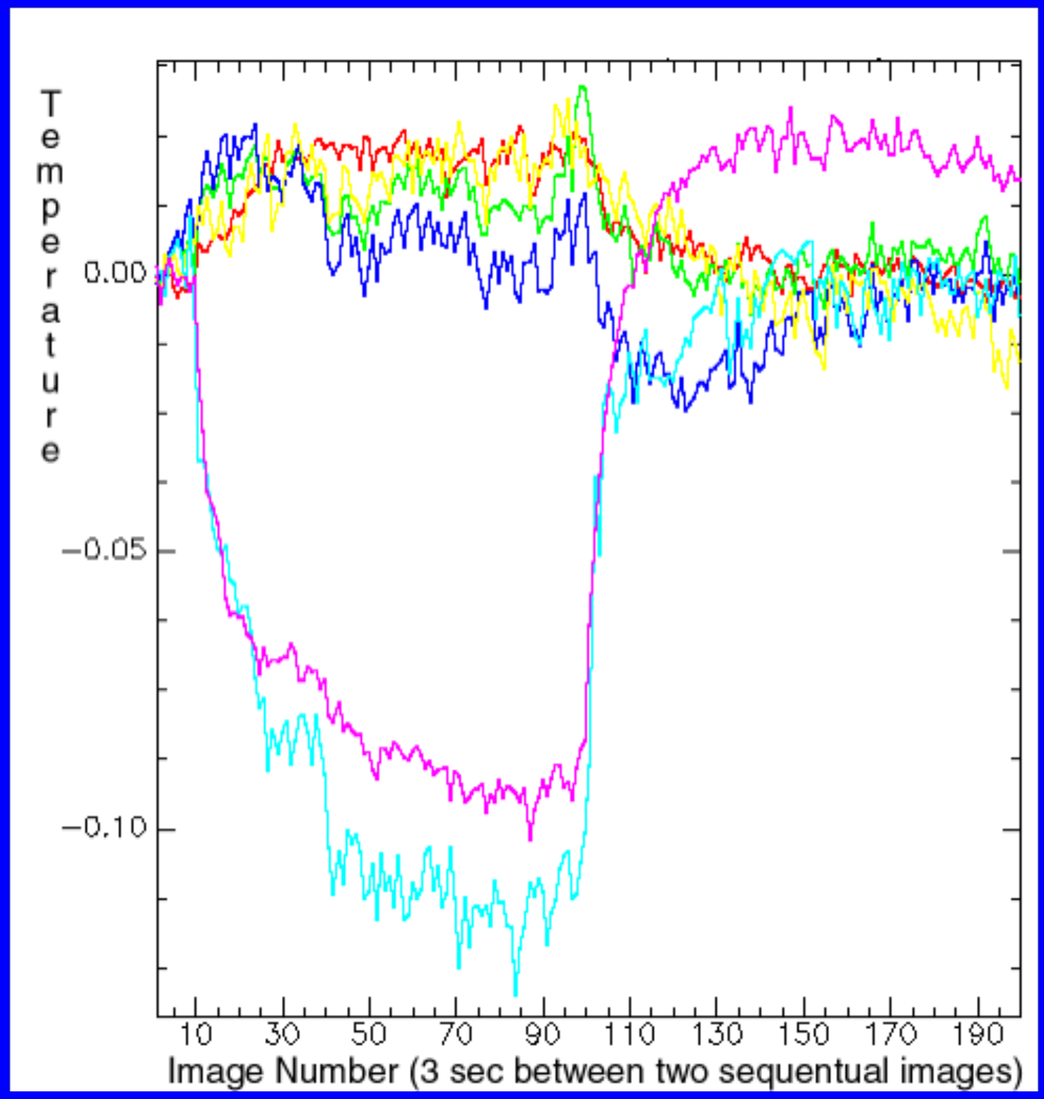
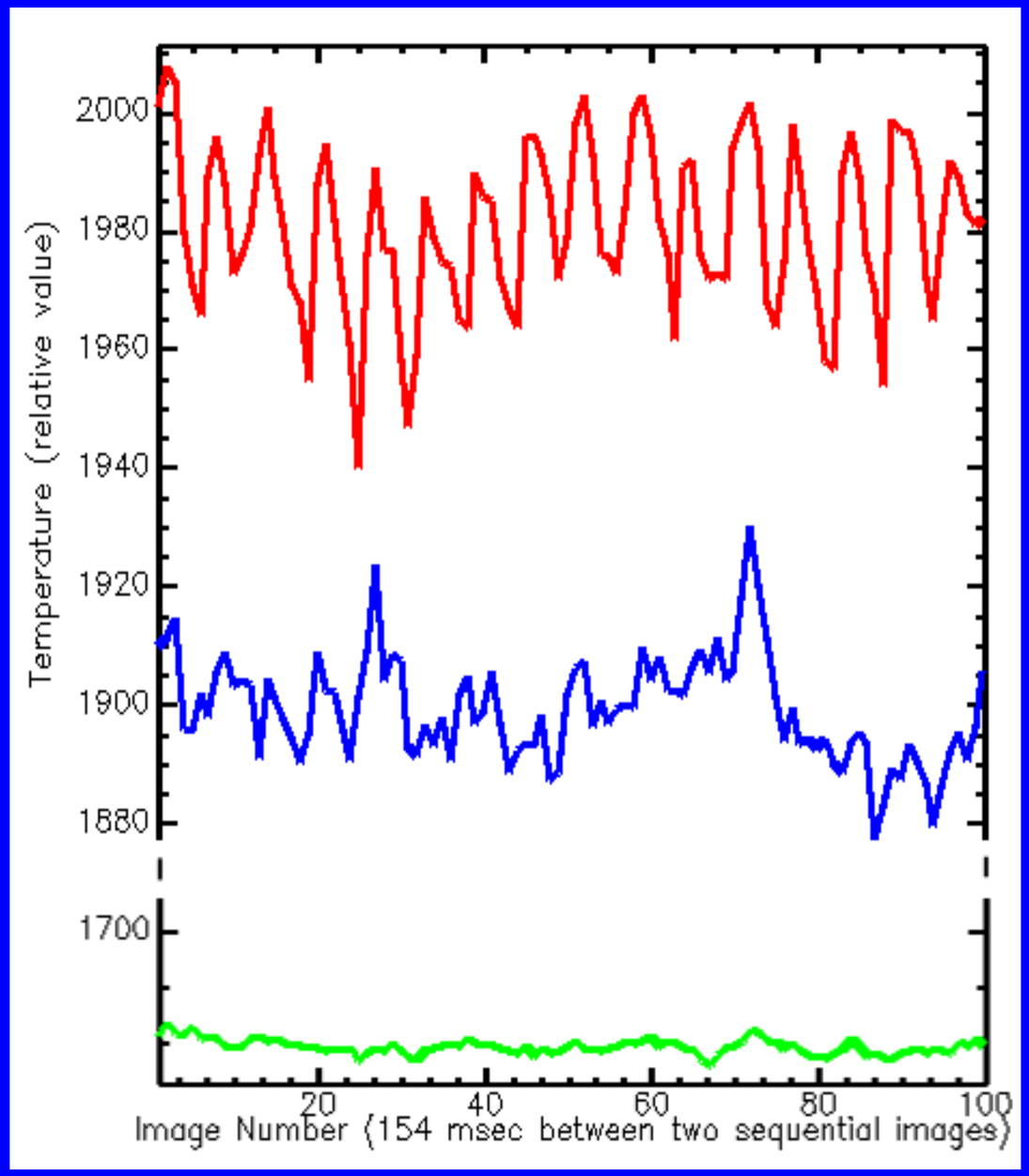
Real-time Detection of Vascular Occlusion and Reperfusion of the Brain During Surgery by Using Infrared Imaging





Watson J., Gorbach A., Pluta R., Rak R., Heiss J., Oldfield E. Real-time Detection of Vascular Occlusion and Reperfusion of the Brain During Surgery by Using Infrared Imaging. J. of Neurosurgery 96(5):918-923, 2002

Relationships Among Temperature of Arteries, Veins and Brain Parenchyma



A.Gorbach et al., 2003

Origin and Frequencies of Vasomotion

	Vascular tone controlled by	Frequency interval, *Hz*
1	Endothelium-derived hyperpolarizing factor (*EDHF*)	0.005 - 0.0095
2	Rate of endothelial release of *NO*	0.0095 - 0.021
3	Sympathetic activity	0.02 - 0.05
4	Myogenic activity	0.06 - 0.095
5	Respiration	0.2 - 0.6
6	Heart activity	0.6 - 1.8

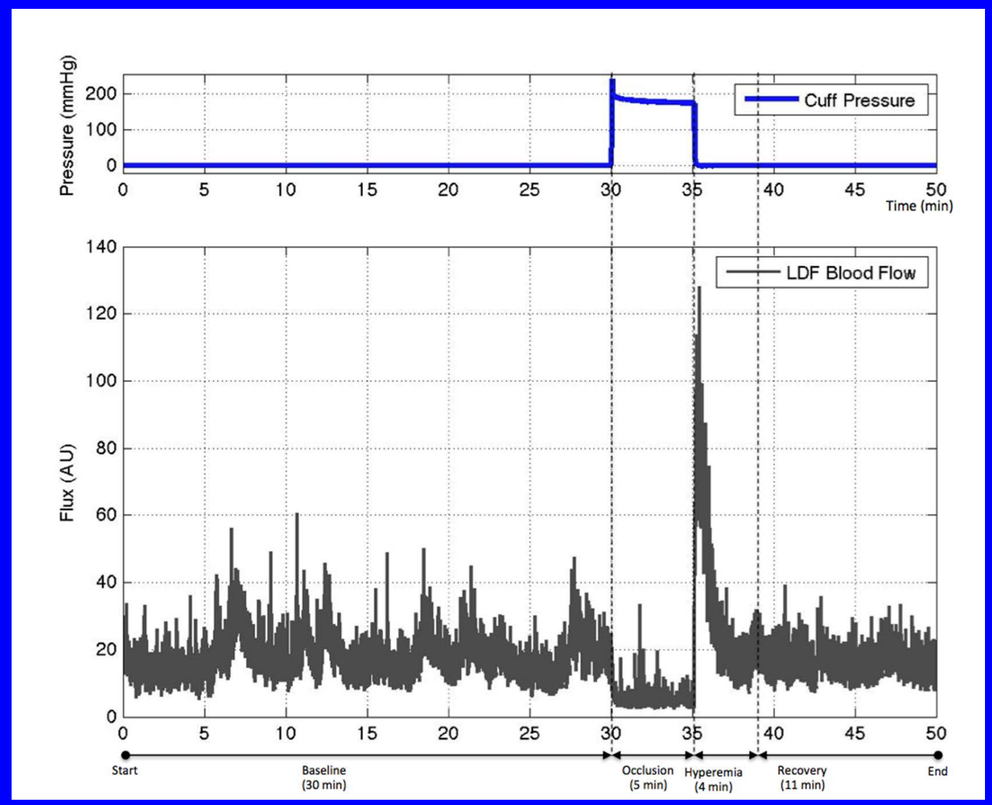
Kvandal et al., 2006

Study of Blood Flow Oscillations in Patients with SCD and Healthy Volunteers

Study Groups:

