Volume 2,
Issue 3
August 2007
Editor:
Joan Brown

Vascular Voice

MICHIGAN VASCULAR CENTER

Michigan Vascular Center (MVC) - Mission Statement

MVC exists to improve the quality of life for patients by providing the most comprehensive, innovative and best possible vascular care based on sound principles of treatment.

MVC exists to render that care with compassion, respect, & integrity; exercising the best possible thought and judgment for the patient's benefit.

Inside this issue:

SEPTEMBER IS NATIONAL VASCULAR AWARENESS MONTH

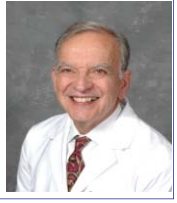
The Michigan Vascular Center invites you to join us and many national vascular societies to promote VASCULAR AWARENESS during the month of September. When one considers the national devastation caused by vascular conditions such as coronary artery disease, cerebrovascular occlusive disease and stroke along with aneurysms of the abdominal and thoracic aorta and peripheral arterial occlusive disease (PAD) — the 1st, 3rd and 13th leading causes of death in this country — one can appreciate that we, as physicians, have much work to do to educate the public about these vascular conditions. Indeed, this VASCULAR AWARENESS MONTH is long overdue.

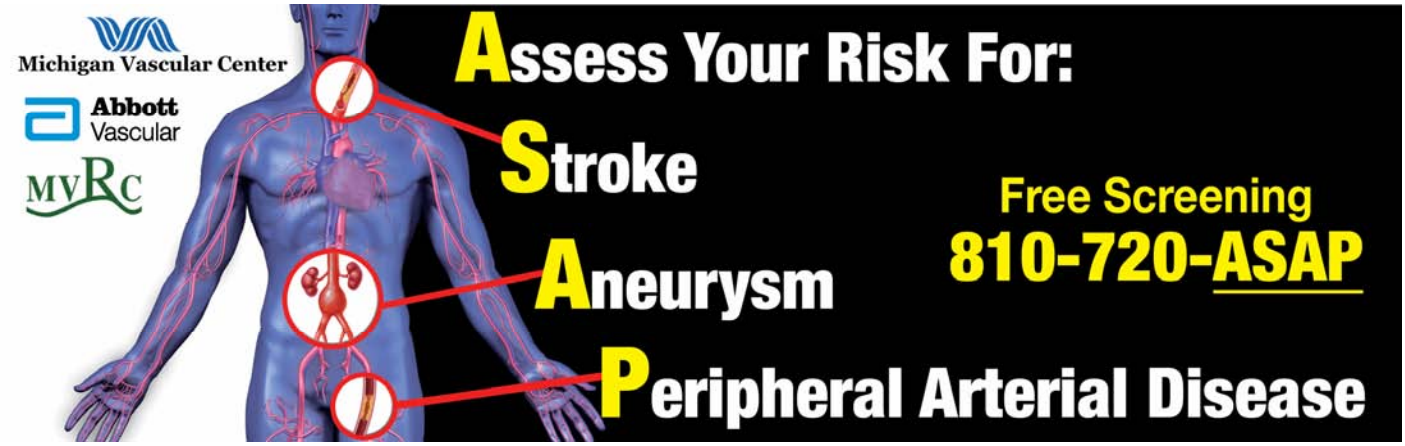
To promote Vascular Awareness during the month of September, we at the Michigan Vascular Center will be conducting free public seminars and screenings on these vascular conditions, both in our office and at several offsite locations. The ASAP screening is ongoing and details are listed on page 2 of this issue.

Over the years we have dedicated ourselves to the education of the citizens of this community about vascular conditions and have taken our responsibility seriously. From free screenings, which we began 12 years ago, to our current patient directed seminars, free screenings and billboard awareness program along the local freeways, we will do all we can to raise awareness of this silent and lethal process. With you, our referring physicians as partners in this endeavor, I believe we have raised the level of awareness of these conditions from "off the radar" to topics of discussion among a large cross-section of the population. I commend you for doing a great job.

