

From Bench to Bedside: Accelerating Drug and Device Development with Vascular Phenotyping

Executive Summary

Vascular phenotyping, particularly through advanced techniques such as pulse wave velocity (PWV) and pulse wave analysis (PWA), is revolutionizing the pharmaceutical and medical device industries. By providing precise measurements of arterial stiffness and cardiovascular function, these methodologies offer critical insights for disease diagnosis, management, and therapeutic interventions. They allow for the capture of vascular biomarkers, crucial in the development, testing, and regulatory processes of new medical treatments and devices.

For pharmaceutical companies, vascular biomarkers enhance drug development efficiency by providing quantifiable data that predicts treatment efficacy and patient responses. This capability allows for the early fine-tuning of dosages and formulations, reducing both the duration and cost of clinical trials. It also helps in pinpointing the optimal patient demographics for specific treatments, thereby boosting drug efficacy and safety upon market entry.

In medical device development, integrating vascular biomarkers enables the creation of advanced devices that deliver real-time vascular health feedback. This supports the development of personalized therapeutic devices that adapt treatments based on ongoing vascular assessments, improving patient management and outcomes.

Adopting vascular phenotyping not only provides companies with a competitive advantage but also aligns with the shift towards precision medicine—tailoring treatments to individual patient characteristics, thus enhancing health outcomes. This strategic integration is cutting operational costs, boosting the efficacy of drugs and devices, and increasing success rates in managing cardiovascular and related conditions.

“Medicine is not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided.”

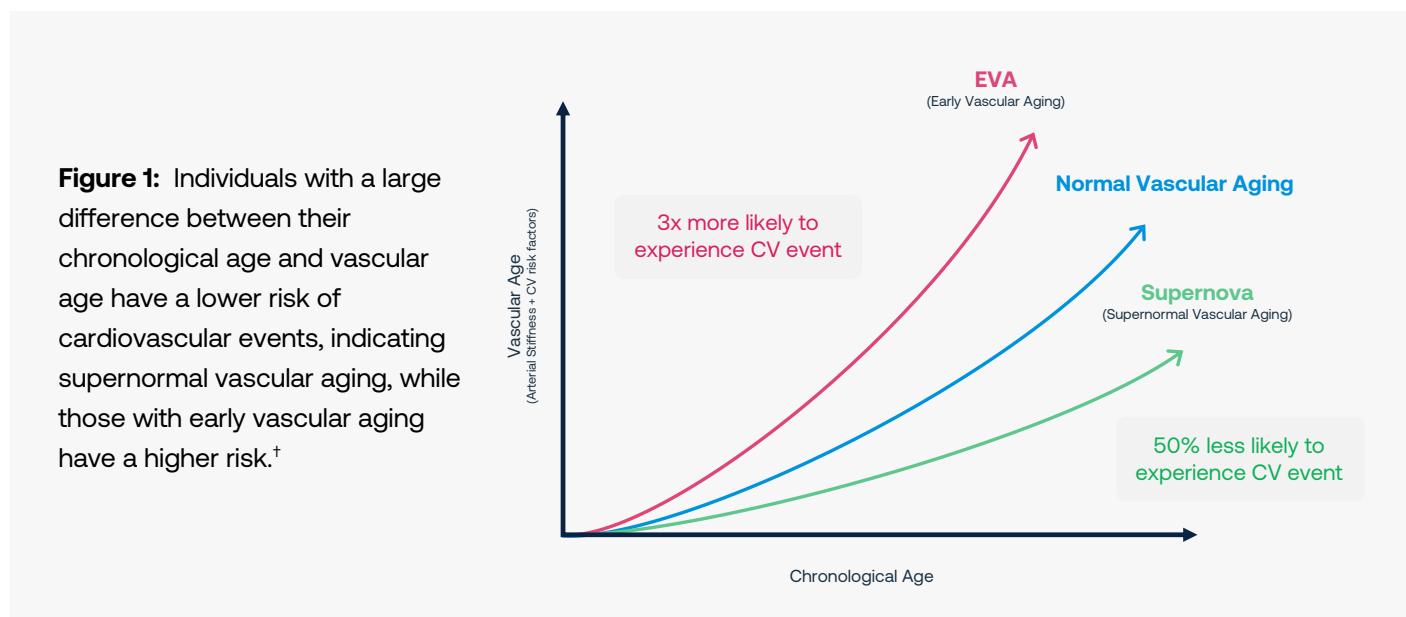
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Pioneer of Toxicology and Renaissance Medicine

Introduction:

In the rapidly advancing field of medical innovation, understanding and quantifying vascular health is increasingly critical. A key focus within this realm is the concept of early vascular aging (EVA), a condition where vascular structures deteriorate at a quicker rate than normal due to various risk factors. Vascular phenotyping, particularly through techniques such as pulse wave velocity (PWV) and pulse wave analysis (PWA), is pivotal in detecting, accurately measuring, and addressing EVA. These methodologies are revolutionizing how the pharmaceutical and medical device industries approach the diagnosis, treatment, and management of cardiovascular diseases.