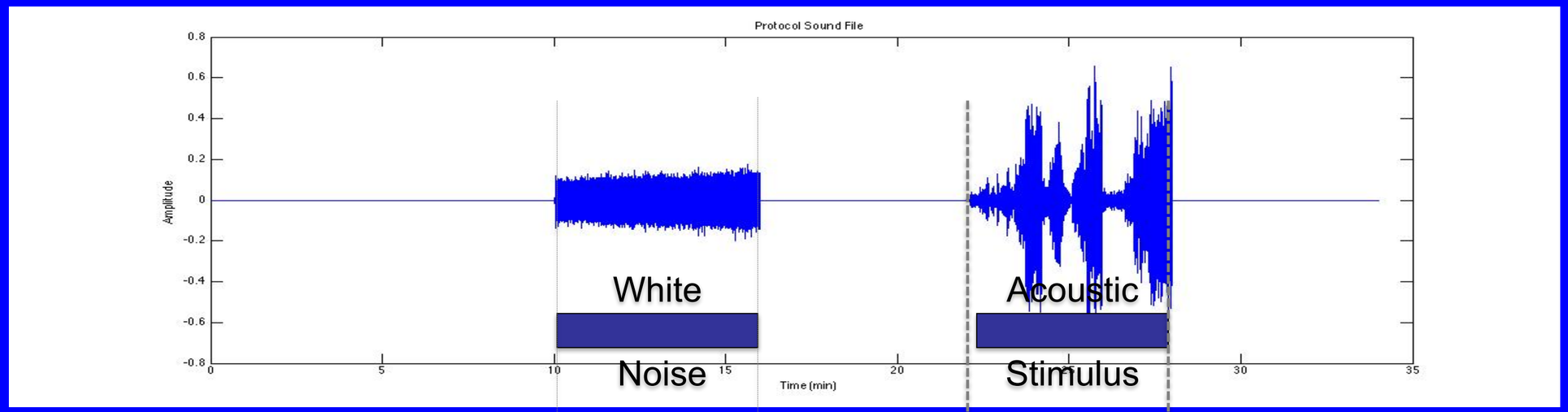
- Healthy Volunteers (n=34)
- Steady State Sickle-Cell (n=22)
- Pain Crisis Sickle-Cell (n=14,11paired)
- Recovered from Pain Crisis (n=16, 11paired)

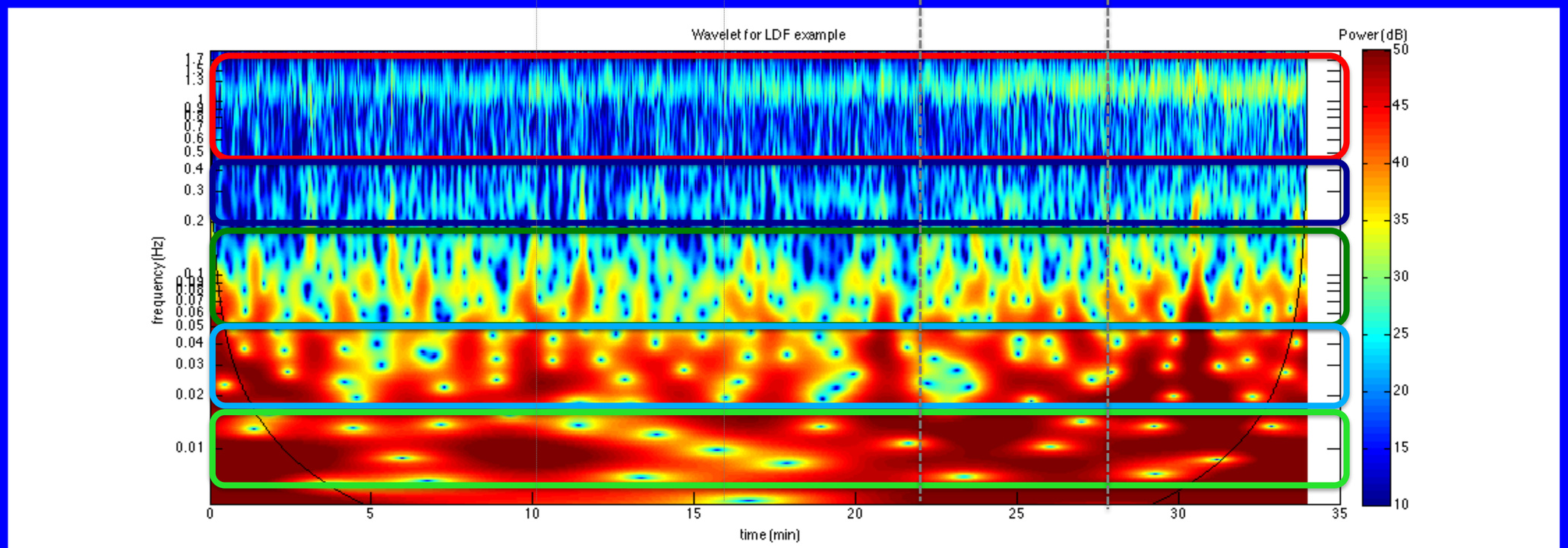
11 of the 14 SCD Pain Crisis patients returned for a follow-up study after recovery from pain crisis



Gorbach et al., article in preparation

Modulating Peripheral Blood Flow Oscillations by Entrainment with Acoustic Stimulation: A Pilot Study





- Cardio/Parasympathetic band (red) spans 0.5-1.7 Hz
- Respiratory band (dark blue) spans 0.2-0.45 Hz
- Myogenic band (dark green) spans 0.06-0.2 Hz
- Sympathetic band (light blue) spans 0.02-0.06 Hz
- Endothelial band (light green) spans 0.005-0.02 Hz

Unpublished, A. Gorbach Lab.

