

CV Section News

Chairman's Message

Editor: Ketan R. Bulsara MD
Co-Editor: Andrew Ducruet MD



The Spirit of Partnership and Collaboration

Brian Hoh, MD, FAANS, FACS, FAHA

These past few weeks many across the world have been swept up with the excitement of the FIFA World Cup. At the heart of this excitement is a spirit of one world: that fans from across continents can all join for a few weeks to come together and celebrate the human endeavor through sport.

In the same spirit of world collaboration, the Joint AANS/CNS Cerebrovascular Section has been partnering with international neurosurgical societies as well as our brothers and sisters in the Society of Neurointerventional Surgery for our scientific conferences and educational courses.

Many of you joined us in San Diego this past February for our Joint AANS/CNS Cerebrovascular Section and Society of Neurointerventional Society (SNIS) Annual Meeting with our international partners, the Society of Brazilian Neurosurgery. There were a record-breaking nearly 600 attendees at the meeting, and the scientific and educational discourse was spirited and innovative.

We hope that you will all join us in Nashville as the Joint AANS/CNS Cerebrovascular Section and the SNIS will partner with the Section of Vascular Neurosurgery of the European Association of Neurosurgical Societies (EANS) for our Annual Meeting, February 9-10, 2015. The science and education should prove to be even greater.

The state of the section has never been more robust and strong. We have nearly 2200 members of which over 50 are international members. We have been busy representing you, our members, by tackling the issues and challenges that face cerebrovascular, endovascular, and dual trained neurosurgeons of today. In the same spirit of partnership and collaboration, we have teamed up with our partners in other societies to work in a unified fashion to fight to represent our members' interests.

Just a brief highlight of three of the many issues the Joint AANS/CNS Cerebrovascular Section is busy working on:

Fellowship Training Standards: There has never been a standardized and effective manner to ensure adequate quality training standards of fellowships in endovascular neurosurgery. This has been controversial and

challenging because of the multiple specialties that practice and train fellows in this field. A proliferation of fellowships without adequate oversight of appropriate training standards has been the result. In a historic first-ever step, the Joint AANS/CNS Cerebrovascular Section has been working with the Society of Neurological Surgeons on the development of CAST (Committee on Advanced Subspecialty Training) Training Standards for endovascular neurosurgery fellowship training and open cerebrovascular surgery fellowship training. In a spirit of partnership and collaboration, a consensus group with representatives from the Joint AANS/CNS Cerebrovascular Section, SNIS, and SVIN (Society of Vascular and Interventional Neurology) has been working together to develop endovascular neurosurgery fellowship training standards which is now under review by SNS CAST. This is going to be a critically important initiative, as this will have significant implications for the future of our specialty.

Joint Commission Comprehensive Stroke Center Certification: In its previous iteration, the Joint Commission Comprehensive Stroke Center (CSC) certification criteria included inadequate minimum case volume requirements for the treatment of aneurysmal subarachnoid hemorrhage: CSCs only needed to treat 15 aneurysmal SAH patients each year with *either* clipping *or* coiling. There is abundant robust evidence in the peer-reviewed literature demonstrating the direct relationship between case volume and outcomes when it comes to the treatment of aneurysmal SAH, and that a multidisciplinary treatment approach capable of clipping and coiling is necessary for the comprehensive management of patients. Again, in the spirit of partnership and collaboration, the Joint AANS/CNS Cerebrovascular Section has worked with our parent organizations, the AANS and CNS, to team up with the Cerebrovascular Coalition (CVC) which represents the Joint AANS/CNS Cerebrovascular Section, American Academy of Neurology (AAN), American Society of Neuroradiology (ASNR), Society of Neurointerventional Surgery (SNIS) and the Society of Vascular and Interventional Neurology (SVIN), to propose an increase in the minimum case volume requirements and to include a requirement for both clipping and coiling for aneurysmal SAH for CSCs. A new Technical Advisory Panel (TAP) was convened by the Joint Commission with Judy Huang, Charles Prestigiacomo, Babak Jahromi, and myself representing the Joint Cerebrovascular Section, and Cameron McDougal representing the SNIS. The TAP after deliberation and compromise recommended revising their volume targets for aneurysm and SAH to require hospitals perform at least 10 aneurysm clippings, 20 aneurysm coilings, and treat 35 aneurysmal SAH patients per year. The Joint Commission has delayed the implementation of these revised standards, despite the recommendation of the TAP, so the Joint AANS/CNS Cerebrovascular Section has again teamed up with the CVC to urge the Joint Commission to adopt these minimum case volume standards for aneurysmal SAH.