Arterial stiffness and cardiovascular function are paramount in assessing overall vascular health, with EVA serving as an important indicator of cardiovascular risk earlier in life. Traditional methods including biometrics (i.e., blood pressure, heart rate, and BMI) and metabolic parameters (i.e., lipid levels and fasting glucose) often lack precision and predictability required to effectively gauge EVA, but vascular phenotyping offers a new level of accuracy. This approach not only enhances clinical accuracy but also improves patient outcomes through personalized treatment strategies. It provides invaluable insights that are essential for therapeutic interventions tailored to the unique vascular profiles of patients.

Vascular phenotyping is poised to revolutionize the pharmaceutical and medical device sectors. Capturing vascular biomarkers through advanced techniques like PWV and PWA provides robust, quantifiable data that streamline the development processes of drugs and devices, reduce costs, and expedite regulatory approvals. The integration of these biomarkers, particularly those indicative of EVA, not only boosts efficiency but also aligns with the growing trend toward precision medicine, where treatments are increasingly tailored to the specific risk and needs of individual patients.



[†] Bruno RM, Nilsson PM, Engström G, et al. Early and Supernormal Vascular Aging: Clinical Characteristics and Association With Incident Cardiovascular Events. *Hypertension*. 2020;76(5):1616-1624. doi:10.1161/HYPERTENSIONAHA.120.14971

Understanding Vascular Biomarkers

Vascular biomarkers present a valuable avenue for understanding cardiovascular health. Determined non-invasively through pulse wave analysis using blood pressure cuffs and wearable sensors, the technique captures the physiologic properties of arterial stiffness by assessing the speed and contour of the pulse wave as it travels through the arteries. This analysis extracts vascular biomarkers representing the stiffness of blood vessels, reflecting their ability to expand and contract in response to changes in blood flow.

Vascular health has wide-reaching implications across various medical fields. It plays a crucial role in managing diseases like ischemic heart disease, heart failure, diabetes and chronic kidney disease, as changes in blood flow can accelerate disease progression and complications. Furthermore, it also affects neurological conditions, such as cognitive decline and dementia, where adequate cerebral blood flow is essential. In the field of oncology, vascular health is particularly vital as the growth and spread of tumors are intimately tied to blood vessel development and functionality.

Across these diverse fields, the strategic application of vascular biomarkers not only enhances therapeutic precision but also supports the broader trend towards personalized medicine. Treatments can be tailored based on comprehensive health profiles, significantly improving patient care. This approach accelerates the development of new therapies, reduces healthcare costs, and improves treatment outcomes across a wide range of medical disciplines, illustrating the extensive impact of vascular health beyond traditional cardiovascular applications.

Table 1: CARDEIX vascular biomarkers representing arterial health

	Heart Rate (HR)	A beat-to-beat heart rate measurement on par with standard ECG-based methods. A consistently high resting heart rate may be a sign of coronary heart disease.
	Brachial Blood Pressure	The pressure of blood at the brachial artery in the upper arm. High brachial blood pressure is a major risk factor for heart disease and stroke.
	Central Blood Pressure (SP & DP)	The pressure of blood at the root of the aorta in the heart. cBP is a more accurate predictor of subclinical cardiovascular disease than traditional brachial blood pressure alone.
	Central Pulse Pressure (PP)	The pressure which key organs like the heart, brain, and kidneys experience. It is used to identify the risk of end organ damage to major organs.
	Augmentation Pressure (AP)	A marker indicating how stiff one's artery is. Elevated augmentation pressure is associated with cardiovascular risk factors.
	Augmentation Index (AIx)	Another marker indicating how stiff one's artery is. It reflects the burden stiff arteries place on the heart.
	Subendocardial Viability Ratio (SEVR)	The supply of blood that flows to your inner heart muscle in relation to demand. It offers insight into how well a person's heart can handle the stress of exercise.
	Pulse Pressure Amplification (PPA)	The increase in amplitude of arterial pulse waves as they travel from central to peripheral arteries and provides insights into arterial stiffness, wave reflection, as well as the efficiency of blood flow distribution.
	Pulse Wave Velocity (PWV)	The speed at which the arterial pulse travels through the circulatory system, a key indicator of arterial stiffness.

Applications in Drug and Device Development

The applications of vascular biomarkers and vascular phenotyping span across various medical disciplines, offering invaluable insights and facilitating advancements in therapeutic interventions and medical device design. In drug development, vascular biomarkers are instrumental in assessing vascular function and evaluating the efficacy of novel therapeutics. Specifically, these tools enable researchers to accurately measure arterial stiffness, pulse wave characteristics, and overall vascular health. This precise evaluation facilitates the identification of potential drug candidates with improved therapeutic and safety profiles, and fewer adverse effects, ultimately enhancing patient outcomes.

Similarly, in medical device development, vascular biomarkers and phenotyping techniques are indispensable across various specialties. By incorporating vascular health assessments into device testing protocols, manufacturers can refine design features and optimize device performance to ensure optimal functionality and favorable patient outcomes. This comprehensive evaluation process not only enhances the effectiveness of medical devices but also contributes to an enhanced quality of life for patients by addressing health with greater precision and efficacy.