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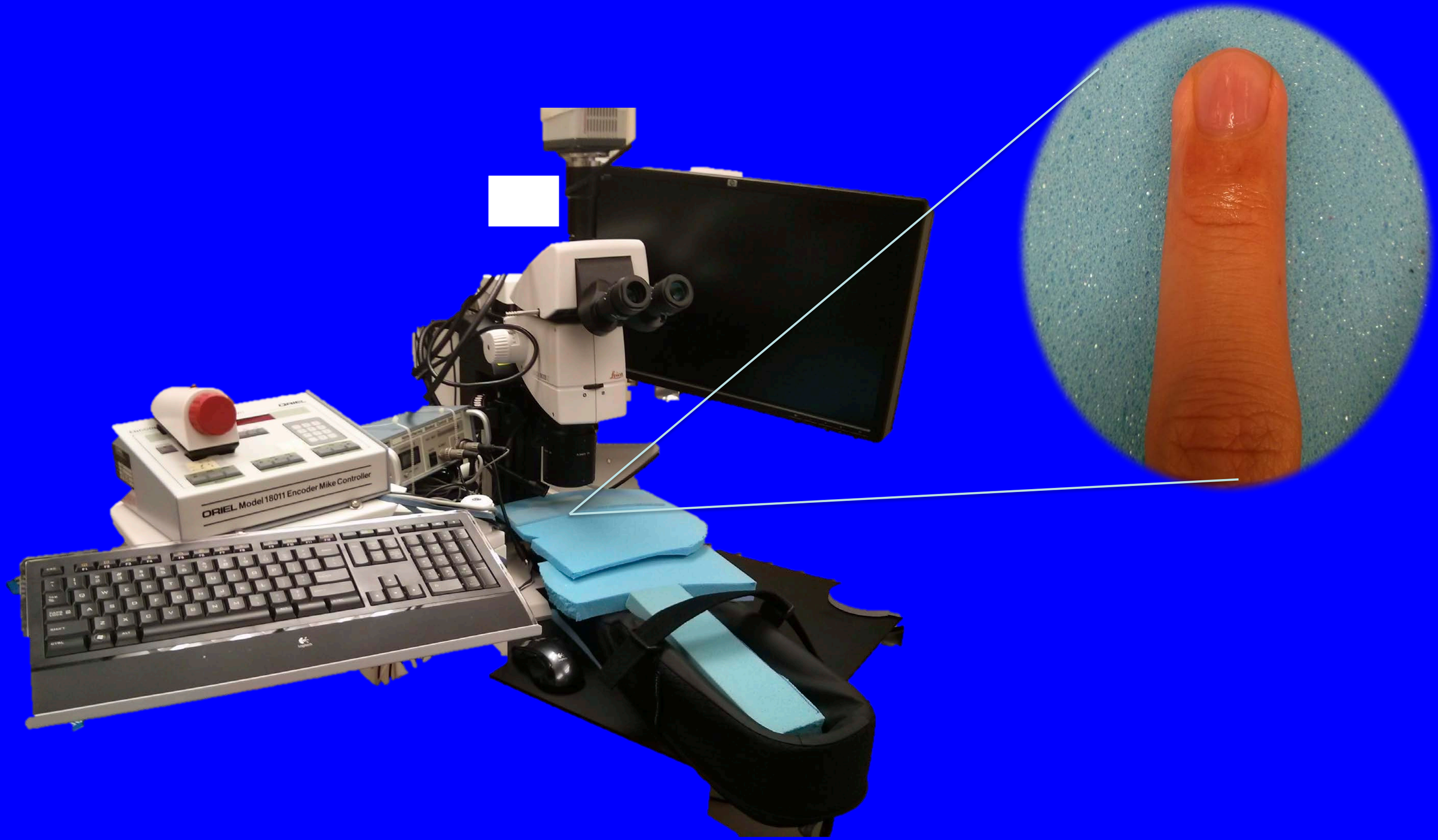
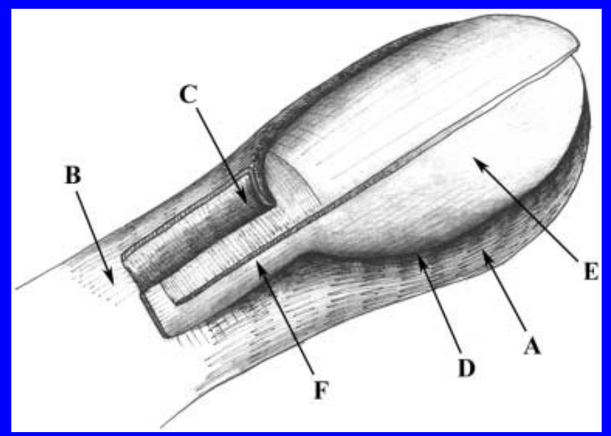
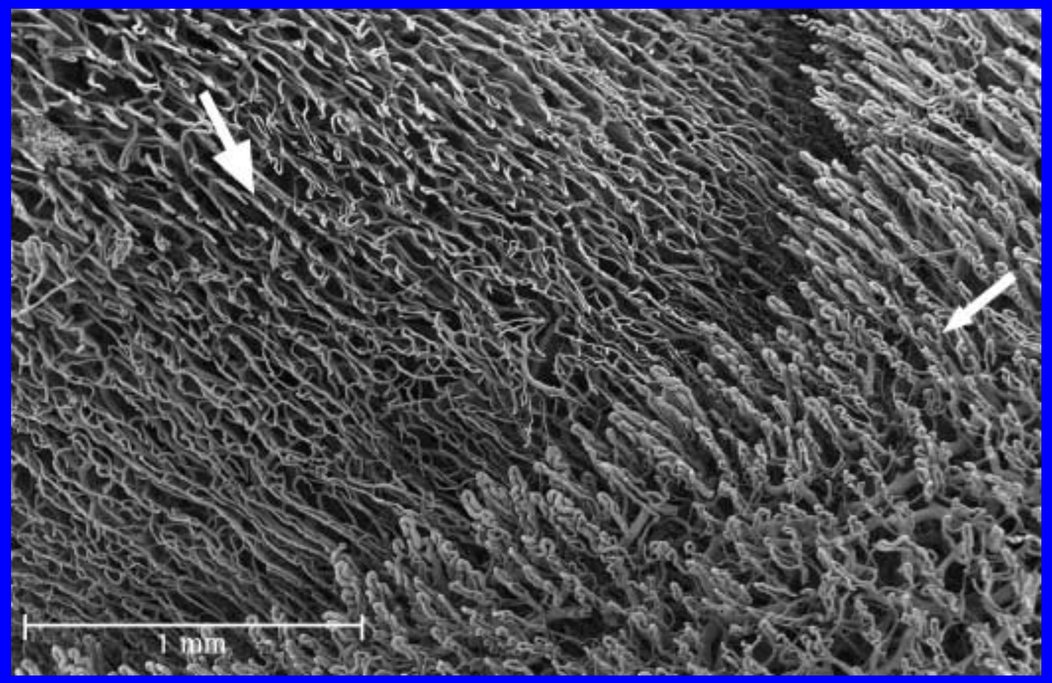
Capillaroscopy Technique



Micro-vascularization of the Human Digit

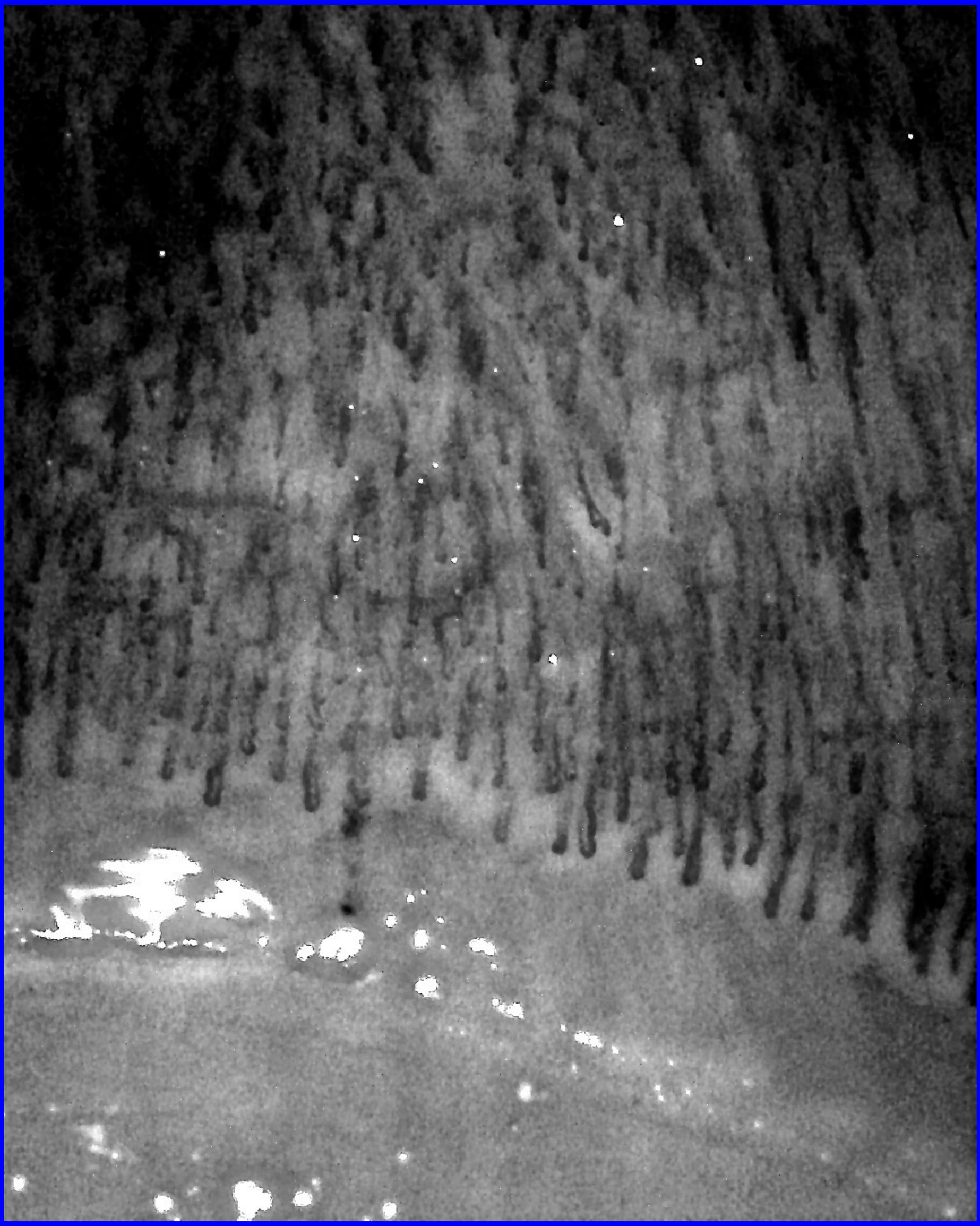


Schematic representation of the digit
palmar (A) and *dorsal* (B) side of digital skin
C - *eponychium*
D - *perionychium*
E - *nail bed*
F - *nail root*