In an effort to simplify Vascular Awareness, we ask all interested a simple question: ***What is your vascular profile***? Are you at risk of a stroke from carotid occlusive disease? Do you have an abdominal aortic aneurysm? Do you have PAD, a marker for coronary artery disease? We invite anyone who does not know the answer to these questions to join us in September to raise awareness of these conditions by enrolling in one of the free screening events.

≈ Carlo A. Dall'Olmo, M.D.





A.S.A.P.

Assess your risk of Stroke, Aneurysm, and Peripheral arterial disease (PAD)

Screening

The Screening Exam will consist of three diagnostic tests

- ✓ ***CAROTID (Neck Arteries) SCREENING EXAM****: This is an ultrasound exam done to determine the amount of plaque build up in the arteries carrying oxygen and blood to the brain. A blockage in these arteries increases your risk of stroke.*
- ✓ ***LOWER EXTREMITY (Leg Arteries) ARTERIAL SCREENING EXAM****: This test is done to determine the percentage of blood flow getting to your legs/feet. Blockage in these arteries decreases that percentage and is called Peripheral Vascular Disease (PVD). PVD can lead to leg pain when walking, or if gone untreated, can result in loss of limb.*
- ✓ ***AORTA (Aneurysm) SCREENING EXAM****: This is an ultrasound exam of the aorta (the large artery in your stomach) to look for a weakened or bulging area of the vessel, this is called an aneurysm. The larger the aneurysm, the higher your risk of rupture.*

Patients will receive a copy of their results and those who are found to have a positive test can have a copy sent to their physician for further evaluation and treatment. In addition, educational material will be given at the time of screening to provide the patients an opportunity to learn about their condition and develop a better understanding of PAD. We hope to increase awareness of PAD by offering these free screenings and will also be scheduling free periodic PAD educational symposiums to the public.

Patients can be pre-qualified and scheduled for testing by calling

(810) 720-ASAP (2727)

Additional information as well as educational material can be found at

www.michiganvascular.com.

Secondhand Smoke—*Unfortunately the Real Thing*

Twenty-one years ago, in 1986, the U.S. Surgeon General, Dr. C. Everett Koop, issued the first report to conclude that the involuntary inhalation of tobacco smoke by nonsmokers (secondhand smoke) causes disease. In 2005, the U.S. Surgeon General, Dr. Richard Carmona, issued a follow-up report which examined the evidence linking secondhand smoke to a number of disease processes. Fortunately, during this period of time the exposure of adults to secondhand smoke is decreasing as smoking becomes increasingly restricted in workplaces and public places. Unfortunately, children continue to be exposed in their homes by the smoking of their parents and other adults. As of the year 2000, more than 126 million Americans, aged 3 or older, still are estimated to be exposed to secondhand smoke.

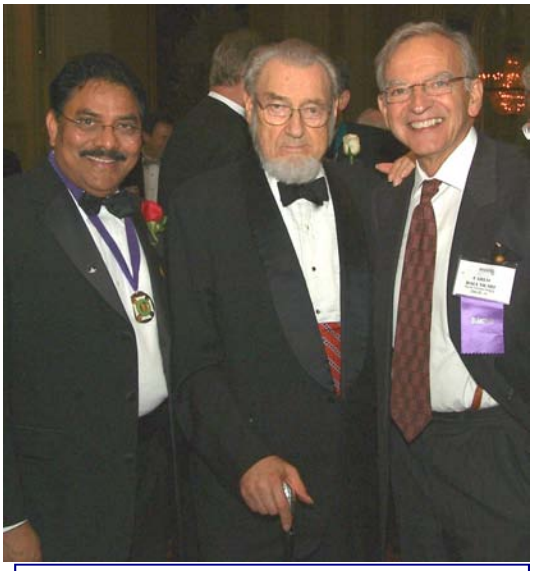


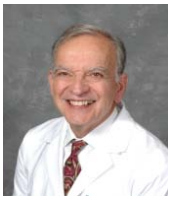
Photo taken at Annual AMA Meeting June, 2007
Center: Dr. C. Everett Koop, M.D.
Born 10-14-1916—Appointed US Surgeon General 11-17-1981
Right: Dr. Carlo A. Dall'Olmo, M.D. — Flint
Left:: Apparao Mukkamala, M.D. — Flint