Furthermore, the advent of vascular phenotyping heralds a new era of personalized medicine approaches, revolutionizing drug development strategies. By integrating vascular biomarkers into clinical trials, pharmaceutical companies can tailor treatments to align with individual patient vascular profiles, thereby enhancing treatment efficacy and safety across a spectrum of medical conditions. This personalized approach not only marks a significant leap forward in patient care but also underscores the transformative potential of vascular phenotyping in reshaping the landscape of drug development.

Moreover, vascular biomarkers play a crucial role in the selection of clinical trial participants and the identification of non-responders to new therapies. By leveraging vascular phenotyping techniques, researchers can identify individuals with specific vascular profiles that are most likely to benefit from novel therapies. This personalized approach to participant selection enhances the likelihood of successful trial outcomes by targeting patient populations with the highest probability of positive responses to treatment. Additionally, vascular biomarkers enable the early identification of non-responders to new therapies, allowing researchers to adapt trial protocols and allocate resources more efficiently.

Vascular biomarkers provide a transformative lens for medical science, allowing healthcare innovators to identify and address diseases at the earliest stages of vascular dysfunction. This precision enhances therapeutic approaches and drives the development of targeted treatments, ultimately improving patient care and outcomes.

Integrating Vascular Biomarkers into Clinical Trials

Integrating vascular biomarkers into clinical trials begins with the recruitment of appropriate subjects. By selecting subjects with distinct vascular profiles that reflect the intended study population, researchers can ensure that the trial outcomes are applicable to the intended patient demographic. Vascular health parameters, such as arterial stiffness, endothelial function, as well as other relevant vascular biomarkers can be utilized for screening and selection criteria. This targeted approach enhances the ability to assess the efficacy and safety of investigational therapies and enables researchers to identify patient subgroups that are most likely to benefit from treatment.

Throughout the duration of the trial, continuous monitoring for adverse events is paramount to ensure patient safety and maintain data integrity. Vascular biomarkers serve as valuable tools for early detection of potential adverse effects related to cardiovascular function or vascular health. Regular assessments of vascular biomarkers, integrated into the trial protocol, enable researchers to promptly identify any changes in vascular health and intervene as necessary. This proactive approach minimizes the risk of adverse events and optimizes patient care, thereby enhancing the overall safety profile of the investigational therapy.

In addition to monitoring for adverse events, the data generated from vascular biomarker assessments contribute to the regulatory approval process. Vascular biomarkers provide quantitative measures of treatment effects on vascular health, offering objective data that regulators can utilize to evaluate the safety and efficacy of investigational therapies. By including robust vascular biomarker data in regulatory submissions, researchers strengthen their case for approval and expedite the regulatory review process. The incorporation of vascular biomarkers in regulatory submissions enhances the credibility of the trial results and increases confidence in the therapeutic benefits of the investigational therapy, ultimately facilitating the pathway for bringing new treatments to market.



Conclusion

Vascular phenotyping, particularly through the use of vascular biomarkers captured via pulse wave velocity and pulse wave analysis, emerges as a powerful tool in the medical and pharmaceutical fields, significantly expediting the development and approval processes for drugs and medical devices. As pharmaceutical companies increasingly prioritize innovation to enhance patient care and streamline their developmental pipelines, vascular biomarkers are gaining recognition as indispensable tools for assessing health.

These technologies not only facilitate the early detection and effective management of vascular dysfunction but also provide quantifiable metrics that enhance the precision of clinical trials. By accurately assessing arterial stiffness, analyzing pulse wave characteristics, and evaluating vascular biomarkers, these methods enable developers to tailor therapeutic strategies effectively, ensuring both efficacy and safety. Additionally, they aid in predicting patient outcomes, optimizing treatment protocols, and potentially reducing adverse effects.

The concept of early vascular aging also plays a crucial role, offering additional insights into cardiovascular health. By identifying EVA through sophisticated phenotyping tools, healthcare professionals can intervene earlier in disease progression, crucial for preventing severe cardiovascular events and improving long-term patient outcomes.

In light of these advantages, broader adoption of vascular phenotyping and strategic use of vascular biomarkers will drive the healthcare industry towards more data-driven and outcome-focused practices. Embracing these advanced diagnostic tools will be essential for companies seeking leadership in the competitive landscape of medical innovation.

About CONNEQT

CONNEQT pioneered a biosensing technology that has been clinically validated and FDA-cleared to noninvasively measure vascular biomarkers representing key indicators of vascular health. The indicators include, but not limited to, central BP, arterial stiffness, vascular age, and heart stress. Named SphygmoCor®, the technology has been deployed in healthcare systems and clinical trials to measure vascular health.

The SphygmoCor technology enables a new paradigm in the diagnosis and management of hypertension and cardiovascular diseases that is increasingly decentralized and personalized. When combined with cloud-based data analytics, our suite of FDA-cleared medical devices enables key stakeholders throughout the healthcare ecosystem to obtain valuable health information not accessible from standard brachial blood pressure monitors.

Learn more at CONNEQT.com.