Guidelines: In the current era of medicine, evidence-based guidelines are increasingly important to improve the quality and safety of treatment for our patients. The patients we as cerebrovascular and endovascular neurosurgeons take care of can be some of the most complex and critically ill, posing challenging treatment decisions and demanding surgical technique. The Joint AANS/CNS Cerebrovascular Section, through our parent organizations, has teamed up with the American Heart Association to develop, write, peer review and endorse important guidelines documents for our field. The following is a brief list of just some of many guidelines that the Joint AANS/CNS Cerebrovascular Section is working on:

1. AHA/ASA Guidelines on the Management of Cerebral and Cerebellar Infarction with Swelling.
2. AHA/ASA Guidelines on the Prevention of Stroke in Women.
3. AHA/ASA Guidelines for Prevention of Stroke in Patients with Ischemic Stroke or Transient Ischemic Attack (Secondary Prevention).
4. AHA/ASA Guidelines on Palliative and End-Of-Life Care in Stroke.
5. AHA/ASA Guidelines on Risk of Cervical Arterial Dissection after Cervical Manipulation Including Chiropractic Manipulative Therapy.
6. AHA/ASA Guidelines for the Primary Prevention of Stroke.
7. AHA/ASA Guidelines for the Management of Spontaneous Intracerebral Hemorrhage
8. Upcoming: AHA/ASA Guidelines for Management of Unruptured Intracranial Aneurysms.
9. Upcoming: AHA/ASA Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Thrombolysis.
10. Upcoming: American Association of Blood Banking (AABB): Platelet Transfusion Guidelines.

I look forward to the coming year as your chair of the Joint AANS/CNS Cerebrovascular Section. I pledge to work in partnership and collaboration with our colleagues in our sister societies to advance the greater interests of our members and our field.

Sincerely,

Brian Hoh MD, FAANS, FACS, FAHA

Washington, DC Update

Katie O. Orrico, Director, Washington Office
AANS/CNS

Rep. Pat Tiberi (R-OH) and Richard Neal (D-MA) introduced a resolution that would designate Sept. 2014 as “National Brain Aneurysm Awareness Month.” This came on the heels of a similar resolution (S. Res. 353) introduced by Sen. Ed Markey (D-MA) in February 2014.



SECRETARY'S MESSAGE



The AANS/CNS Section on Cerebrovascular Surgery is proud to report that 2014 has truly been an outstanding year. The activity of the Section has continued to increase in both scope and strength. The treatment of cerebrovascular disease is rapidly evolving and the Section is privileged to represent the neurosurgical community through these exciting times.

We are excited for our upcoming annual meeting in Nashville, TN. The AANS/CNS Joint Cerebrovascular Section will continue its strong partnership with the Society of NeuroInterventional Surgery (SNIS) in planning and executing the annual meeting. The collaborative environment created at this joint meeting is a wonderful one to participate in, and helps both society's advance their missions. This year Dr. William Mack will lead the SNIS program committee team. We are also particularly excited about this year's new partnership with the European Association of Neurological Surgeons, who will assist in meeting planning and who will doubtless bring great insight and learning to the table with their perspectives and experience from "across the pond". Dr. Mika Niemela will represent the EANS on the program committee.

The meeting is shaping up to have a fantastic program that is comprehensive, innovative, and thought provoking. Furthermore, Nashville should provide an outstanding venue for the meeting. The meeting will be held in the downtown area, close to world-class music venues, professional sports complexes, numerous fine and casual dining options, a multiple cultural activities – such as Schermerhorn Symphony Center and the Frist Center for the Visual Arts. In contrast to past meetings in the Nashville area, when the meeting was held outside of town, this upcoming year should truly provide an outstanding venue. Drs. Peter Nakaji and myself will serve as the co-chairs of this year's annual meeting.

