VENDYS®

White Paper

ENDOTHELIX

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Digital (Fingertip) Thermal Monitoring of Vascular Function Improves Traditional Cardiovascular Risk Assessment and Monitoring of Response to Treatments

A Summary Report by the Endothelix Scientific Advisory Board

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Summary:

Even though the majority of deaths and disabilities resulting from cardiovascular disease (CVD) can be prevented, CVD continues to be the most burdensome health issue in the developed countries (approximately 1 million deaths and 300 billion dollars per year in the US alone) and is rapidly increasing in the developing nations. This major public health problem may be largely attributed to the hidden (asymptomatic) nature of CVD, remaining undetected until too late (heart attack and stroke). Therefore, early detection by risk assessment of the asymptomatic at-risk population plays a key role in reducing the societal burden of CVD. Traditional risk assessment strategies have proven insufficient; CVD has remained the leading cause of death for decades. Current methods which rely on measuring risk factors of CVD cannot directly assess the status of an individual's cardiovascular health and perform poorly in the identification of high risk asymptomatic individuals. In addition, accurate monitoring of the response to therapy is essential for successful secondary prevention in patients with known CVD. Vascular function evaluation can improve risk assessment and monitoring of therapy, but current methods of assessing vascular function are suboptimal or limited to research laboratories.

In this document, we provide the scientific validation of Digital Thermal Monitoring (DTM) of vascular reactivity, a new technique for vascular function evaluation in clinical settings, that is applicable both in the primary and secondary prevention arenas.

DTM is a noninvasive and inexpensive vascular function test that is simple and operator-independent. As shown in Figure 1, it is much like a blood pressure device with temperature probes. The probes measure fingertip temperature changes during a brief (2-5 minute) arm-cuff occlusion and release procedure (reactive hyperemia) which is a standard technique for assessment of vascular reactivity. Fingertip temperature drops during the cuff occlusion and rebounds after releasing the cuff. The higher the temperature rebound, the better the vascular reactivity.

In our studies in the past three years, we have found DTM indices of vascular reactivity to correlate strongly with the:

- **burden of cardiovascular risk factors, measured by Framingham Risk Score. (Fig.2)**
- **burden of subclinical coronary atherosclerosis, measured by coronary calcium score. (Fig.3)**
- **extent of myocardial perfusion defects, measured by nuclear stress test. (Fig.4)**