The conclusions of the 2005 report are worth repeating because of the wide range of illnesses non-smoking adults and children develop as a result of their exposure to secondhand smoke:

1. Exposure of adults to secondhand smoke has immediate adverse effects on the cardiovascular system and causes coronary heart disease and lung cancer. Secondhand smoke causes endothelial cell dysfunction, thus creating a prothrombotic effect in humans - i.e. an increased risk of developing blood clots and heart attacks. In animal studies, it also causes atherosclerosis (hardening of the arteries).
2. The scientific evidence indicates that there is no risk-free level of exposure to secondhand smoke.
3. Secondhand smoke causes premature death and disease in children and adults who do not smoke.
4. Children exposed to secondhand smoke are at an increased risk for sudden infant death syndrome (SIDS), acute respiratory infections, ear infections, and more severe asthma. Smoking by parents causes respiratory symptoms and slows lung growth in their children.
5. Many millions of Americans, both children and adults, are still exposed to secondhand smoke in their homes and workplaces despite substantial progress in tobacco control.
6. Eliminating smoking in indoor spaces fully protects nonsmokers from exposure to secondhand smoke. Separating smokers from nonsmokers, cleaning the air, and ventilating buildings cannot eliminate exposures of nonsmokers to secondhand smoke.

The path to eliminating the consequences of secondhand smoke is obvious- eliminate smoking in the workplace and in private and public spaces. For children, the home must become smoke free. We at the Michigan Vascular Center are dedicated to your vascular health and encourage all to support initiatives for a smoke free environment.

≈ Carlo A. Dall'Olmo, M.D.



Smoking, Inflammation and Vascular Disease

The "why" questions of life have fascinated me since my high school biology and chemistry classes. I believe that is true for most of us who have pursued a career in any of the scientific disciplines.

As a critical care and pulmonary physician, illness affecting blood vessels, acutely or chronic vascular disease leading to organ dysfunction and life threatening illness, are the focus of most of my days. Whether it is an acute stroke, an acute myocardial infarction, ischemic bowel disease, pulmonary embolic disease, renal failure or even primary pulmonary hypertension, vascular reactivity or vascular pathology plays a central roll in the disease and dysfunction my patients face daily.

Over the past 31 years since my days at medical school the "why " questions related to vascular disease have focused on many causes and mechanisms. 1970 to 1980 was the decade of hypertension awareness. The eighties were about cholesterol. The nineties were about inflammation and the first decade of the new millennium has been about mediators.

THE FIRST DECADE OF THE NEW MILLENNIUM HAS BEEN ABOUT MEDIATORS

Basic science research and, now, clinical studies have revealed the very strong relationship between smoking and many inflammatory markers such as C-reactive protein (CRP) and mediators such as interleukin-6 and others. For the clinician, what should trigger my further evaluation when my patient smokes? A recent study entitled "Interactions between smoking and reduced lung function (Chest Vol. 127, Feb 2005) revealed some very startling data. Smokers who's FEV1 (forced expiratory volume in one second) was at 82% or lower had markedly greater levels of inflammatory markers. Smoking alone yielded a 63% greater chance of having an elevated CRP. Smoking with an FEV1 of 82% or less increased the odds ratio of an elevated CRP by 3.31. For a smoker with low "normal" FEV1 the inflammatory risks markers are more than 3 times higher than normal. In these same patients, plasma fibrinogen, platelet counts, and blood leukocytes were also significantly elevated. All of these markers are associated with vascular pathology; but, here, we are talking about a patient we might identify as "normal" except for their smoking because the FEV1 is above 80%. For the clinician with a smoking patient, you must always maintain a high suspicion that lung or vascular damage will occur as time passes for that patient.

What are the other substances and mediators that have been identified as side effects of smoking? The list is long, and an excellent review was published this May in the journal Chest entitled "Systemic Effects of Smoking": acute-phase protein, CRP, cysteine, oxidized cysteine, glutathione, intracellular adhesion molecule, interleukin, low-density lipoprotein, nitric oxide(NO), plasminogen activator inhibitor, PNS's, reactive oxygen species(ROS), thiobarbituric acid-reactive substances, trolox-equivalent antioxidant capacity, tumor necrosis factor, and tissue plasminogen activator. As you can see the list is long and the space in this article is too limited to review each.