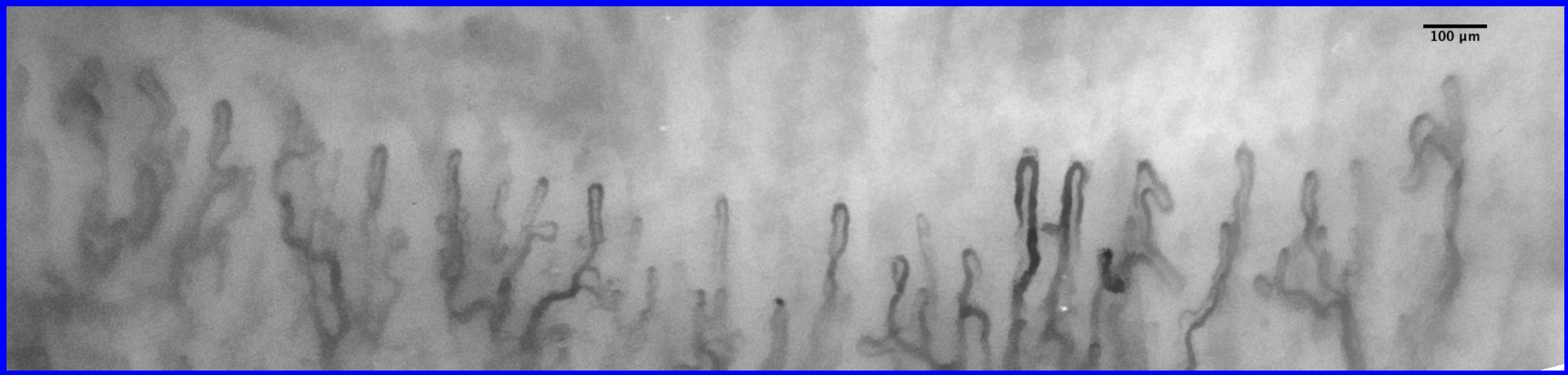


Eponychium - thin arrow
Nail - thick arrow

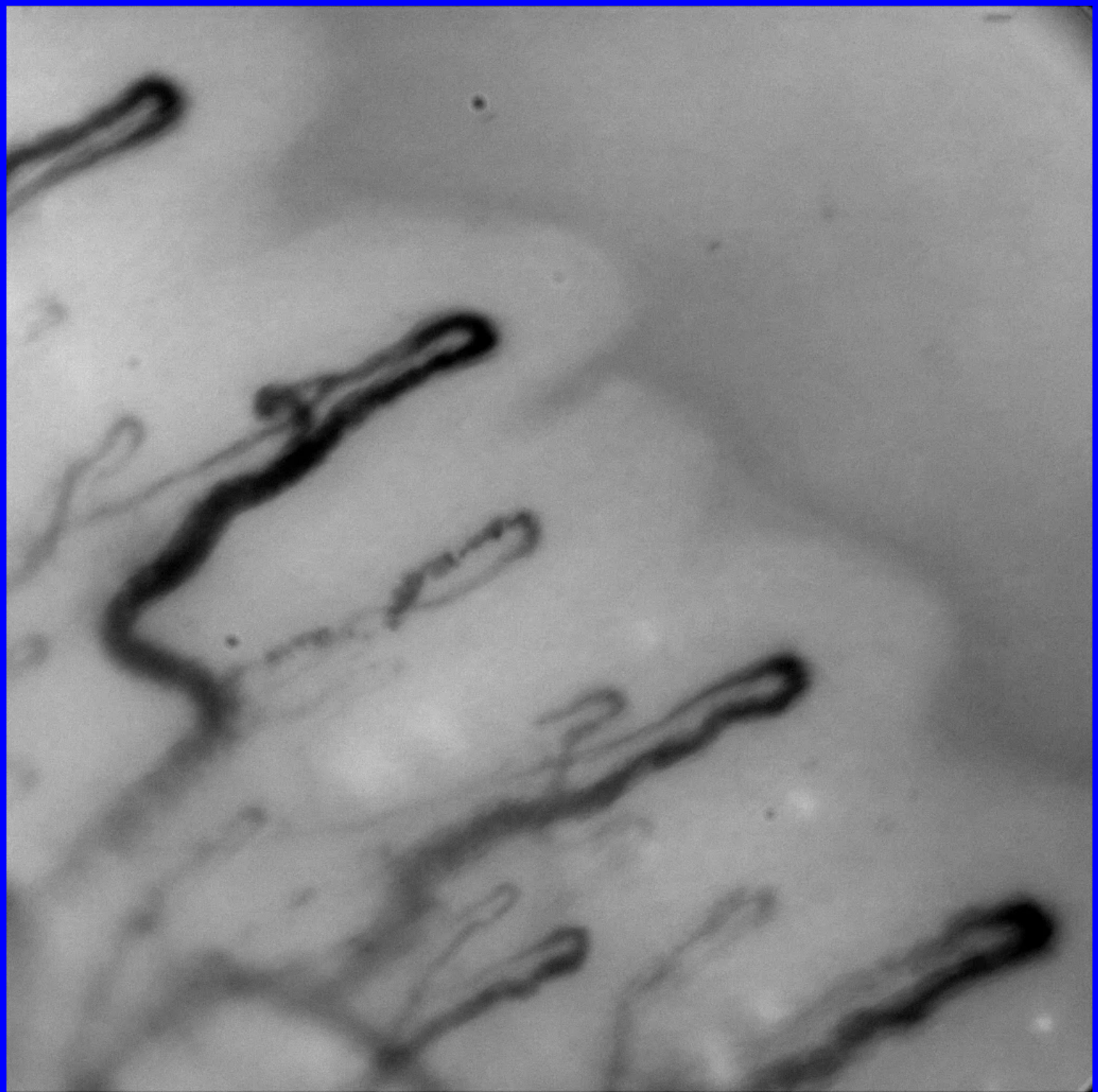
S. Sangiorgi et al., *J. Anat.,* 2004, 204, pp.123–131



Bright-Field Microscopy of Nail fold Capillaries in Human



Capillary Network (zoomed)