- **degree of coronary stenosis, measured by coronary CT angiography. (Fig.5)**

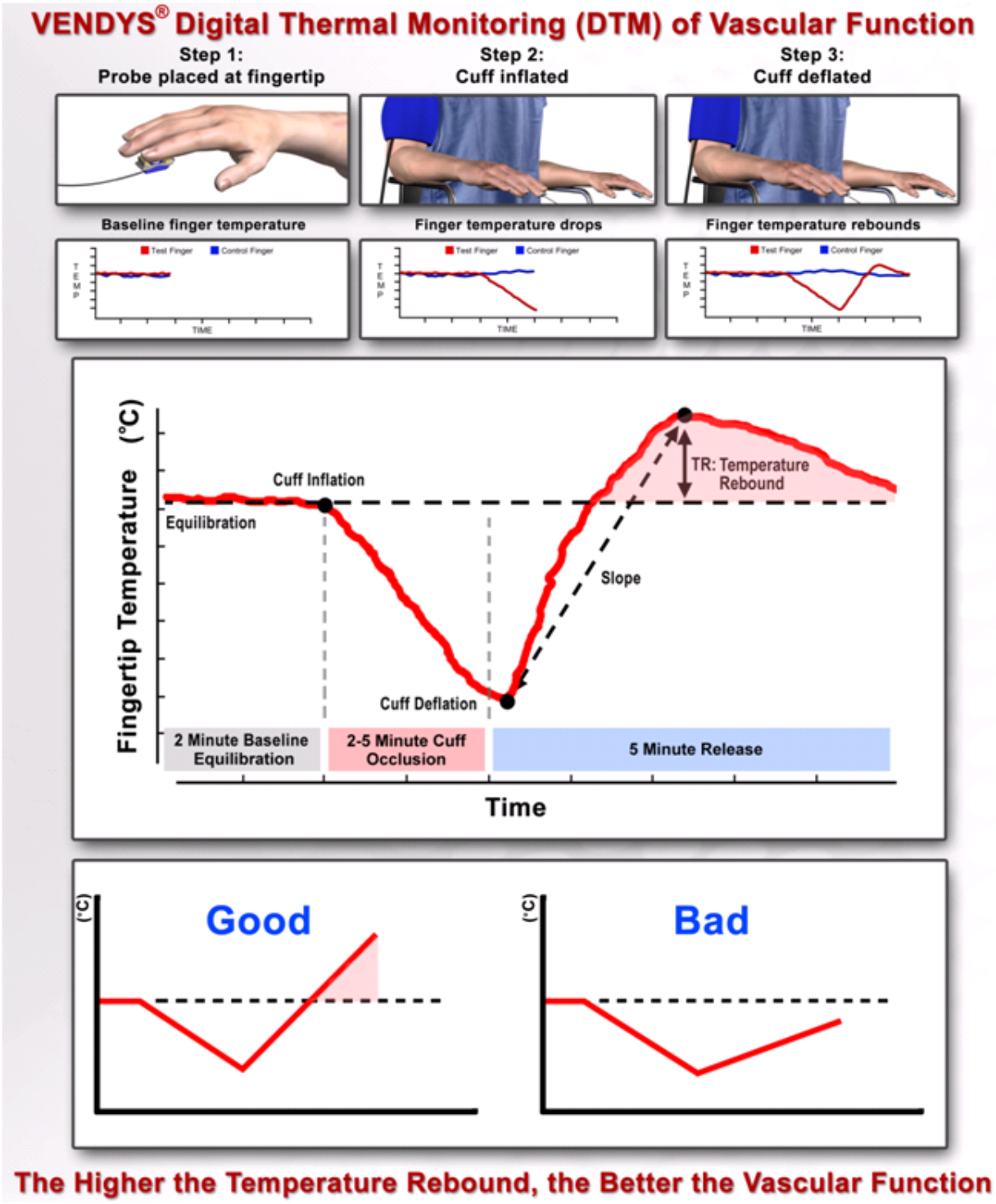
Moreover, DTM provides incremental predictive value over risk factor assessment (measured by Framingham risk score) for identification of high risk patients with:

- **subclinical atherosclerosis (Coronary Artery Calcium Score >=100). (Fig.6)**
- **coronary artery stenosis (CT angiography showing >=50% stenosis). (Fig.7)**

Finally, DTM indices of vascular function have shown comparable reproducibility to those of blood pressure measurements. **(Fig. 8)**

These findings are promising and require corroboration by other cardiovascular researchers, particularly in long-term, prospective studies and clinical trials. It is important to emphasize that DTM is not intended to replace measurement of risk factors or advanced imaging tests. Rather, it is an inexpensive, non-invasive, and easy to use vascular function test that can complement both risk factors and structural imaging modalities.

Figure 1.


VENDYS® Digital Thermal Monitoring (DTM) of Vascular Function
Step 1:
Probe placed at fingertip
Step 2:
Cuff inflated
Step 3:
Cuff deflated
Baseline finger temperature
Finger temperature drops
Finger temperature rebounds
Test Finger
Control Finger
TEMP
TIME
Fingertip Temperature (°C)
Cuff Inflation
Equilibration
TR: Temperature Rebound
Slope
Cuff Deflation
2 Minute Baseline Equilibration
2-5 Minute Cuff Occlusion
5 Minute Release
Time
(°C)
Good
Bad
The Higher the Temperature Rebound, the Better the Vascular Function