Vascular Endothelial Dysfunction is the label we now use to describe the process leading to those clinical manifestations we now see daily. Endothelial dysfunction is mainly caused by diminished production or availability of NO. It has been demonstrated that the serum concentration of nitrate and nitrite, metabolic

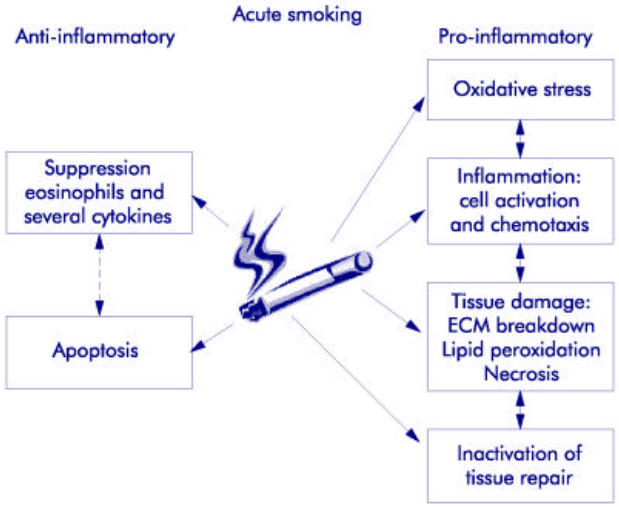
(Continued on page 5)

Smoking, Inflammation and Vascular Disease *(Continued)*

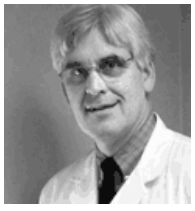
end products of NO, is significantly decreased in smokers relative to that in nonsmokers. In cigarette smokers, low-density lipoprotein(LDL) is more prone to oxidation due to higher levels of ROS and reactive nitrogen species. Oxidatively modified LDL limits the bioactivity of endothelium-derived NO; and, in turn, the loss of NO bioactivity is associated with increased inflammatory cell entry into the arterial wall. Oxidatively modified LDL is taken up by macrophage scavenger receptors, promoting cholesterol ester accumulation and foam cell formation. And this is only part of the puzzle we are putting together to show how smoking is linked to inflammation and vascular disease.

Besides smoking, vascular inflammation and the same inflammatory markers are also strongly linked to chronic infection with agents such as Chlamydia spp, as well as with hyperglycemia in both the acute (such as ICU illness) and chronic forms such as diabetes.

The following diagram illustrates some of the acute as well as chronic effects of smoking:



With those factors in mind we, as clinicians, can evaluate, counsel and treat our patients in a rational fashion leading to less vascular disease and improved wellness for our community.



≈ Mark S. Rittenger D.O. F.C.C.P.

Michigan Lung and Critical Care Specialists P.C.
Associate Clinical Professor Internal Medicine M.S.U. COM
Board Certified in Internal Medicine, Pulmonary Medicine, Critical Care Medicine.
Director of Respiratory Therapy Genesys Regional Medical Center

CoSmic—New Technologies for Pseudoaneurysms

Michigan Vascular Center takes the lead in minimally invasive therapy for complications in Dialysis access. The incidence of end-stage renal disease (ESRD) has been rising over the last two decades. In 1999, approximately 300,000 people were on hemodialysis (HD) and 75,000 new patients are added annually. The most common cause of hospitalization in these patients is access maintenance, HD access placement and associated complications being the leading cause of morbidity. Complications of HD include pseudoaneurysm formation, skin erosion, graft thrombosis and infection.

Figure 1

Pseudoaneurysms form secondary to repeated punctures causing trauma to the vein or graft. Proximal venous outflow stenosis causes increased resistance in the arteriovenous fistula (AVF) or graft (AVG) leading to a weakening and dilatation of the vein/graft. Patients that are not excluded potentially result in skin erosion and eventual rupture. The current standard treatment of pseudoaneurysms is surgical revision or bypass to prolong access use.

