



Surrogate Physiological Markers of Carotid Stent Safety and Efficacy

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Disclosures

- Drs. Crutchfield and Mozayeni are employed by New Health Sciences, Inc.
- Drs. Alexandrov, Garami and Chen have no disclosure regarding this study.
- Dynamic Vascular Analysis (DVA) has not been approved by the FDA as a surrogate marker

Carotid Artery Disease

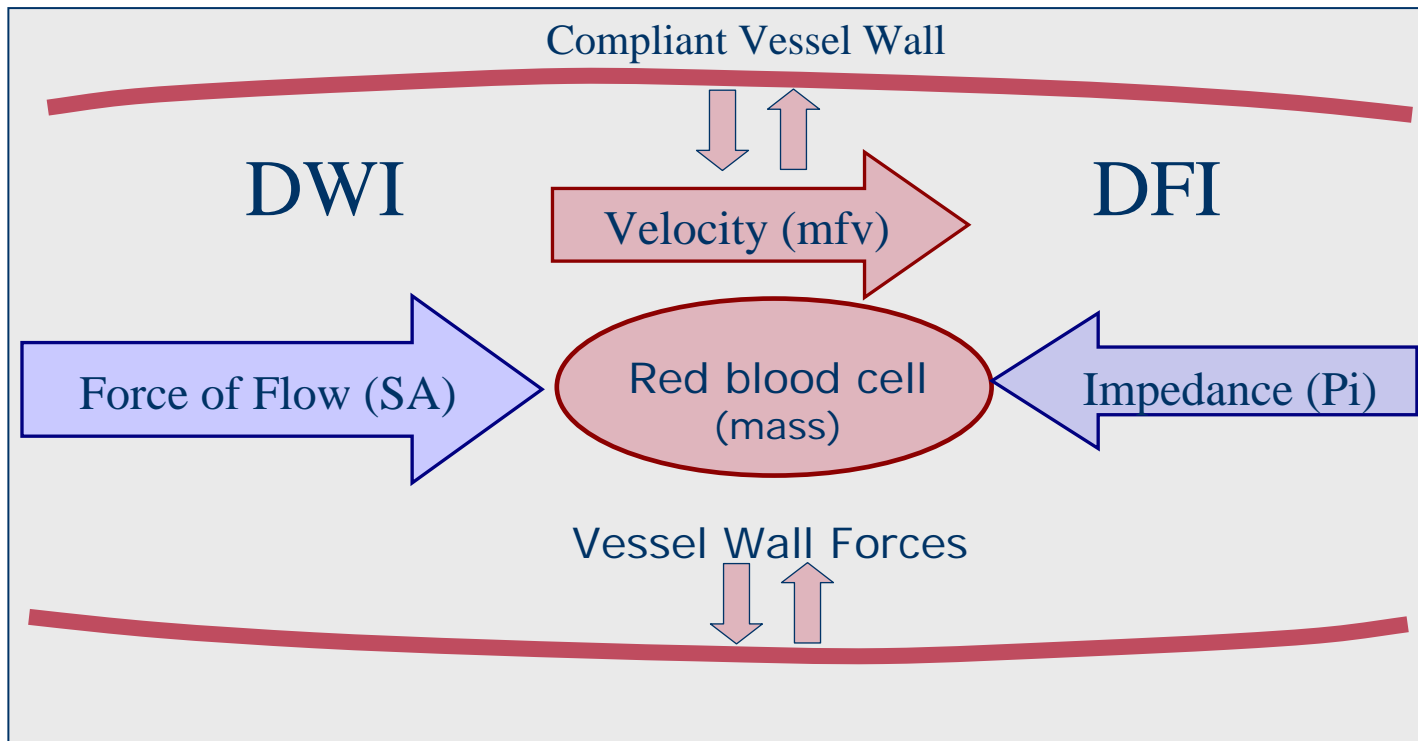
- Neurological symptoms caused by impaired end-organ perfusion (vascular performance)
- Current standard of care
 - Carotid endarterectomy
 - Carotid artery angioplasty and stenting in non-operative cases

Carotid Artery Disease

- Risks of carotid stenting
 - Ischemia secondary to embolization
 - “CPK washout” equivalent to potential loss of independence (cognitive impairment)
 - Development of hyperperfusion syndrome
- Embolic complications may depend on pre-existing vascular state or ability to withstand burden of emboli

Dynamic Vascular Analysis (DVA)