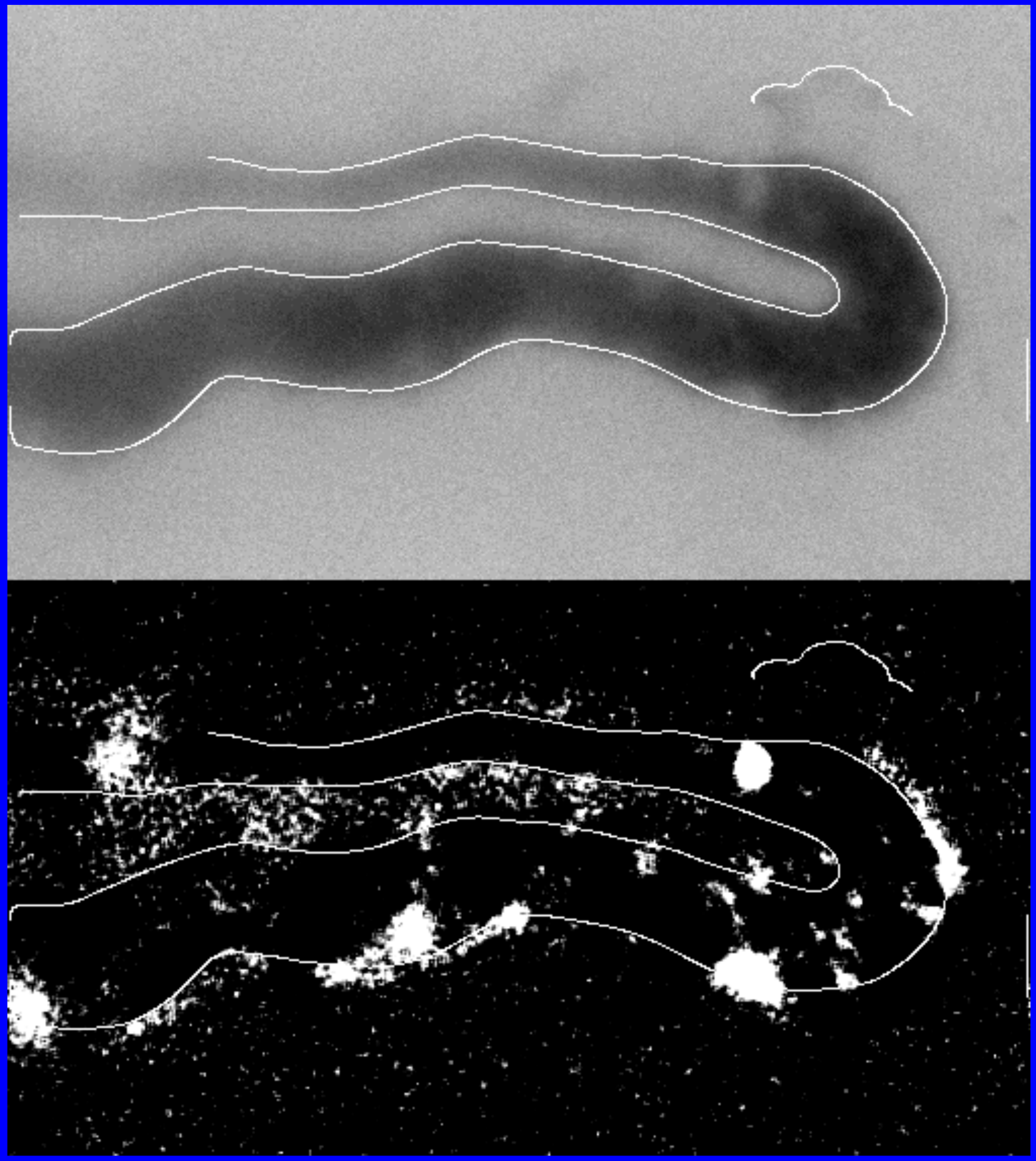


In-Vo Cellular Cytometry

A

A – single capillary; row images

B – the same capillary; processed images

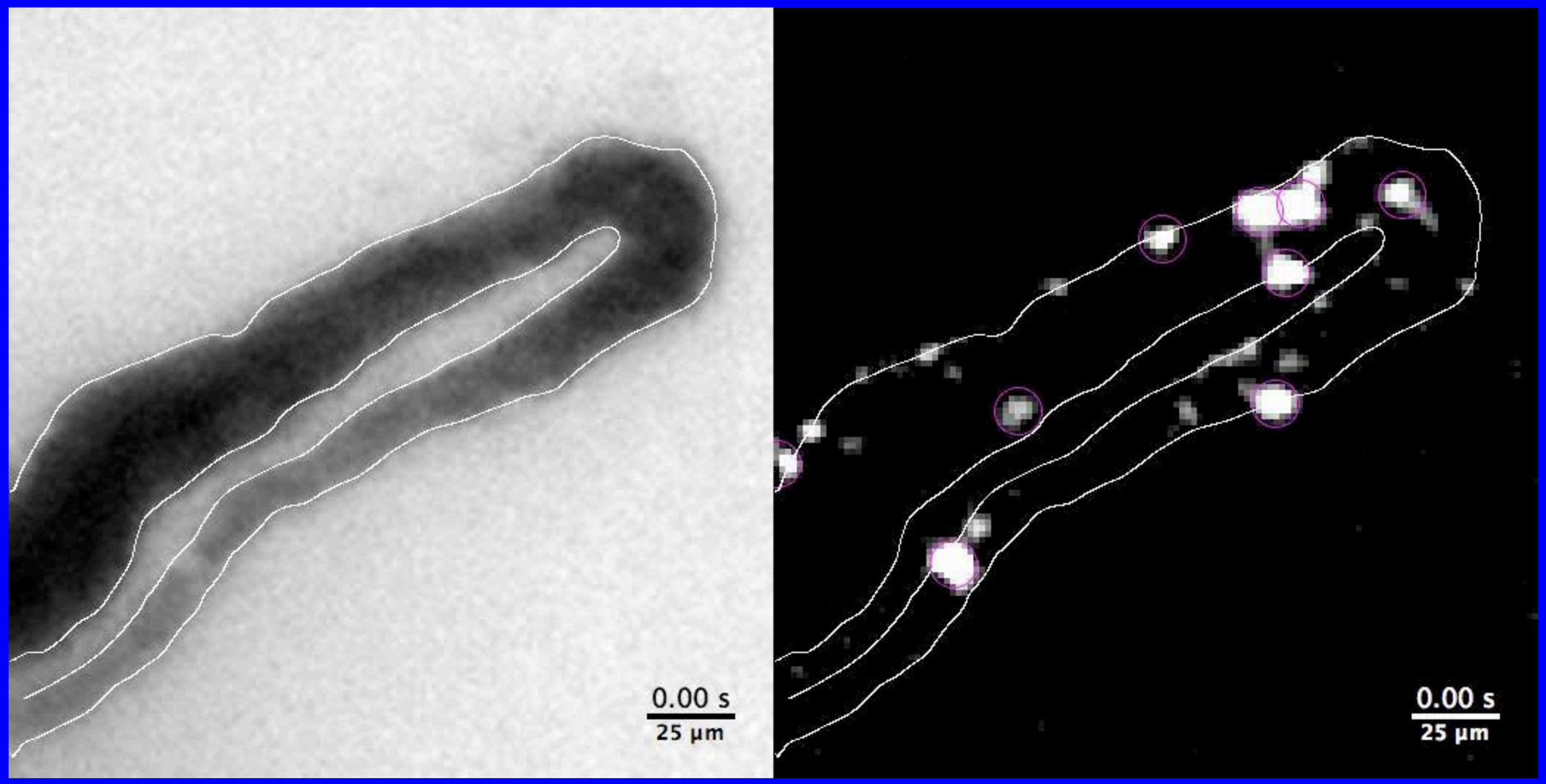


B

Single Capillary with Low Blood Flow Velocity

Row images

Processed images

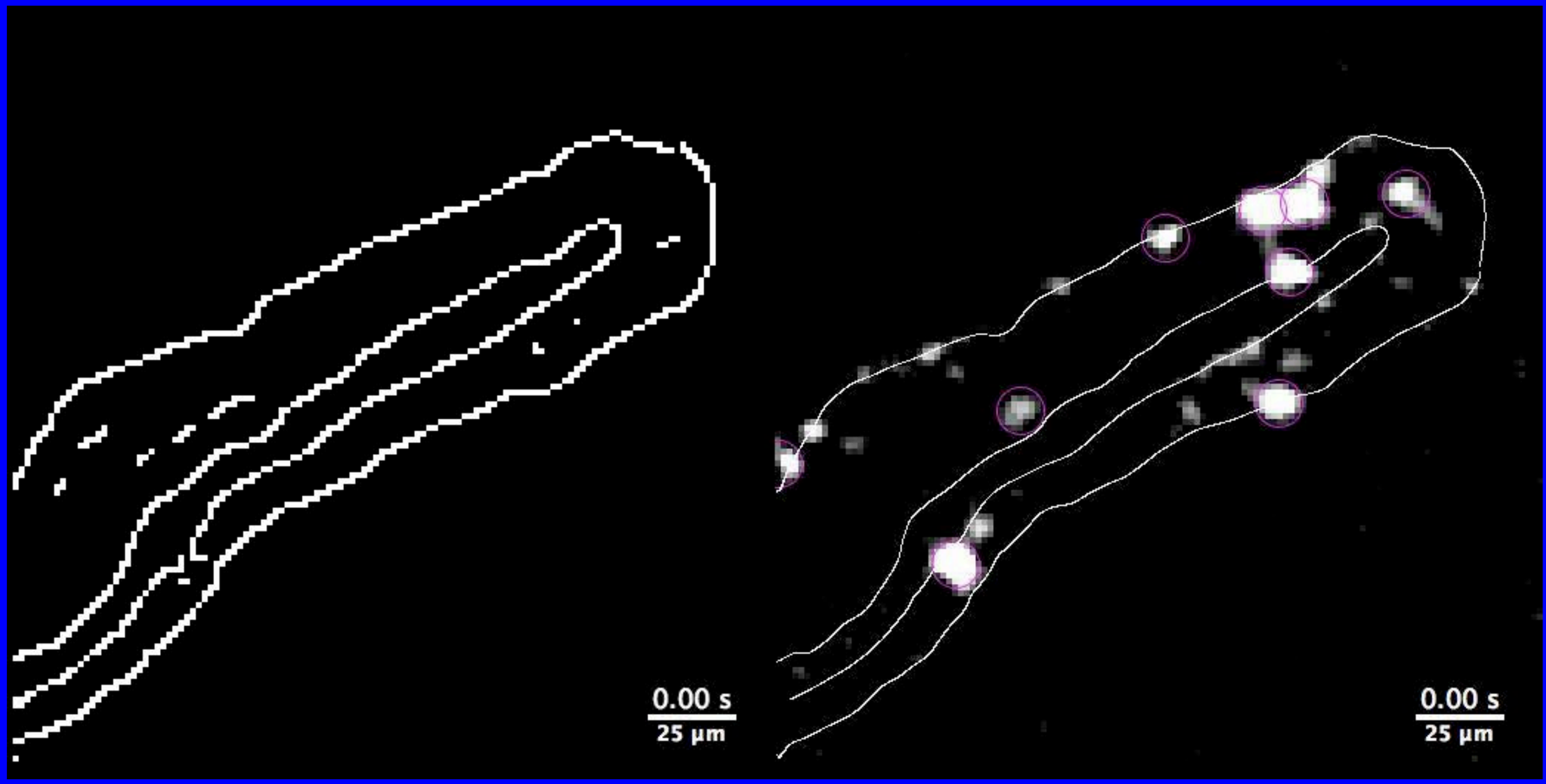


Dark color cells - RBCs
White color cells - WBCs

Interaction of WBCs with Endothelial Glycocalyx

Edge Detection

Video capillaroscopy
(processed)



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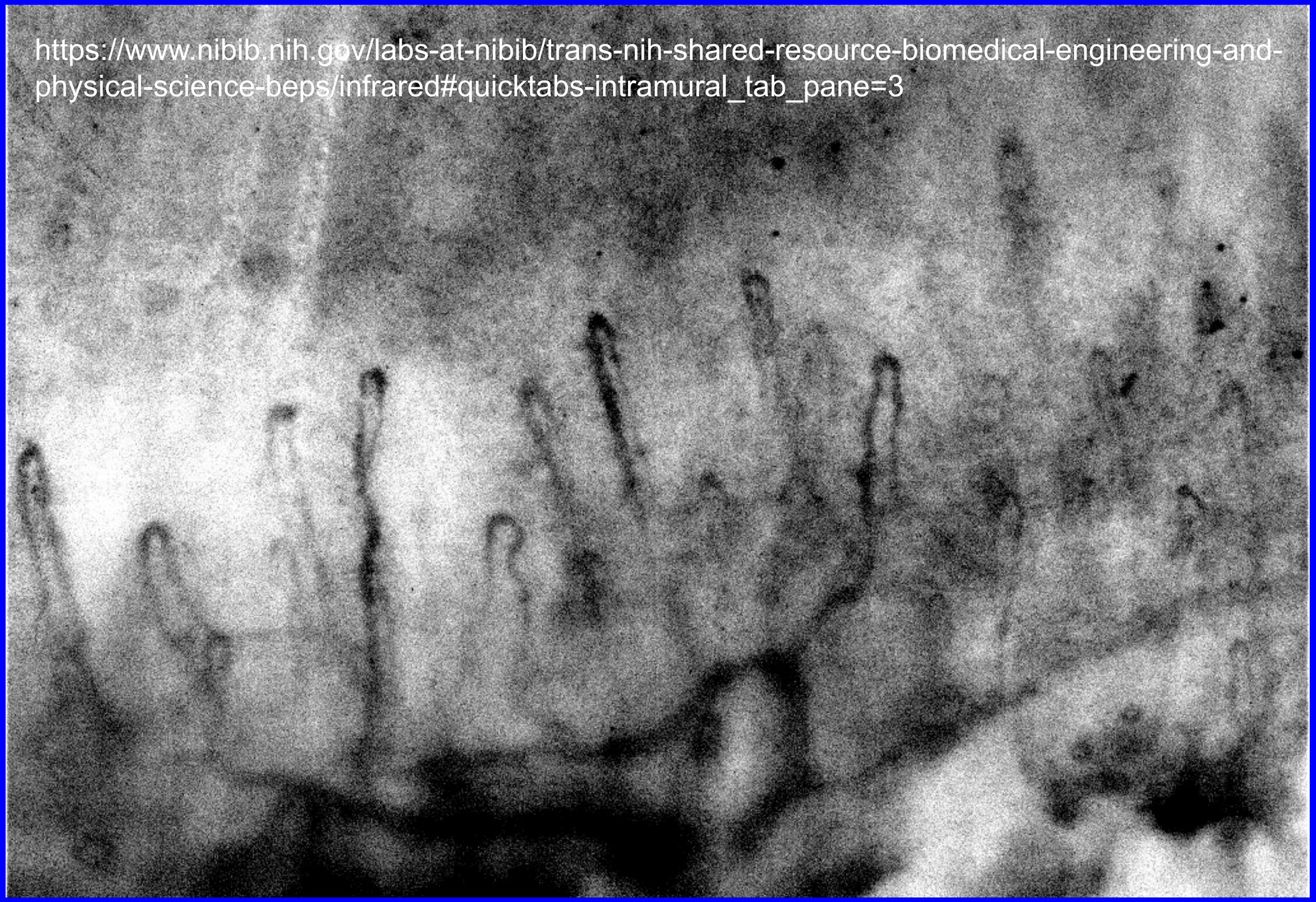