Michigan Vascular's strong commitment and interest in the dialysis patient has led us to initiate a minimally invasive technique to treat pseudoaneurysms. The use of a covered stent, figure 1, to safely exclude the pseudoaneurysm can be done with a puncture of the fistula/graft not much larger than that used for dialysis. This immediately removes the risk of rupture and does not interrupt the patient's dialysis. These covered stents are made of the same material as the grafts that we currently place, polytetrafluoroethylene or gortex, and can be accessed the same day. Results as seen in the angiographic series in figure 2-4 and 5-6 can be obtained.

Figure 1
B = Pseudoaneurysm with erosion

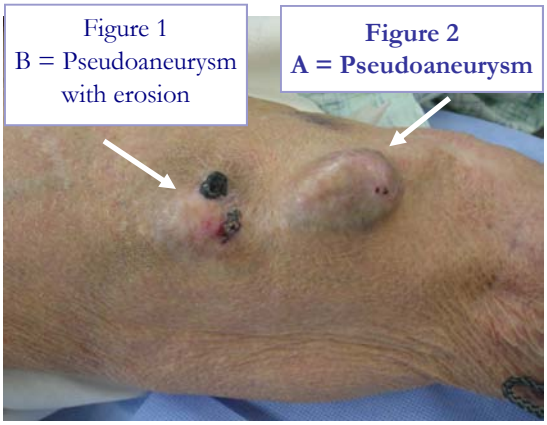


Figure 2
A = Pseudoaneurysm

Figure 3

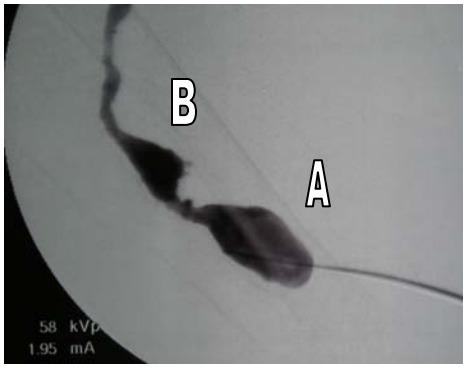


Figure 4

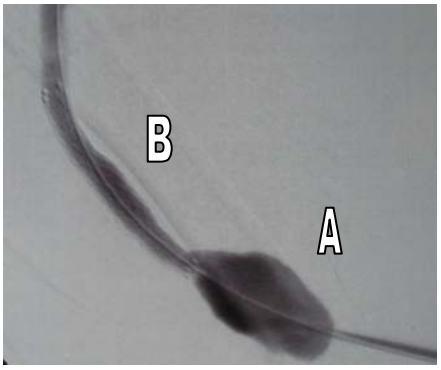


Figure 5
Femoral loop with pseudoaneurysms

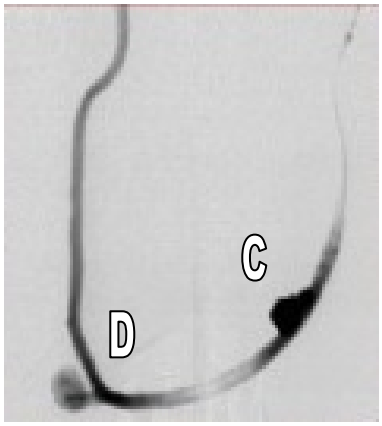
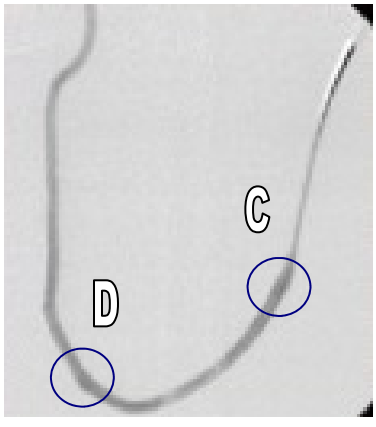