Systolic Acceleration informs us regarding vessel wall compliance



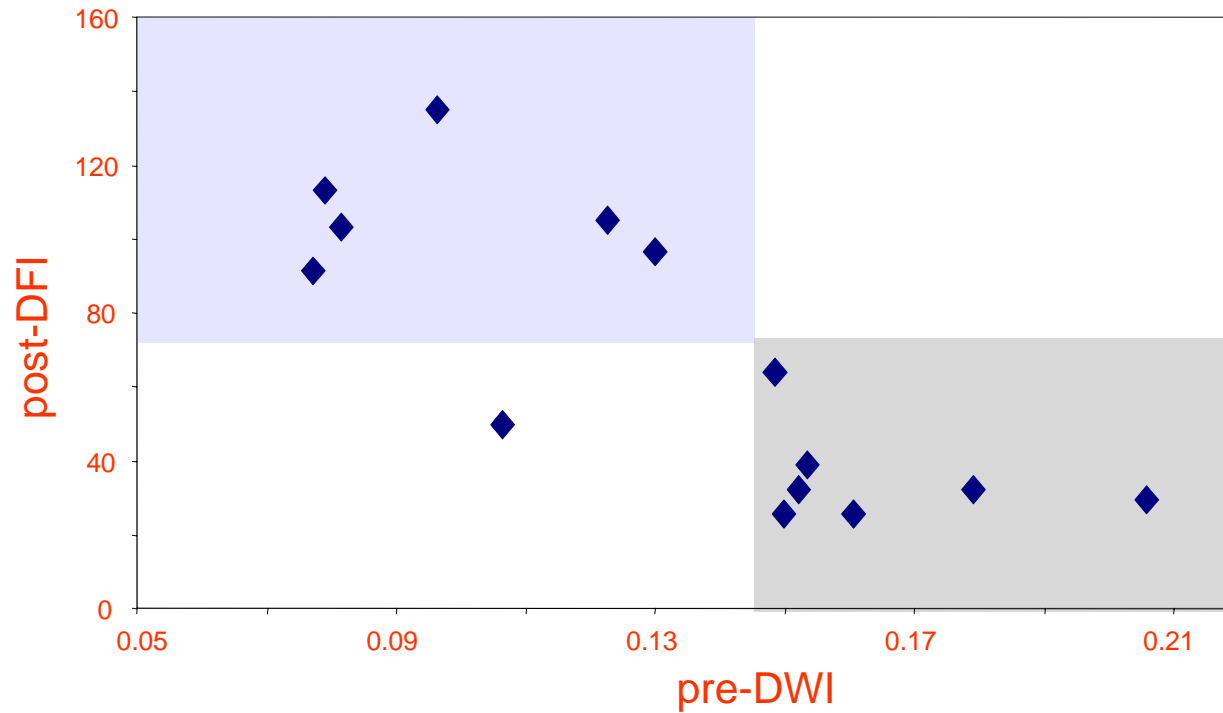
Dynamic Vascular Analysis (DVA)

- May provide a surrogate for vascular performance
 - continuous scalar marker to replace dichotomous clinical endpoints
 - defines the physiological spectrum of vascular disease
- Captures and explains the physiological effects of vascular interventions
 - subgroup differences in favorable or adverse responses
 - allows efficient and improved design of trials

Pilot Trial – UT Houston

- DVA assessed pre- and post-carotid stenting
- Methods
 - TCD monitoring of middle cerebral artery (M1) during stenting of ECCA with protection in 14 patients to quantify emboli
 - DVA indices calculated from TCD spectral output
 - Relationship between DFI and DWI analyzed
- Results
 - Patients with low DWI pre-stent had higher DFI following stent
 - Patients with high DWI pre-stent had unchanged DFI post-stent
 - All patients had ‘too numerous to count’ and ‘clusters’ of emboli