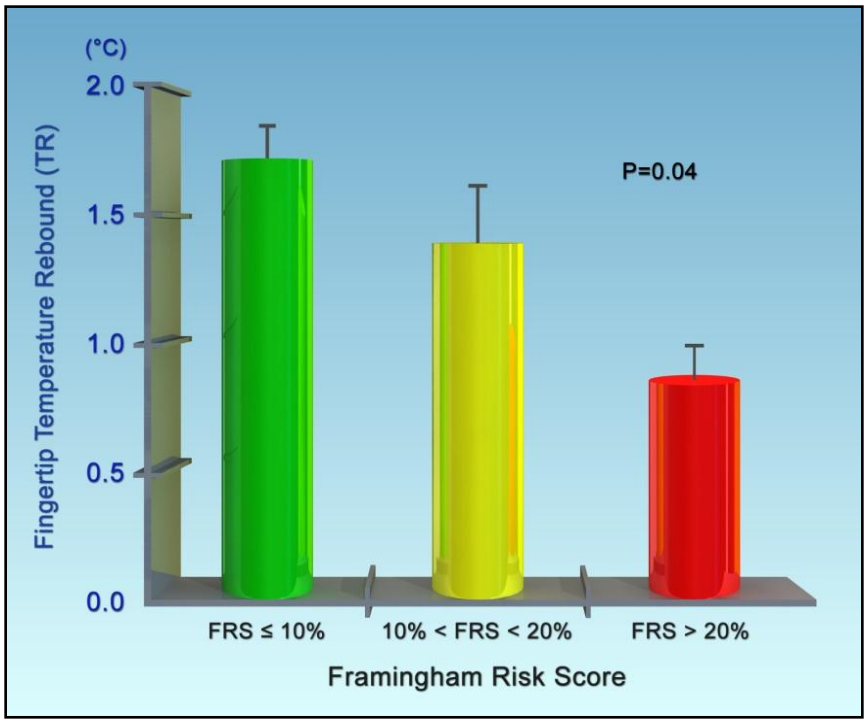


Figure 2. Lower fingertip temperature rebound (TR) is associated with higher burden of cardiovascular risk factors measured by Framingham risk score (FRS).

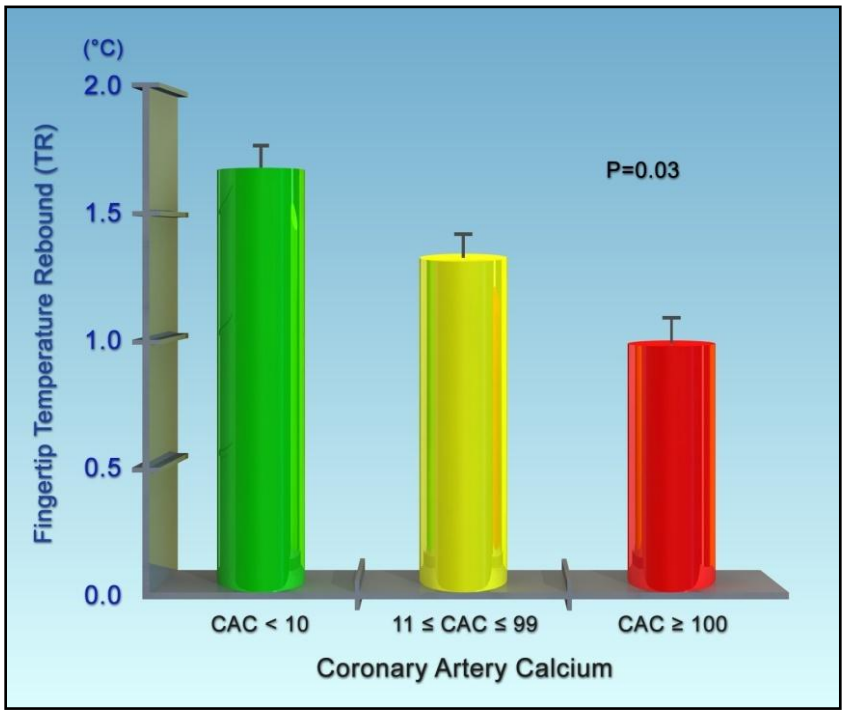


Figure 3. Lower fingertip temperature rebound (TR) is associated with higher burden of atherosclerotic plaques measured by coronary artery calcium (CAC) score.

