

## Surrogate Physiological Markers of Carotid Stent Safety and Efficacy

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**Background:** With intrinsic risks carotid stents were narrowly approved (6 to 5 by FDA) for inoperable subjects. Transcatheter procedures generate emboli. Emboli can cause adverse outcomes and there exists no way to assess vulnerability to emboli or the impact of emboli on cerebral function. Emboli counts do not predict post-procedure hyperemia. Compromised vasomotor reserve is associated with negative outcomes, however, stress testing exposes patients to stroke risk. Pre-procedure analysis of cerebrovascular physiology utilizing a non-invasive, risk free method, Dynamic Vascular Analysis (DVA), may assess cerebrovascular vulnerability to emboli and predict the responses to carotid revascularization.

**Methods:** Eight subjects from an IRB-approved carotid stent trial underwent TCD monitoring (middle cerebral artery, MCA) to quantify emboli. Spectral TCD waveforms were analyzed with DVA and produced relationships among acceleration, velocity and impedance that included Dynamic Flow Index (DFI) and Dynamic Work Index (DWI). Formal statistical assessment was deferred pending additional cases.

**Results:** All subjects had clusters of emboli throughout despite neuroprotection. The DVA data were evaluated for pathophysiological patterns. At the start of the procedure subjects with a low DWI experience DFI increases following stent deployment. In contrast, subjects with high DWI had unchanged DFI following stenting. The pre-procedure DFI did not predict DFI response.

**Conclusion:** The purpose of carotid revascularization is to improve flow into the anterior cerebrum. The DWI, a surrogate for vessel compliance, quantifies vascular stiffness in the distal intracranial circulation. This study suggests a physiologic relationship between MCA small vessel stiffening and stent-related improvement in DFI, a surrogate for microvascular perfusion. DVA ascertains the baseline vascular states that predict outcomes. DVA criteria may be used to optimize risk-benefit ratios of carotid stents. DVA-defined vascular states characterizing short- and long-term adverse and positive trial endpoints provide the continuous surrogate measures needed to greatly shorten trial duration and subject number while enhancing safety.