Figure 6
Pseudoaneurysms safely excluded



Dialysis Access in Current Clinical Trial (CoSmic) *(Continued)*

We have prospectively evaluated seventeen patients, of which nine were enrolled. Eight patients were eliminated due to suboptimal pseudoaneurysm size (too small), not having adequate landing zones, pseudoaneurysm ruptures, or not wanting to participate in the study. Stent placement was achieved in all nine patients. Seventy-eight percent (7/9) had additional angioplasty performed at time of stent placement. There were no complications from the pseudoaneurysm exclusions. Two month follow up was completed on 8/9 (89%) of patients and six month follow up was completed on 5/9 (56%). One patient has been enrolled less than two months, one patient less than six months, one patient died of unrelated causes after the two month follow up and one patient had an infected graft removed four months after three stents had been placed. Two and six month follow up showed 100% patency and 100% effectively excluding the pseudoaneursyms.

Results — 2 Month FollowUp					
Enrolled	9	Patent	%	Exclusion of Aneurysm	%
< 2 mos.	1	N/A	N/A	N/A	N/A
Total 2 mo. f/u	8 (89%)	8	100%	8	100%

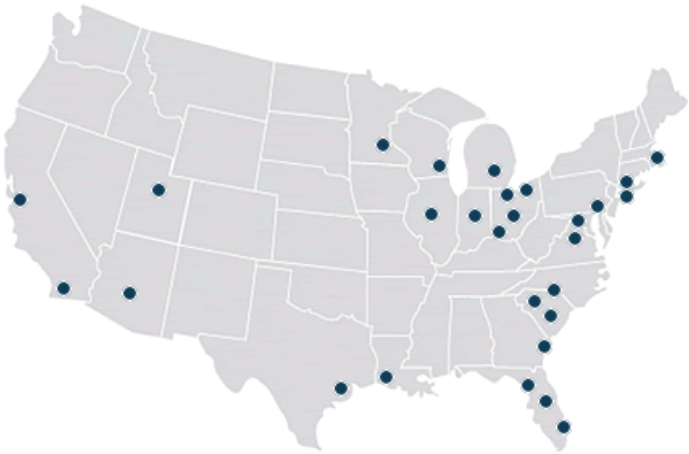
Results—6 Month FollowUp					
Enrolled	9	Patent	%	Exclusion of Aneurysm	%
< 2 mos.	1	N/A	N/A	N/A	N/A
< 6 mos.	1	N/A	N/A	N/A	N/A
Deceased/ Unrelated	1	N/A	N/A	N/A	N/A
Infected Graft > 4mos & 3 stents	1	N/A	N/A	N/A	N/A
Total 6 mo. f/u	5 (56%)	5	100%	5	100%

This small cohort of patients does not have the power to change our current patient management algorithm; however, the initial enrollment results are encouraging. Our goal is to enroll a total of thirty patients into the CoSmic study. This is an aggressive target since most of the literature has only small case series or case reports. This number and results would also have the power to change or maintain our current patient algorithm for pseudoaneurysms.

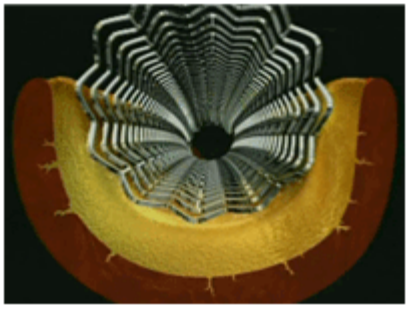
≈ Russell W. Becker, D.O.