Our Executive Council will be meeting once again at the CNS in Boston to continue our work on policy development, education, research, and collaboration with numerous organizations and specialists focused on cerebrovascular disease. We will review recent guidelines the section has contributed to while being guided by Dr. Kevin Cockroft, important projects evaluating coding and insurance coverage changes led by Dr. Henry Woo, and the continued work on developing a national outcomes database for cerebrovascular surgery led by Dr. Sander Connolly.

Drs. Bendok and Siddiqui continue their work on the development of a Cerebrovascular Subspecialty Module for the Maintenance of Certification Exam of the American Board of Neurological Surgery. This will also result in an updated Self-Assessment in Neurological Surgery (SANS) Exam and possibly a

written manuscript as a study guide.

We also look forward to our continued educational efforts. We have developed a continuum of endovascular and cerebrovascular training in order to provide residents level-appropriate care over the course of their training. There is a junior resident cerebrovascular exposure course, held annually at the AANS and run by Drs. Veznedaroglu and myself. There is next a senior resident course held annually at the MERI, run by Drs. Veznedaroglu and Arthur. There then is a pre-fellowship bootcamp held in Jackson Hole, prior to the Cerebrovascular Complications Conference, run by Dr. Andy Ringer. Finally, there are two different fellows courses, with complimentary purposes. The first is a hotel based course run jointly by the CV Section and SNIS to provide high level didactic teaching and technology exposure, this year the CV Section leadership is represented by Dr. William Mack. The second is an animal and cadaver based hands on program that occurs at the MERI and run by Drs. Veznedaroglu and Arthur. This time-line of courses has been successful beyond expectations and plans are in place to continue and expand the opportunities provided by this coordinated educational plan.

Other exciting new opportunities include the development of a Clinical Trials Advisory Committee to aid our members in the development, approval, and implementation of new clinical trials drawing from the experience of our successful clinician researchers, headed by Robert Friedlander and Bob Carter. Additionally, our first International Liaison to the CV Section, Dr. Mika Niemela an academic open cerebrovascular surgeon at the University of Helsinki, Finland will keep us informed of the educational and collaborative opportunities outside North America.

Our website: <http://www.cvsection.org/> continues improve by leaps and bounds under the direction of Babu Welch. If you haven't visited the site recently, we recommend you do. There are many new functions and resources for our membership.

The CV Section is a dynamic organization committed to advocating for patients and advancing the care of cerebrovascular disease worldwide. We encourage all neurosurgeons and cerebrovascular practitioners to become involved in our educational, research and advocacy activities. It is only through our dedicated membership's efforts that we will continue to provide these important opportunities.

J Mocco, MD, MS

TREASURER'S MESSAGE



I am happy to report that the Joint Cerebrovascular Section continues to be in excellent financial standing. The JCVS/SNIS Joint Annual Meeting in San Diego, CA was a tremendous success - combining an outstanding scientific program and strong discourse among speakers and participants while also being financially successful. We very much look forward to the upcoming JCVS/SNIS Joint Annual Meeting in Nashville, TN and hope that you will join us. The fundraising committee is very active in the section's efforts towards raising the funds necessary for this meeting, and is also making great progress towards funding the Robert Dempsey Resident Award in Cerebrovascular Research, the Brain Aneurysm Foundation Christopher C. Getch Chair of Research sponsored by the JCVS, and the DePuy Synthes Cerebrovascular Research award for 2015. These fundraising efforts are made possible through generous sponsorship from our industry partners. A special thanks goes to Drs. Ray Turner, Mustafa Baskaya, J Mocco, and Alex Khalessi for their critical roles in these fundraising efforts. As in previous years, the JCVS plans to contribute \$10,000 to the Washington committee and \$20,000 to the AANS NREF in 2015.