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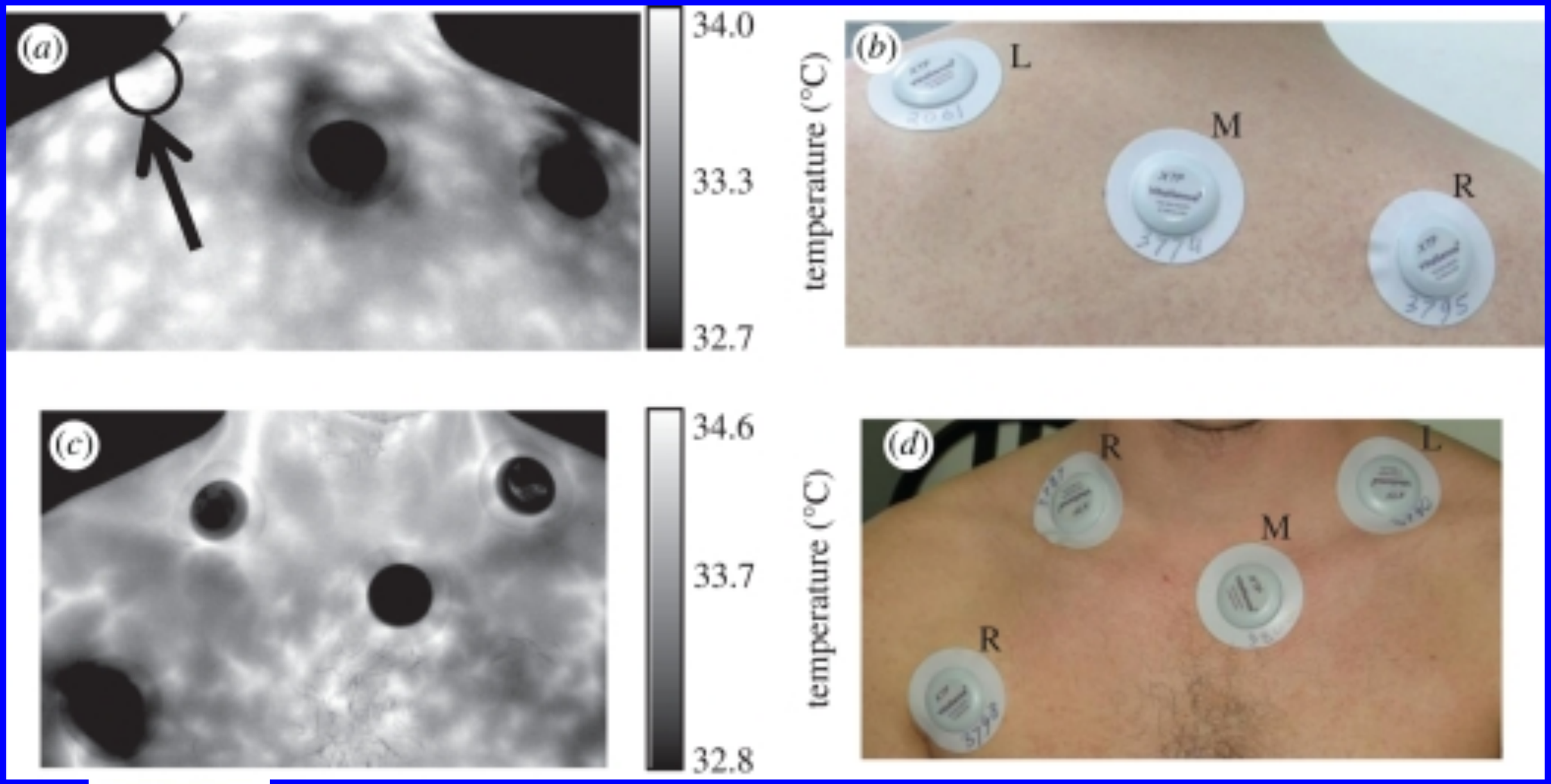
Skin Surface Temperature Rhythms as Potential Circadian Biomarkers for Personalized Chronotherapeutics in Cancer Patients



Scully C., Karaboué A., Liu W.M., Meyer J., Innominato P., Chon K., Gorbach A.M., Lévi F. Interface Focus 1:48-60, 2011

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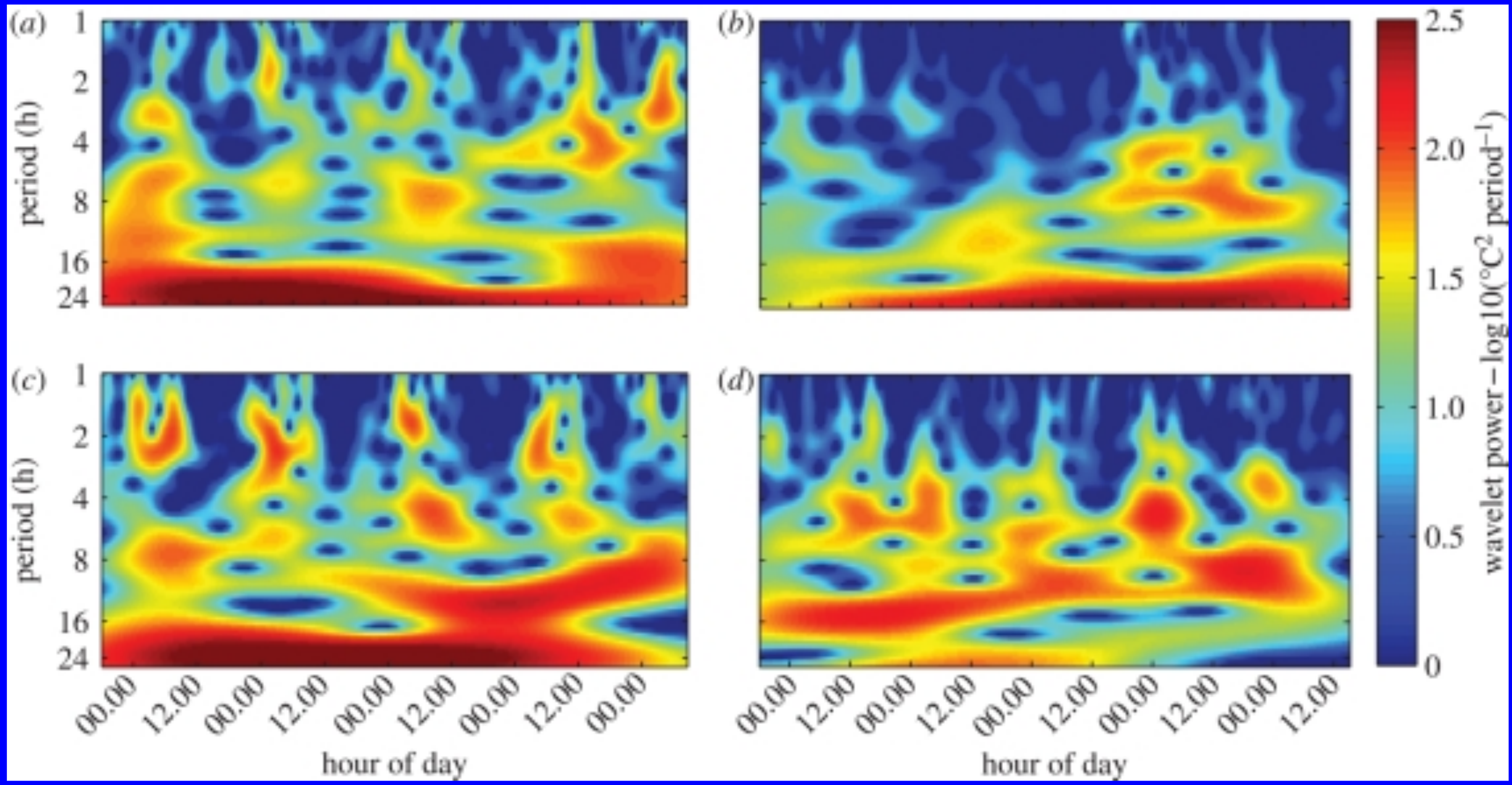

