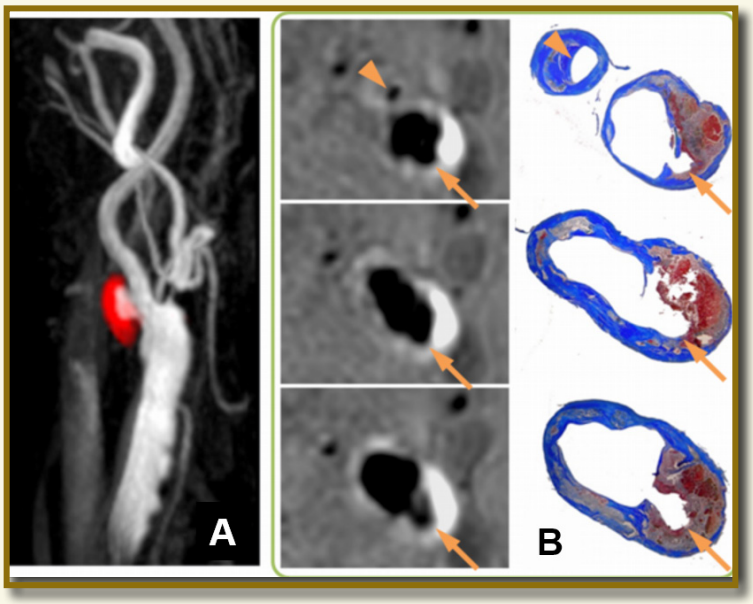
Researcher Profile: Thomas Hatsukami, MD

Dr. Thomas Hatsukami

When working properly, the cardiovascular system transports blood circulated by the heart and distributed by blood vessels throughout the body, but when this system is compromised, a number of potentially life–threatening cardiovascular diseases can result, such as stroke, peripheral artery disease (PAD) and aortic dissection. More than 140,000 people in the U.S. alone die each year from stroke, and it is a leading cause of serious long–term disability in North America. Globally, stroke is the second leading cause of death. PAD, which can lead to severe pain in the legs, and in more advanced cases, gangrene and limb loss, is estimated to affect 12 –20% of people over age 60. And aortic dissection, though less common, is a life–threatening condition of the arteries that requires immediate treatment. Many of the worst outcomes of these cardiovascular diseases can be prevented with early detection and proper treatment. The Vascular Imaging Laboratory (VIL) at UW Medicine South Lake Union, under the leadership of Co –Directors Dr. Thomas Hatsukami, Professor of Surgery in the Division of Vascular Surgery, and Dr. Chun Yuan, Professor, Department of Radiology, is making groundbreaking progress in detecting, diagnosing and treating strokes, PAD and aortic dissections with advances in high–resolution imaging and new methods of drug delivery.

Preventing Strokes with High–Resolution Imaging Techniques

When blood supply to the brain is interrupted or severely reduced, it takes just a few minutes for brain cells to begin to die, causing a stroke. A quarter of patients age 65 and older will die within a year following a first stroke, and more than half die within the first five years. In 2008, the total costs of stroke in the U.S. was $34.3 billion; in 2050 projected costs are expected to exceed $2.2 trillion. For the past 20 years, Drs. Hatsukami and Yuan and their team at VIL have applied high–resolution imaging techniques in long –term studies to better understand the development of atherosclerosis, or hardening of the arteries, and have identified specific features of atherosclerosis that are associated with rapid disease progression and that may be indicators of future stroke. Dr. Hatsukami recently received joint funding from the National Institutes of Health and the National Natural Science Foundation in China, where stroke is the leading cause of death, for a study to develop improved methods for the detection and localization of the atherosclerotic lesion responsible for stroke, referred to as the culprit plaque. The VIL is partnering with the Tsinghua University and the Neuroradiology Department at Tiantan Hospital in Beijing to examine novel markers and risk factors for development of the high–risk plaque. Findings from this study will lay the foundation for prospective studies that will assess whether presence of a magnetic resonance imaging (MRI)–detected culprit plaque poses a higher risk for recurrent stroke, and whether specific circulating markers predict progression to a high–risk plaque.



(A): Magnetic resonance angiogram (left panel) demonstrating a disrupted, ulcerated plaque in the proximal internal carotid artery, surrounded by intraplaque hemorrhage shown in red. The scan was performed in a patient who recently suffered a stroke and who was scheduled for surgery to remove the plaque.

(B) Images from the left panel are reformatted to show the carotid artery in cross section (middle panel). The reformatted images demonstrate the ulcerated plaque (arrow). Matching histological cross–sections obtained from the plaque removed during surgery (right panel) that confirms the presence of a large ulcerated laque with intraplaque hemorrhage.