Greg Zipfel, MD

MEETING UPDATES

NICHOLAS C. BAMBAKIDIS MD, FAANS, FAHA CV SECTION PROGRAM CHAIR

J MOCCO MD, MS CV SECTION PROGRAM CO-CHAIR

CV SECTION ANNUAL MEETING (2014)

The AANS/CNS Joint Cerebrovascular Section Annual Meeting with the theme of “Adaptive Ingenuity” was held this past February in beautiful San Diego. As with last years meeting, it was held immediately prior to the International Stroke Conference and in conjunction with the SNIS Endovascular Stroke Conference. More than 500 registrants attending this meeting and contributed to its record-setting attendance over 2 days. Highlights of the annual meeting included the Chair’s address by Dr. Robert Friedlander, the Luessenhop Lecture by Dr. Christopher Ogilvy, spirited debate sessions which included interdisciplinary leaders in the stroke and cerebrovascular field, and stroke trial updates led by primary investigators from around the world. Our international partners, the Society of Brazilian Neurosurgery, also were very active in participating in the meeting with a wonderful group of lectures by Dr. Evandro de Oliveira, Dr. Felix Pahl, and Dr. Jean de Oliveira. Financially the meeting was equally successful and will significantly aid the CV Section in fulfilling its educational and advocacy missions in the coming year. The Scientific Program Committee and the invited lecturers and faculty were instrumental in the success of our Annual Meeting. Thanks also to our SNIS co- Chair Dr. Michael Kelly, the SNIS Scientific Program Committee, and Marie Williams from the SNIS. Without their immense organizational help the meeting would not be possible and we look forward to continued cooperation in hosting the premier educational event of the Joint CV Section.

International Stroke Conference

Kevin Cockroft, William Mack, Babu Welch

The 2014 International Stroke Conference in San Diego, CA was very successful. The scientific program featured two sessions planned by the CV section planning committee. The first session, entitled “Controversies in the Management of Acutely Ruptured AVMs,” was moderated by Kevin Cockroft and Alex Khalessi and featured talks by Chris Ogilvy and Michael Lawton with a special tribute to William Young, MD. The second session was entitled “ Management of Dural Venous Sinus Thrombosis” and was moderated by William Mack, and Chirag Gandhi. The program featured talks by Charlie Prestigiacomo and Felipe Albuquerque. Each session had standing room only attendance. Many other CV section members (over 30 in total) were selected and included as speakers at other plenary sessions and moderators of abstract presentations.

The 2015 International Stroke Conference is planned for February 11-13, 2015 in Nashville, TN following the CV section meeting. The program committee had a positive response after soliciting session topic proposals from CV section members. The SAH and Critical Care and Vascular Malformations sections will each have at least one planned speaker session in addition to abstract

presentations. The ISC program committee is currently in the final stages of topic selection. We encourage all CV section members to stay for the ISC following the CV section meeting.

CV Section Annual Meeting 2015

J Mocco MD, MS CV Section Program Chair

Peter Nakaji MD, CV Section Program Co-chair

The 2015 CV Section Annual Meeting will be held in Music City this upcoming year, Nashville, TN. Nashville provides a host of activities within walking distance of its brand new state-of-the-art convention center, including numerous famous music venues (including the Ryman Auditorium – “the high church of country music”), the Schermerhorn Symphony Center, the Frist Center for the Visual Arts, the Bridgestone Arena (home of the Nashville Predators), the Country Music Hall of Fame, and LP Field (home of the Tennessee Titans). More importantly the CV Section has an exciting agenda planned in conjunction with the SNIS and, for the first time, the EANS. Over a two-day program, participants will hear fascinating discussion on advanced cerebrovascular procedures, the current state of evidence for AVMs, and complicated decision making in challenging cerebrovascular cases. A high-quality selection of oral abstracts will provide insight into some of the most ground-breaking science currently being performed for cerebrovascular disease. We are excited about what will surely be an incredible meeting for our membership.