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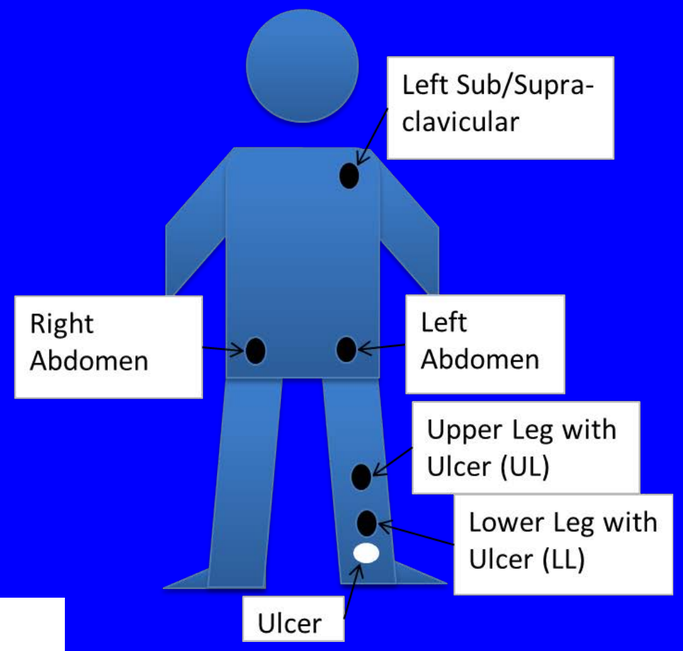
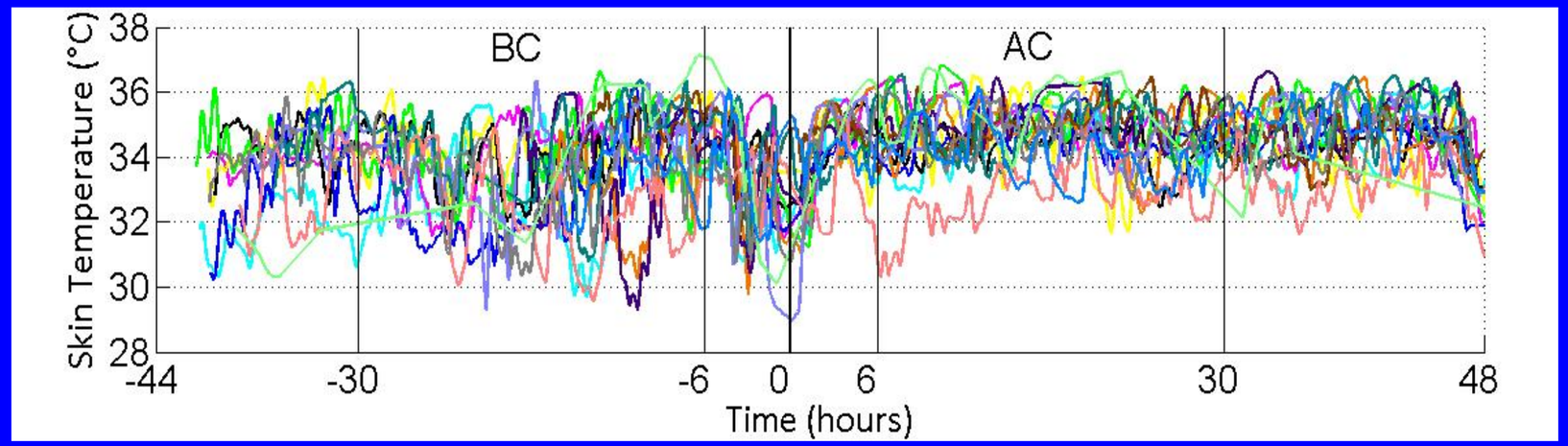
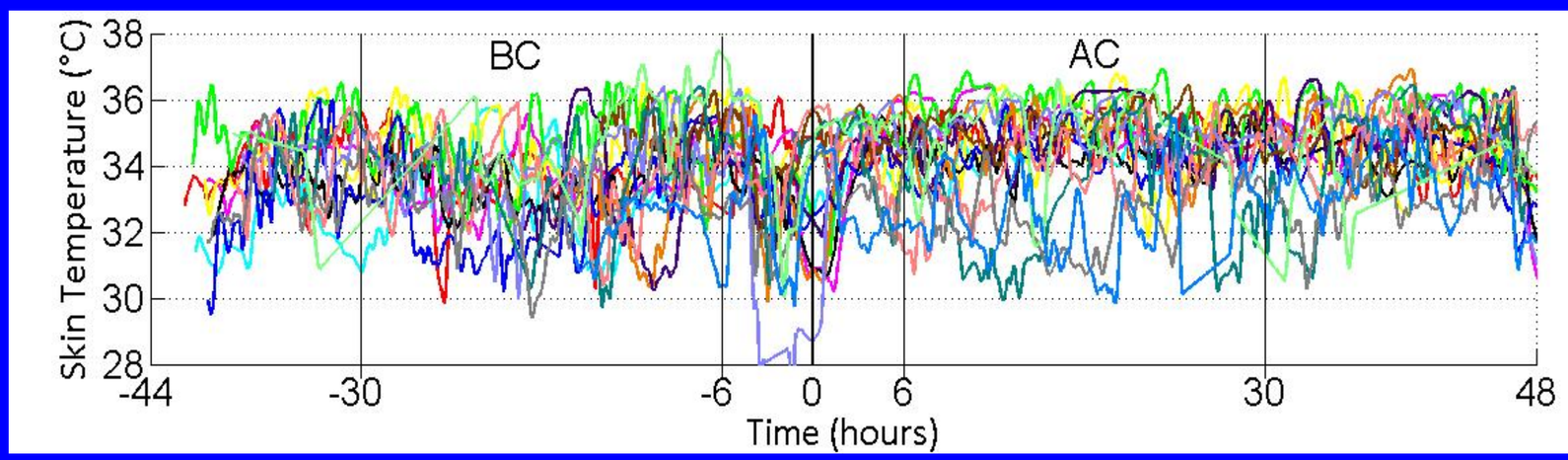
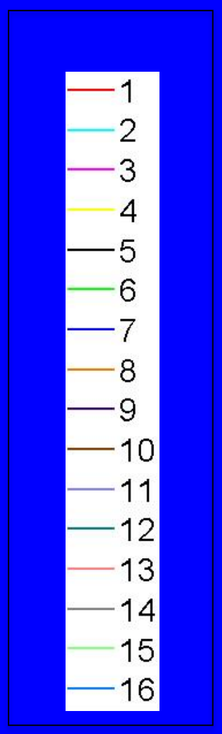
Continuous Monitoring of Skin Temperature in Patients with Sickle Cell Diseases