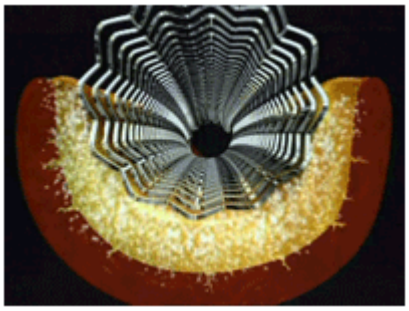
Zilver PTX Phase II Trial—Now Enrolling

The Michigan Vascular Research Center (MVRC) is pleased to announce open enrollment in the Zilver PTX phase II clinical trial – the first trial ever to evaluate drug-eluting stents used in the peripheral arterial circulation. This trial was awarded to MVRC after participating in the phase I trial. Michigan Vascular Center is one of only thirty-one sites in the United States to have been chosen to participate in this landmark trial. This trial is designed to evaluate the efficacy and durability of superficial femoral artery drug eluting stenting (using the Cook Zilver paclitaxel drug eluting stent) compared to primary angioplasty. Thirty-one sites in the United States as well as in Asia, Canada, Latin America and Europe, have been chosen to enroll 460 patients randomized to either primary angioplasty or drug eluting stent placement. Patients eligible include those with severe intermittent claudication, non-healing ulcers, or limb-threatening ischemia. The superficial femoral artery lesion length cannot be greater than 14 centimeters and patients must fit one of the inclusion criteria and be absent of any of the defined exclusion criteria. Patients who are randomized to primary angioplasty yet have a suboptimal PTA result will be further randomized to either drug-eluting or bare metal stent placement. Patient follow up for this study will occur over a three year period.



While drug eluting stents in the coronary circulation have received some negative press due to acute failure, this has not been seen so far in the SFA Zilver drug eluting stents. It is postulated that the reason for coronary drug eluting stent failures is, in part, due to the polymer that binds the therapeutic drug to the stent. The Zilver PTX drug eluting stent does not use a polymer, as the paclitaxel is applied to the stent without polymer binding. As the stent is deployed and makes contact with the intimal lining of the artery, the paclitaxel is immediately released and absorbed directly into the endothelial cells. This rapid uptake is due to the extremely lipophilic nature of paclitaxel and therefore does not need the polymer to allow for slow continued release. Once paclitaxel is taken into the cells, its biological activity is present for months, thus allowing for a longer therapeutic window.





A bare metal stent (above) is coated with paclitaxel, a drug that is released in the vessel (below) to help prevent renarrowing of the artery.

It is too early to tell whether drug eluting stents will have a positive impact on revascularization of peripheral arteries. Endovascular treatment of the SFA has been somewhat disappointing and inferior to surgical revascularization. However, minimally invasive techniques and drug therapies continue to improve and the phase I data from the Zilver PTX stent is very encouraging. Please assist us in identifying patients who might benefit from this exciting new minimally invasive therapy. If any of your patients have claudication, non-healing ulcers, or symptoms of significant PAD, please contact our office to see if they might qualify. New technologies and inclusion into prestigious international trials such as the ZilverPTX trial enable the Michigan Vascular Center to offer you and your patients the latest in minimally invasive endovascular therapy.

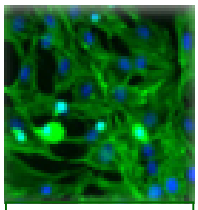
≈ Robert G. Molnar, M.D.

Two New Research Studies at MVRC

Michigan Vascular Research Center is pleased to announce two new studies available for patients with Peripheral Vascular Disease.

Critical Limb Ischemia Trial

Aastrom Biosciences, Inc.



Vascular Repair Cells Technology

Critical limb ischemia, the most severe form of peripheral vascular disease, leads to over 160,000 major limb amputations per year. Therapeutic options are limited and largely ineffective for the most severe patients. Aastrom is developing Vascular Repair Cells (VRCs), based on TRC technology. Aastrom's Tissue Repair Cells (TRC) products have been used in over 240 patients and are currently in clinical trials.

Michigan Vascular Center has been chosen to participate in this very important trial and is able to offer it to patients currently with critical limb ischemia. For more information, please contact Brenda Buckle, ANP, BC, Research Director at 810-600-2009.

Arteriovenous Graft Study

Angiotech

Paxlitaxel is compounded from Pacific Yew tree

The incidence of end stage renal disease (ESRD) is approximately 100,000 per year and approximately 330,000 subjects currently require routine hemodialysis (USRDS, 2005). These subjects require vascular access via the placement of arteriovenous grafts or via the creation of arteriovenous fistulae. Almost half of the arteriovenous grafts fail in the first year of use. This high failure rate is a substantive cause of morbidity and may necessitate medical and surgical intervention in order to maintain graft patency. Angiotech has developed the Vascular Wrap™ Paclitaxel-Eluting Mesh to be used at the anastomosis of the graft. The primary objective of this study is to demonstrate that the target site primary patency rate of the Lifespan® ePTFE Vascular Graft and Vascular Wrap™ Paclitaxel-Eluting Mesh is superior to the target site primary patency rate of the Lifespan® graft alone within 1 year following hemodialysis access surgery.