Pilot Trial – UT Houston

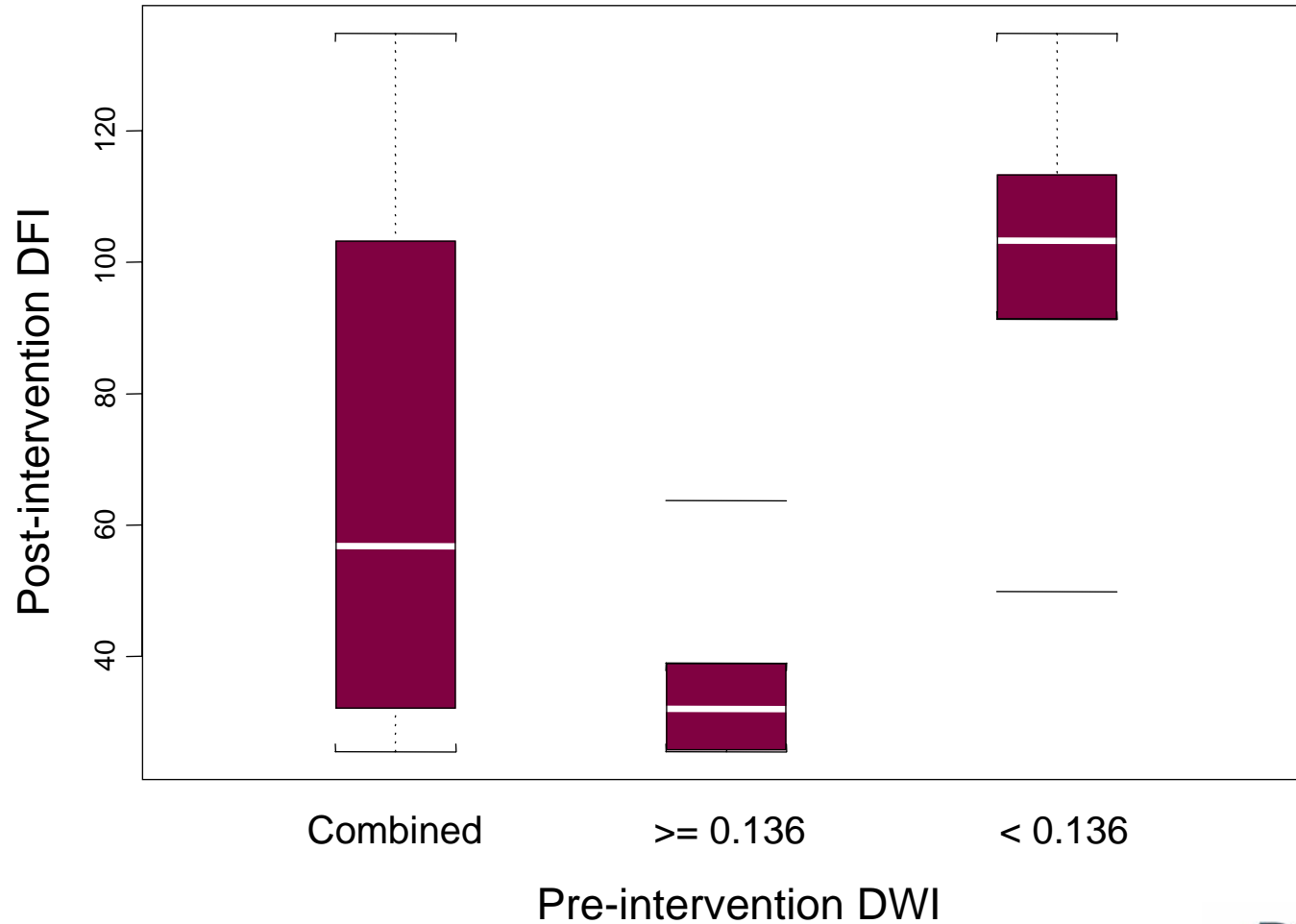


Subjects N=14; $R^2=0.8294$

Results

Pre-procedure DWI	Mean post-procedure DFI
< 0.136	67.25 (n = 7)
> 0.136	35.36 (n = 7)

Post-intervention DFI by pre-intervention DWI level



DVA: Conclusion and Implications

- May predict improved physiological performance
 - Pre-stent DWI may predict post-stent DFI
- May improve the risk benefit ratio
 - Exclude patients at risk for embolic events
 - Exclude patients at risk for hyperperfusion injury
- May provide a marker of efficacy and risk
 - Correlate changes in vascular flow dynamics with patient outcomes
 - Monitor changes over time
- May predict post-stent safety
 - Identify patients at risk for serious adverse events post-stenting
 - Inform etiology of complications

Next Steps: Carotid Stent Studies with DVA

- **Study Objective: demonstrate DVA as surrogate marker**
 - A pre-intervention tool to improve selection of subjects participating in carotid stent trials
 - An early, quantitative measure of the treatment effect
- **Subject Population**
 - Patients with hemodynamically significant diameter reduction of the extracranial or intracranial internal or common carotid artery
- **Study Design**
 - A prospective, multicenter, single-arm clinical trial

Proposed Carotid Stent Study with DVA

- Study Endpoints
 - Establish DVA-defined physiological ‘classifiers’ with specified thresholds for predicting 30-day clinical outcomes
 - MI, stroke, cognitive impairment, or death within 6 months