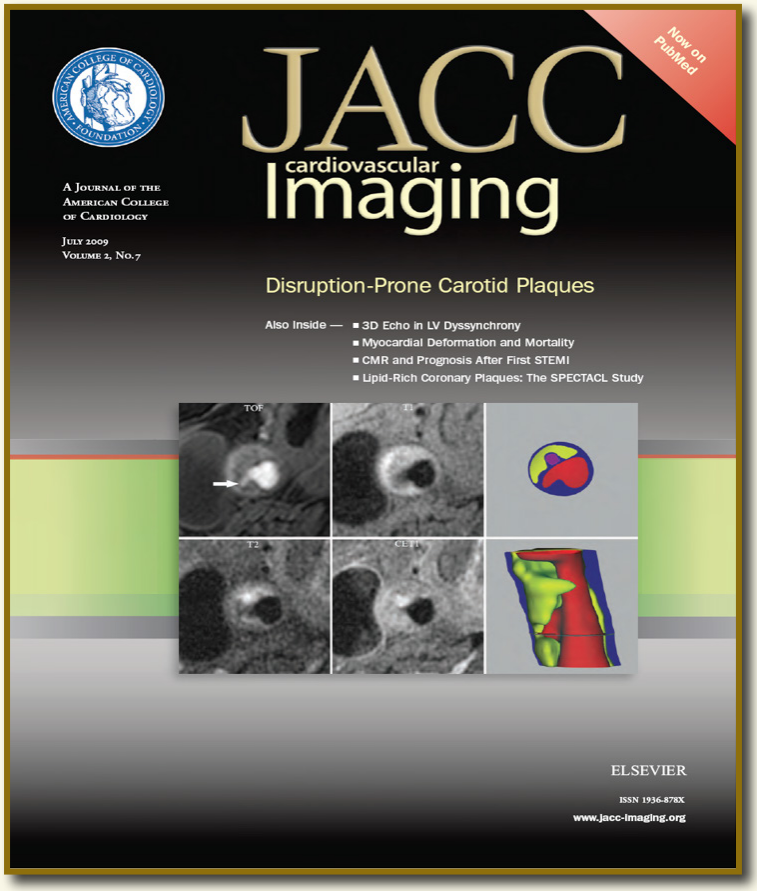
Improved Aneurysm Prediction and Aortic Dissection: Life and Death

Another important area of focus for the VIL is "Type B" aortic dissection, which is a tear in the inner layer of the descending

(continued on page 11)

Continued from page 10

aorta in the chest. A majority of patients with Type B aortic dissection can be successfully treated with medication, but they are at risk for aneurysmal degeneration and rupture over time, and up to 25% will die within three years, mostly due to aortic rupture. Predicting whether a patient with a type B dissection will eventually develop an aneurysm or a complete aortic rupture is difficult yet a matter of life and death. In a study funded by Philips Healthcare, the VIL is developing and testing MRI techniques to assess whether this type of imaging can identify characteristics of the aortic wall that are associated with future



Cover of JACC Cardiovascular Imaging demonstrating work performed at the UW Medicine Vascular Imaging Lab (VIL). The left and middle panels exhibit multi-contrast weighted magnetic resonance images (MRI's) of a disrupted, ulcerated plaque in the carotid artery (arrow). Using custom-designed image analysis software developed by the VIL, the tissue components of the plaque are identified (right upper panel) and a 3D reconstruction of the plaque's composition can be generated (right lower panel).

aneurysmal degeneration or aortic rupture in patients with Type B aortic dissection. They are also developing novel, noninvasive imaging methods to quantify the level of inflammation in the aorta and determine whether patients with greater vessel wall inflammation are at higher risk for rupture. Accurately predicting the likelihood of an aneurysm or an aortic rupture will help determine whether a given patient may be safely managed with medical therapy or is better served by early surgery.

Peripheral Artery Disease (PAD): A New Method of Drug Delivery

PAD is caused by atherosclerosis in the lower extremities and can result in pain in the leg muscles when walking and, in more severe cases, gangrene, the need for amputation and increased risk of death. More than half a million people each year undergo balloon dilation (angioplasty) or stenting procedures to open blocked arteries in the leg, but many patients develop recurrent narrowing and blockage within a year. This narrowing is caused by growth of a scar –like tissue thought to be driven by inflammation, and while there are a number of drugs that may reduce scarring and inflammation, they carry serious side effects when administered systemically. The VIL is collaborating with investigators at the University of California, San Francisco to test the effectiveness of local delivery of anti –inflammatory drugs directly into the artery wall at the time of angioplasty, which may reduce the risk of systemic side effects. Dr. Hatsukami is also participating in a study funded by Astra–Zeneca to develop high–resolution, noninvasive imaging techniques to more precisely measure the amount of scarring and inflammation in the artery wall following treatment. Together these studies will aid in the development of new drugs to prevent scarring and inflammation and improve the long–term durability of angioplasty in patients with PAD.

Conclusion

Vascular disease exacts a heavy burden on the health of the public around the world. Globally, stroke is the second leading cause of death, for example. Over the past 20 years, Drs. Hatsukami, Yuan and their colleagues at the VIL have developed highly productive international collaborations with medical centers throughout North America, Asia and Europe dedicated to reducing the incidence of stroke and complications from aortic dissection and PAD. They are developing advanced arterial imaging techniques that identify individuals at increased risk so physicians can intervene early and prevent the complications of these disabling vascular diseases.