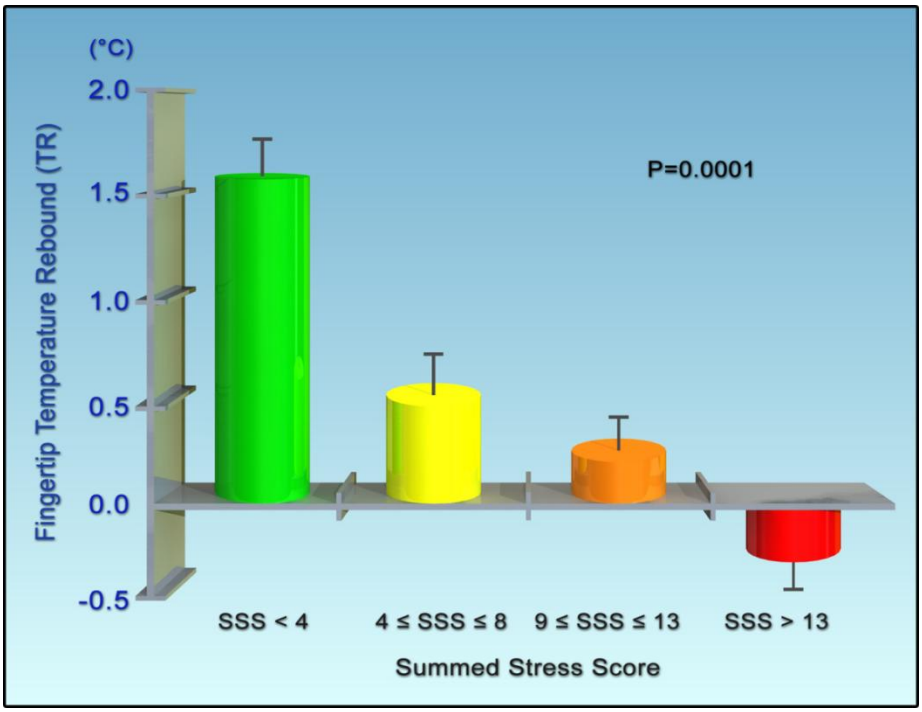


Figure 4. Lower fingertip temperature rebound (TR) is associated with higher extent of myocardial perfusion defect (SSS>=4) measured by nuclear myocardial SPECT imaging.

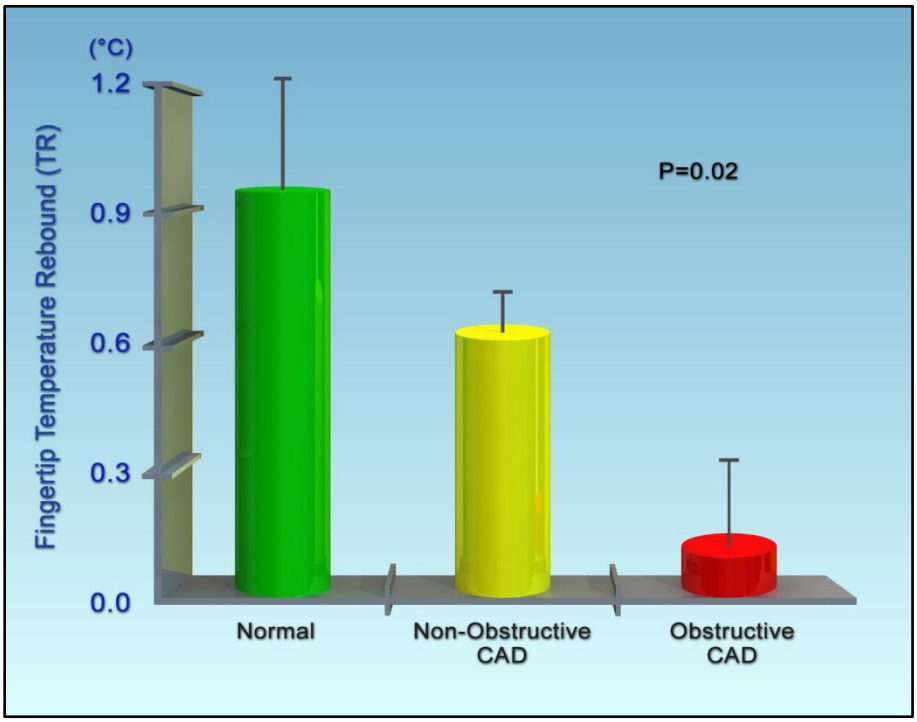
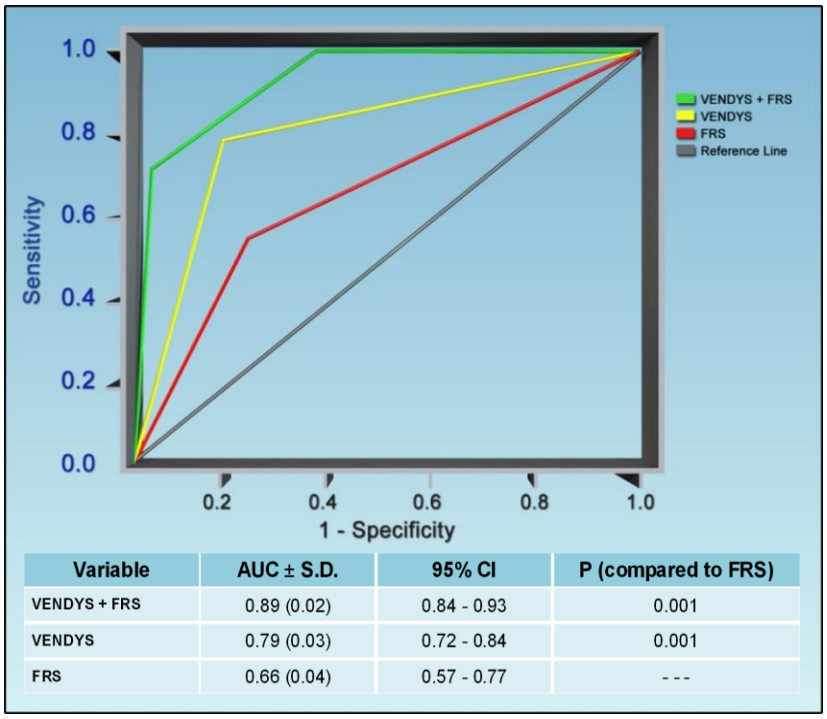
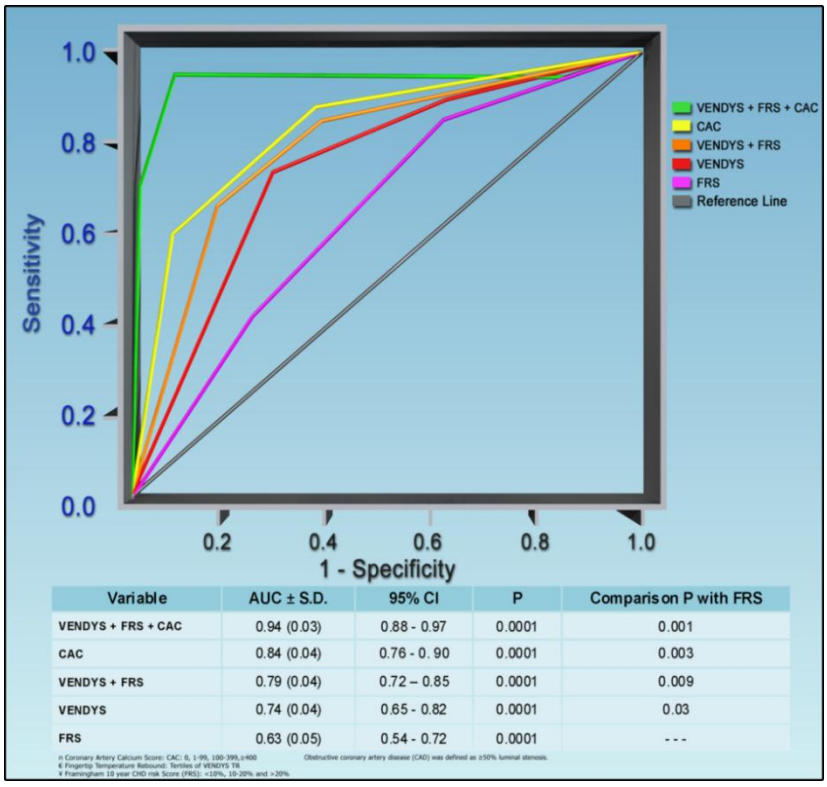