AANS CV Section Meeting (2015)

Peter Nakaji MD and Adam Arthur MD

The CV Section session planned for the Boston CNS meeting this October picks up on the theme of "A Question of Balance" to examine a range of specific clinical problems commonly confronted by cerebrovascular neurosurgeons. Starting at a new time on Monday morning, October 20, bright and early at 0700, the session will feature discussions on the best strategies for the treatment of small unruptured anterior circulation aneurysms, the treatment of AVMs, and selection of stenting versus endarterectomy. This year we are honored to have Dr. Ralph Dacey presenting the Drake Lecture. The second session will be Tuesday morning also beginning at 0700, with ten outstanding oral abstracts, including the Synthes award winner, "Treatment of Ruptured Anterior Communicating Artery Aneurysms: Equipose in the Endovascular Era" and the Galbraith Award winner, "Bilateral Failure of Cerebral Autoregulation is Related to Unfavourable Outcome After Subarachnoid Hemorrhage." We look forward to seeing the CV section membership in Boston for this provocative and educational program.

MERI Course

Adam Arthur MD

The AANS/SVIN/SNIS endovascular course for fellows will be held September 12-14, 2014 at the Medical Education and Research Institute (MERI) in Memphis, Tennessee. The AANS open and endovascular course for residents will be held November 13-15 at the MERI. Please email Adam Arthur (aarthur@semmes-murphey.com), Erol Veznedaroglu (ezevnedaroglu@capitalhealth.org), Mike Lawton (lawtonm@neurosurg.ucsf.edu) or Joni Shulman (jls@aans.org).

Technology Forum

Andrew F. Ducruet, M.D., University of Pittsburgh, PA

Despite recent advances in neuroendovascular device technology, broad necked bifurcation aneurysms continue to pose a significant challenge for the neuro-interventionalist. However, neuroendovascular devices and techniques are continually evolving to meet this challenge. Three recently introduced devices have shown promise in treating this type of aneurysm. Two of these devices are deployed within the aneurysm sac and incorporate properties of both flow diverters and traditional coils, whereas the third device represents a variation on the traditional intraluminal neck remodeling device. These devices are currently being marketed and evaluated in Europe but are not commercially-available in the United States at the present time.

The first device, the Woven EndoBridge (WEB) aneurysm embolization device (Sequent Medical, Aliso Viejo, CA) is an intrasaccular flow diverter designed for use in wide necked bifurcation and side-wall aneurysms. It is composed of a metallic mesh construct which is delivered within the aneurysm (Figure 1). WEB is designed to bridge the aneurysm neck to promote stasis and subsequent endothelialization. Although conceptually very different from currently available devices, it is deployed like a stent and expands to adhere to the wall of the aneurysm. It may also be completely recaptured, and when it is positioned appropriately, it is detached like a coil using an electrothermal system. As a completely intrasaccular device, it avoids need for antiplatelet medications and thus may be safely deployed in both ruptured and unruptured aneurysms. One additional advantage of this device is that it can be crossed with a microcatheter in order to deploy adjunctive coils if necessary.

There are currently 3 variations of the WEB device available: Web Dual Layer (DL), WEB single Layer (SL), and WEB Single Layer Sphere (SLS). WEB DL is available in diameters of 5-11mm and heights of 4-9mm and is designed for wide-necked bifurcation aneurysms. WEB SL (Diameter 4-9mm, height 3-7mm) and SLS (4-11mm) exhibit increased navigability which facilitates use in sidewall aneurysms as well. All three variations utilize a mix of wire diameters to balance compliance and porosity across varying sizes. The pore structure allows for 35-45% metal coverage, similar to that of existing endoluminal flow diverters.