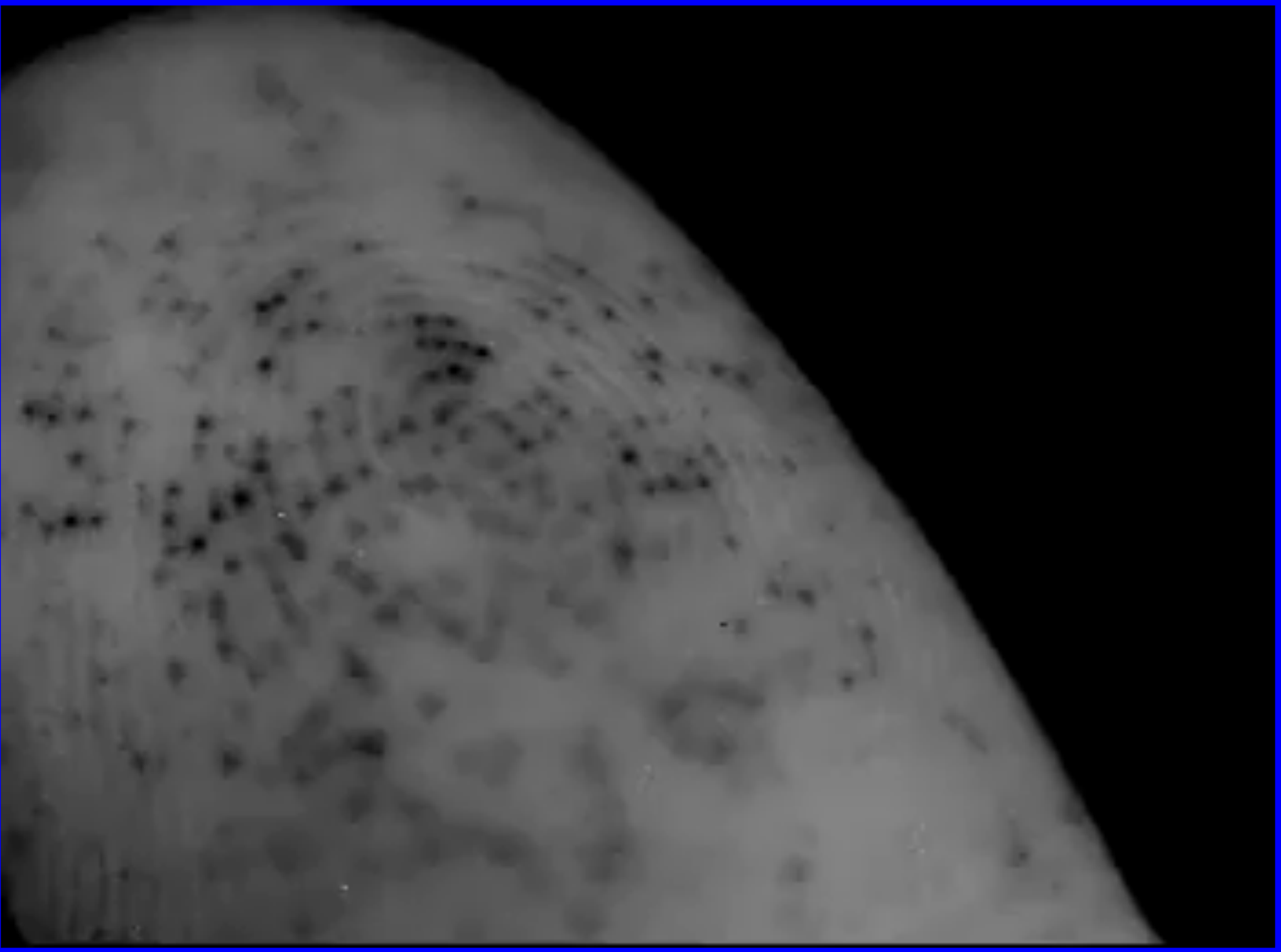






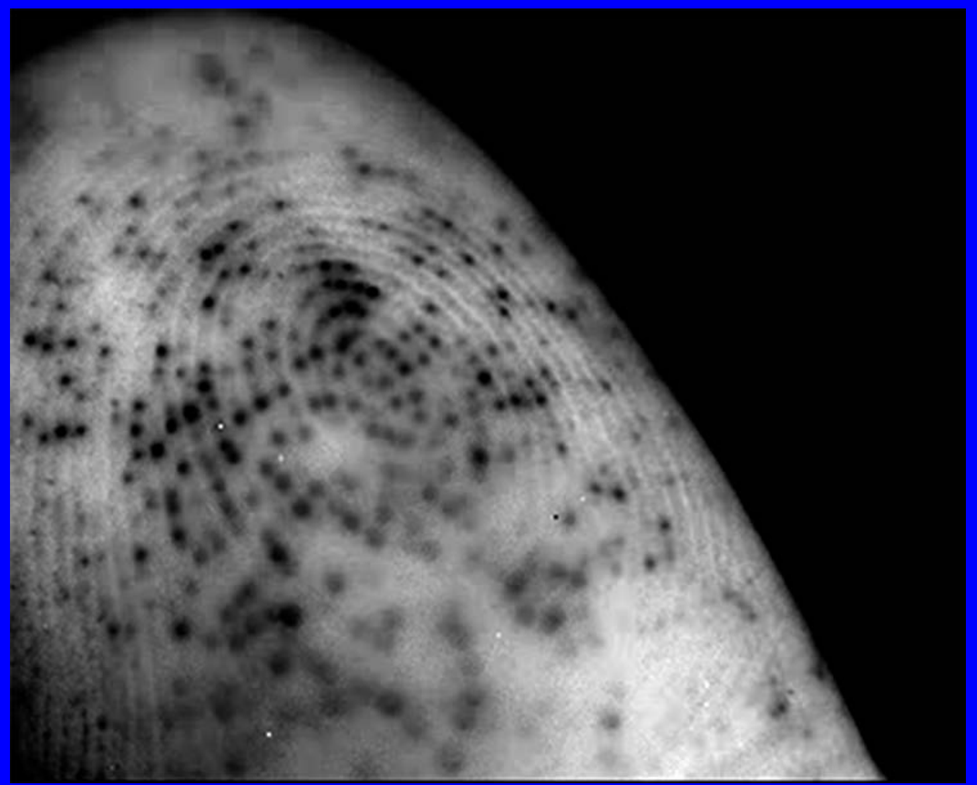
Unpublished, A. Gorbach Lab., NIH

Real-Time Assessment of Sweat Gland Function Using Infrared Imaging



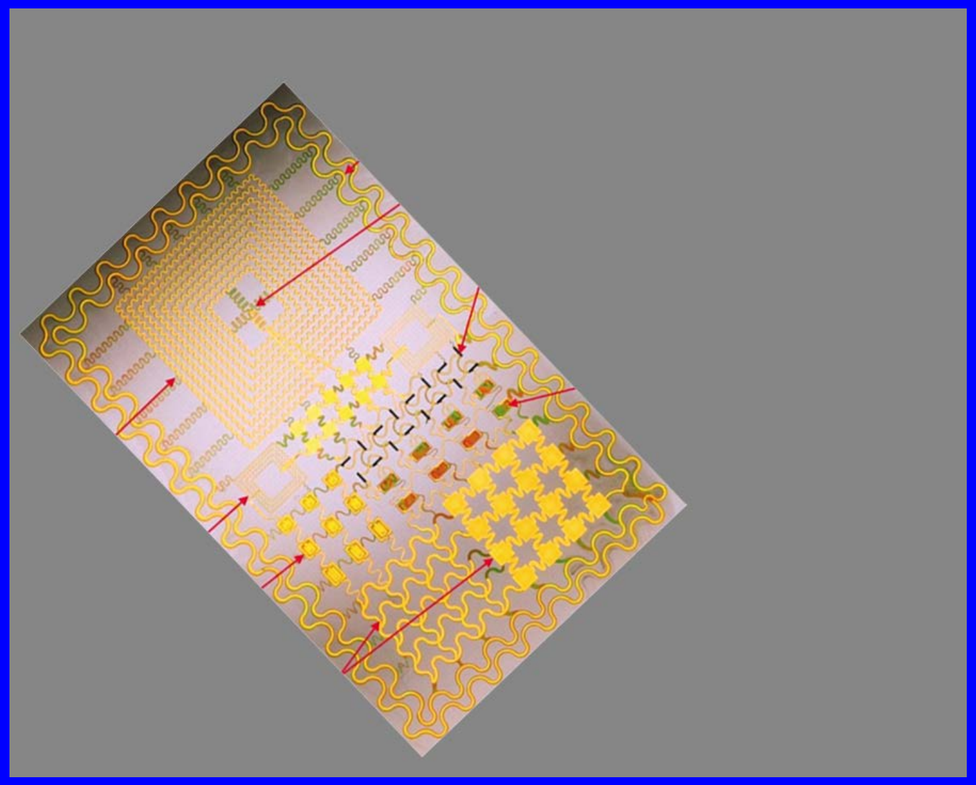
A. Gorbach Lab., NIH

NIH

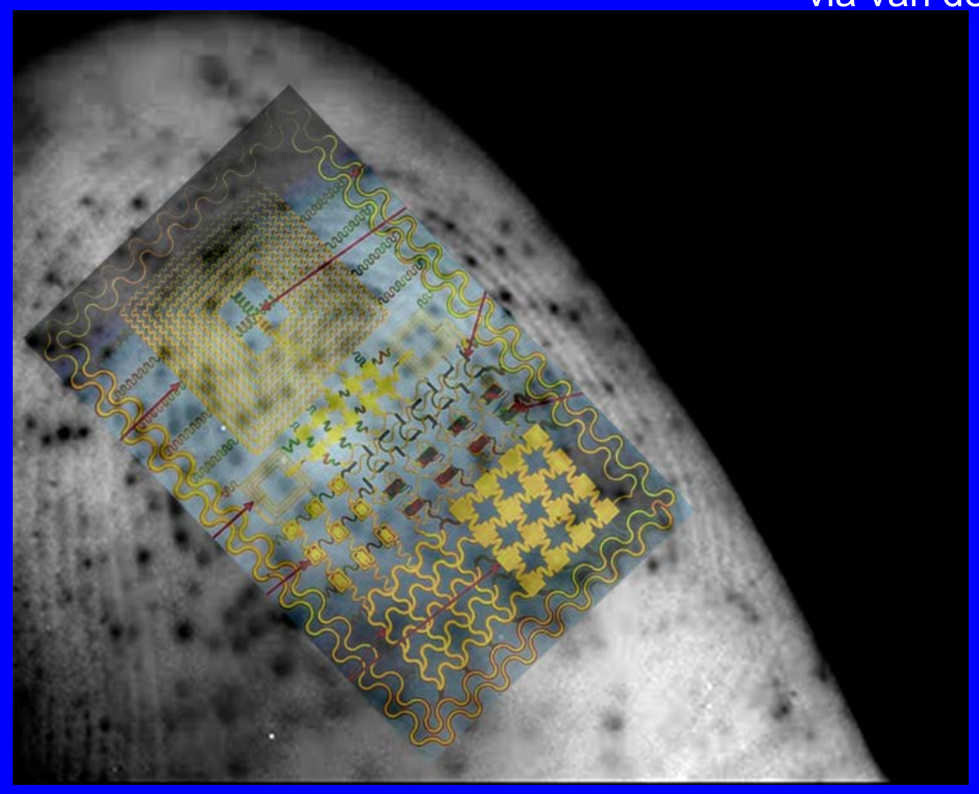


Infrared image of human finger, baseline condition

Illinois at Urbana-Champaign

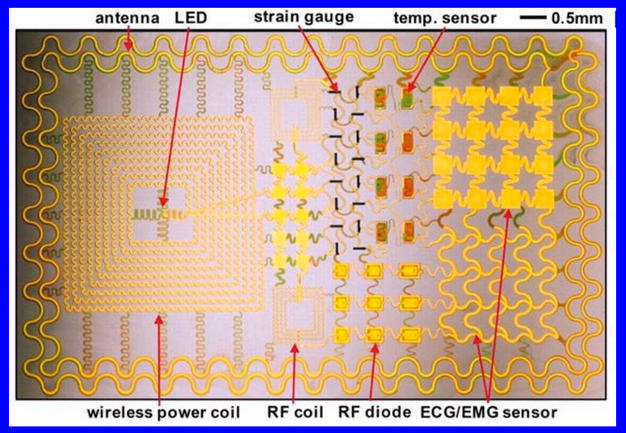


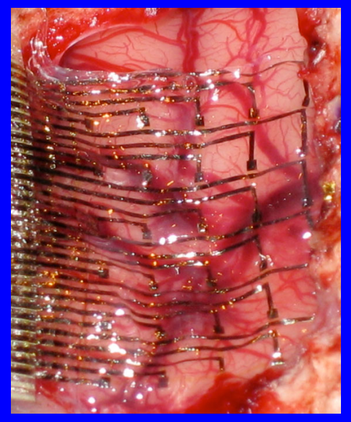
5 μ thick multifunctional electronics attachable to the skin via van der Waals forces

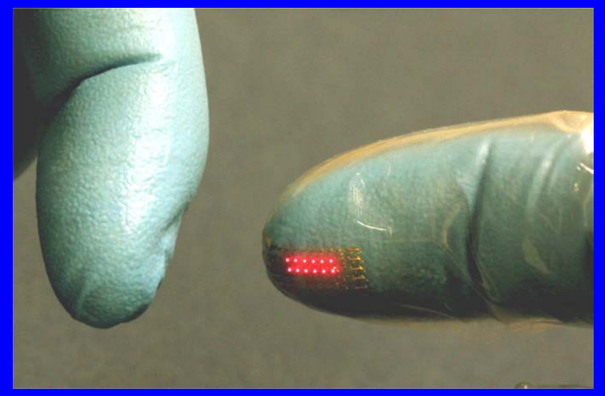


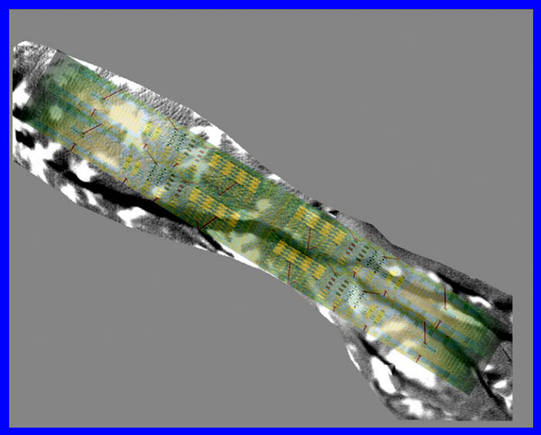
A. Gorbach Lab., NIH

Continuous Monitoring of Vascular Status: Concepts







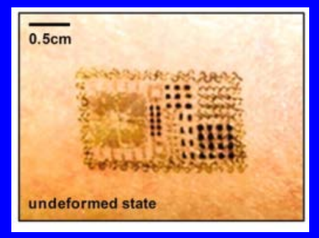


Webb R., Bonifas A., Behnaz A., Zhang Y., Yu K., Cheng H., Shi M., Bian Z., Liu Z., Kim Y., Yeo H., Park J., Song J., Li Y., Huang Y., Gorbach A.M., Rogers J. Ultrathin Conformal Devices for Precise and Continuous Thermal Characterization of Human Skin. Nature Materials 12(10):938-944, 2013

Webb R, Ma Y, Krishnan S, Li Y, Yoon S, Guo C, Feng X, Shi Y, Seidel M, Cho N, Kurniawan J, Ahad J, Sheth N, Kim J, Taylor VI J, Darlington T, Cheng K, Huang W, Ayers J, Gruebele A, Pielak R, Slepian M, Huang Y, Gorbach A.M., Rogers J. Epidermal Devices for Non-Invasive, Precise and Continuous Mapping of Macrovascular and Microvascular Blood Flow. Science Advances, Oct 30:e1-13, 2015

New Technologies for Predictive Medicine

Imaging Probes Patches Tattoos



Temperature Perfusion Colorimetry

- *Hbo_2, HHb, Hbo_2+HHb*
- *Sto_2, SaO_2, SvO_2*
- *Microcirculation*
- *Vasomotion*
- *Temperature*