Figure 5. In patients with chest discomfort, low fingertip temperature rebound (TR) is associated with coronary artery disease diagnosed by CT angiography.



Variable	AUC ± S.D.	95% CI	P (compared to FRS)
VENDYS + FRS	0.89 (0.02)	0.84 - 0.93	0.001
VENDYS	0.79 (0.03)	0.72 - 0.84	0.001
FRS	0.66 (0.04)	0.57 - 0.77	- - -

Figure 6. The combination of low fingertip temperature rebound (TR) and high Framingham risk score (FRS) provides larger area under the ROC curve compared to either TR or FRS alone.



Variable	AUC ± S.D.	95% CI	P	Comparison P with FRS
VENDYS + FRS + CAC	0.94 (0.03)	0.88 - 0.97	0.0001	0.001
CAC	0.84 (0.04)	0.76 - 0. 90	0.0001	0.003
VENDYS + FRS	0.79 (0.04)	0.72 – 0.85	0.0001	0.009
VENDYS	0.74 (0.04)	0.65 - 0.82	0.0001	0.03
FRS	0.63 (0.05)	0.54 - 0.72	0.0001	- - -

Figure 7. In patients with chest discomfort, the combination of fingertip temperature rebound (TR) and Framingham risk score (FRS) provide larger area under the ROC curve for prediction of obstructive coronary artery disease (CAD), compared to TR or FRS alone. The addition of CAC scoring further increases the area under the curve.