WEB has undergone extensive clinical evaluation in Europe. Lubciz et al. [1] reported a single-center series in which 19 patients with 20 unruptured wide-necked bifurcation aneurysms were treated using WEB. Device placement failed in a single patient and adjunctive coiling was utilized in 4 cases. Two symptomatic ischemic events were noted (10.5%). At a mean follow-up of 6 months, complete or near-complete occlusion was observed in 89% (17/19). In a subsequent multi-center series in Europe, Pierot et al. [2] placed the WEB device in 33 patients with 34 MCA aneurysms. Sizing issues led to treatment failure in a single patient. WEB was deployed as a stand-alone treatment in 29/33 (90%), whereas adjunctive coiling and/or stenting was required in 4/33 (12%). Complications included a single intraoperative rupture (3.1%), but no mortality. In a short-term follow-up (2-12 months), 83% of aneurysms in this series remained adequately occluded. The most recent study by Lubicz et al. [3] reports a retrospective multi-center trial evaluating mid-term follow-up in patients treated with WEB-DL. Forty five patients with 45 bifurcation aneurysms were treated, 42 of which were unruptured. In 4 patients, an adjunctive stent was placed, and 2 patients necessitated additional treatment with coils. Good clinical outcome (mRS<2) was observed in 93% of patients. Adequate occlusion, defined as complete occlusion, opacification of the proximal recess, or small neck remnant) was observed in 30/37 patient (81%) at short term follow-up (median 6 months), and in 26/29 patients (90%) at midterm follow-up (median 13 months). Progressive recanalization was only seen in 2 patients (7%) at the midterm follow-up, and these patients both exhibited neck remnants at the immediate and short-term follow-up.

These series suggest that WEB affords safe and effective treatment of a class of aneurysms previously considered challenging for safe and durable endovascular treatment. There are, however, numerous limitations of this device in its current incarnation. The most obvious is the difficulty matching the device to the aneurysm size and shape, as WEB is available in limited sizes and currently works best in aneurysms with regular dimensions. Additionally, the device requires placement through a microcatheter of at least 0.027 inch in caliber and its navigability can be limited in tortuous vasculature.

A conceptually-similar intrasaccular device is offered by Nfocus Neuromedical (Palo Alto, CA) in Europe. LUNA Aneurysm Embolization System (AES) is a self-expanding, round-ovoid implant constructed from a double layer of 72 Nitinol wires which yields a pore size of 25 μm (Figure 2). Available sizes include 4.5mm – 8.5 mm.

LUNA AES for treatment of intracranial aneurysm-PMCF study is currently enrolling patients at 30 sites with a goal of 63 patients. This is a non-blinded, non-randomized trial with planned 12 month follow-up. Sourour et al. recently presented an oral abstract (Stroke 2014; 45: A125) reporting the use of this device in 50 patients with 51 aneurysms (47 unruptured, 4 ruptured). In 48 patients, a single device was used, and in 2 procedures placement failed and coiling was used. In 5 cases, LUNA placement was used with balloon assistance, and in a single case a stent was also deployed. Two significant complications occurred including an aneurysm perforation and a thromboembolism treated by intra-arterial thrombolysis. Clinical follow-up demonstrated one case of subarachnoid hemorrhage from a non-target aneurysm and one case of gastrointestinal bleeding. Immediate complete/near complete occlusion was observed in 13/49 (26.5%). At 6 month follow-up, complete/near complete was 70.8% (34/48). No parent vessel stenosis was seen, and no treated aneurysms bled.

Although this data appears promising, there remains limited clinical data to support the use of this device. As with WEB, sizing the LUNA device is difficult in irregularly-shaped aneurysms. Additionally, given the tight mesh, it is not possible to cross the device with a microcatheter if necessary to place coils. Finally, much like traditional flow diverters, immediate occlusion rate appears low, and longer follow-up is clearly needed.

In contrast to the two intrasaccular devices detailed above, a third new device approaches the problem of treating bifurcation aneurysms by modifying existing endoluminal neck remodeling technology to narrow the neck of a wide necked aneurysm and render it amenable to traditional coil embolization. The Barrel Vascular Reconstruction Device (Reverse Medical, Irvine, CA) is a barrel-shaped neck remodeling device designed for use in wide necked bifurcation aneurysms which has been approved in Europe since December of 2013. In April 2014, the Food and Drug Administration granted investigational device exemption, and a multi-center clinical trial is currently being planned in the United States.