For more information, please contact Brenda Buckle, ANP, BC, Research Director at

(810)-600-2009

≈ Brenda Buckle, NP

Progress of MVC Carotid Stent Trials

Michigan Vascular Center and Michigan Vascular Research Center is one of the country's most experienced sites for carotid stenting. Our specialists are currently participating in multiple FDA-approved carotid stenting procedures and have access to the latest stenting technologies.

Since 2002, we have conducted a total of 14 carotid artery studies and implanted over 220 carotid artery stents. The following table illustrates the carotid artery studies completed or ongoing at Michigan Vascular Research Center.

Study	Type	Date Trial Started	Total Enrolled	Brief Description
Caress	Carotid Stent Vs Open	11/16/2001 Trial Completed	Stents = 16 CEA = 40	Low risk CAS Vs CEA (Carotid Artery Stenting)
C-1	Carotid Stent	8/1/2002 Trial Completed	Stents = 9	High Risk CAS
Off –Label Stenting	Carotid Stent	11/1/2003 Trial Completed	Stents = 20	High Risk CAS
Maveric I	Carotid Stent	9/1/2002 Trial Completed	Stents = 1	High Risk CAS (Carotid Artery Stenting)
Maveric II	Carotid Stent	3/21/2003 Trial Completed	Stents = 22	High Risk CAS (Carotid Artery Stenting)
Archer (LTFU)	Carotid Stent	8/1/2004 Trial Completed	Stents = 10	High Risk CAS (Carotid Artery Stenting)
Guidant Acculink (FDA Approved)	Carotid Stent	9/7/2004 Trial Completed	Stents = 21	High Risk CAS (Carotid Artery Stenting) Only if patient has been enrolled in another trial and or there are no other CAS trials open

Continued on page 11

Progress of MVC Carotid Stent Trials *(Continued)*

Study	Type	Date Trial Started	Total Enrolled	Brief Description
MAVErIC III	Carotid Stent	10/15/2004 Trial Closed to enrollment	Stents = 14	High risk CAS (Carotid Artery Stenting)
CAPTURE	Carotid Stent	10/15/2004 Trial Completed	Stents = 40	High risk CAS (Carotid Artery Stenting)
CASES	Carotid Stent	10/15/2004 Trial Completed	Stents = 17	High risk CAS (Carotid Artery Stenting)
CREST	Carotid-Stents VS Open (randomized)	12/17/2004 Open to enrollment	Stents = 4 CEA = 9	Low risk CEA vs CAS (Symptomatic & Asymptomatic). Pt. must qualify for both CEA and CAS. Pt. must be willing to be randomized to either CEA or CAS. Follow-up 48 months
VIVA	Carotid Stent	10/21/2005 Open to enrollment	Stents = 17	High risk CAS (Carotid Artery Stenting)
CAPTURE II	Carotid Stent	12/16/2005 Open to enrollment	Stents = 25	High risk CAS (Carotid Artery Stenting)
Sapphire WW	Carotid Stent	2-14-07 Open to enrollment	Stents - 1	High risk CAS (Carotid Artery Stenting)
Create PAS	Carotid Stent	5-9-07 Open to enrollment	Stents = 0	High risk CAS (Carotid Artery Stenting)
Protect	Carotid Stent	5-9-07 Open to enrollment	Stents = 0	High risk CAS (Carotid Artery Stenting)

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Fax: (810) 600-0561
(Lower Level of
The Surgery Center)

VeinSolutions
5151 Gateway Centre
Suite 400
Flint, MI 48507
Phone: (810) 232-3363
Fax (810) 232-3602

MVC Core Values

- We are a professional organization –a team– working equally in a common cause: To provide the best possible vascular care for the physicians, patients, and institutions of our community.
- We share a commitment to excellence in the vascular care of patients through the pursuit of knowledge, communication, innovation, and research.
- We value our employees and incorporate them into our team.
- We commit to each other to honor & pursue these values.

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