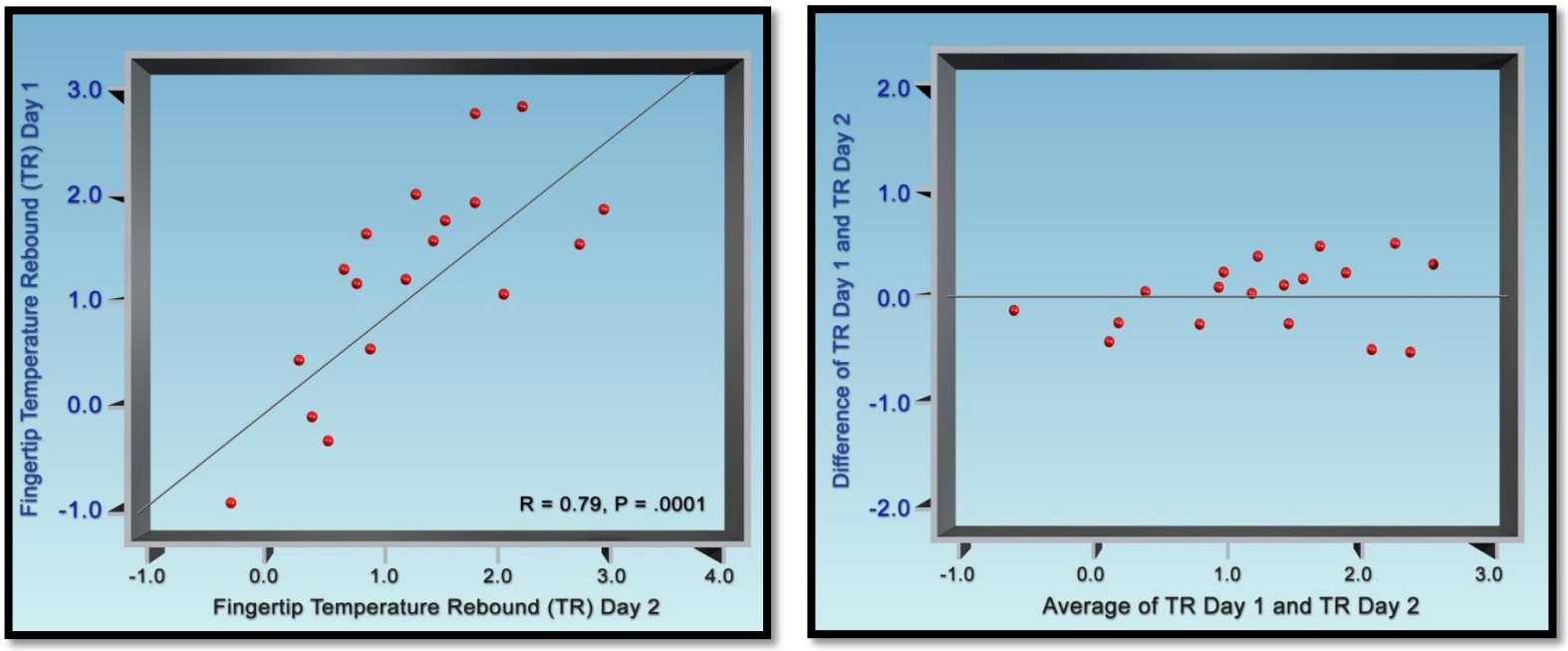


Figure 8. DTM indices of vascular function have shown comparable reproducibility to those of blood pressure measurements.

Variable	D	SD_D	CV (%)	CR (%)	ICC	P value
Heart Rate	0.47	0.054	11.4	10.6	0.7	0.01
Mean Arterial Pressure	0.44	0.038	8.7	7.5	0.79	0.0005
Start Temperature	0.51	0.036	7.1	7.1	0.81	0.0001
DTM (VENDYS®) Indices of Vascular Function						
TR (°C)	0.209	0.012	5.7	2.4	0.82	0.0001
AUC	0.292	0.014	4.8	2.8	0.83	0.0001

D: mean absolute difference; SD_D: SD of mean differences; CV: coefficient of variability [(SD_D /D)*100]; CR: coefficient of repeatability [(SD_D *1.96)*100)]; ICC: Intra-class Correlation Coefficient.

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