Although there are no available published clinical reports of the use of this device, Barrel has been extensively evaluated in animal models. In a recent abstract presented at the SNIS annual meeting, Tateshima et al (JNIS 2013; 5(Suppl 2): A10) report their experience using this device in 16 Canine bifurcation aneurysms and 16 side wall aneurysms (Figure 3). Barrel VRD was found to be easily deliverable, and all embolizations were graded as acceptable with excellent coil packing densities. Coil protrusion was observed in 2/32 (6%), and small neck remnants were observed in 13/32 (41%). Follow-up angiograms performed at 1, 2, 3, and 6 months confirmed stability of coil mass and neck coverage. Three month histology demonstrated stable endothelialization at the aneurysm neck.

One advantage of the Barrel VRD is that it is deployed similar to a standard intracranial stent. Unlike the previously discussed devices which are designed to divert flow away from the aneurysm neck, Barrel does rely on placement of coils to achieve successful aneurysm occlusion. It should also be noted that



Figure 1

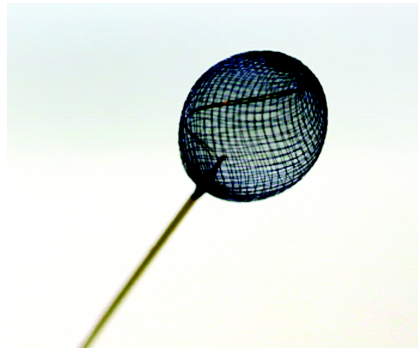


Figure 2

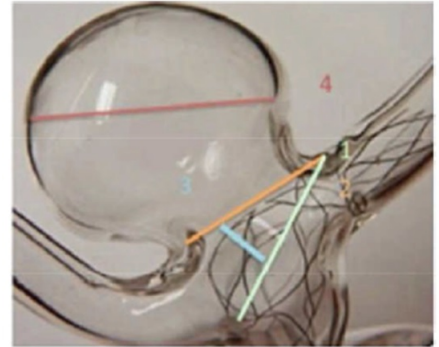


Figure 3

coil protrusion was observed in 6% of the preclinical cases reviewed above, and it remains to be seen how frequently this will be observed and whether this will pose a problem in future clinical use.

These three new devices represent part of the continually evolving landscape of endovascular techniques and have already revolutionized the treatment of challenging bifurcation aneurysms in Europe. These devices are examples of efforts to adapt existing theories and techniques towards new applications. Ultimately, the proportion of previously challenging aneurysms which can be effectively treated using endovascular techniques will continue to increase.

1. Lubicz, B., B. Mine, L. Collignon, D. Brisbois, G. Duckwiler, and C. Strother, WEB device for endovascular treatment of wide-neck bifurcation aneurysms. *AJNR Am J Neuroradiol*, 2013. 34(6): p. 1209-14.
2. Pierot, L., J. Klisch, C. Cognard, I. Szikora, B. Mine, K. Kadziolka, V. Sychra, I. Gubucz, A.C. Januel, and B. Lubicz, Endovascular WEB flow disruption in middle cerebral artery aneurysms: preliminary feasibility, clinical, and anatomical results in a multicenter study. *Neurosurgery*, 2013. 73(1): p. 27-34; discussion 34-5.
3. Lubicz, B., J. Klisch, J.Y. Gouvrit, I. Szikora, M. Leonardi, T. Liebig, N.P. Nuzzi, E. Boccardi, F.D. Paola, M. Holtmannspotter, W. Weber, E. Calgliari, V. Sychra, B. Mine, and L. Pierot, WEB-DL endovascular treatment of wide-neck bifurcation aneurysms: short- and midterm results in a European study. *AJNR Am J Neuroradiol*, 2014. 35(3): p. 432-8.

Technical Forum: ARUBA and Clinical Practice Impact Regarding Unruptured AVMs

Ketan R. Bulsara MD, Yale University, New Haven, CT

The February 2014 publication of a randomized trial of unruptured brain arteriovenous malformations (ARUBA) has generated significant debate across many specialities¹. The significance of the trial, being the first randomized study ever to address this issue with federal funding, is undermined by significant issues with trial design and interpretation of its findings^{2,3}. Yet, despite these known limitations, ARUBA is affecting clinical practice. With the general notion that the conclusions of ARUBA are not applicable to all AVMs, in the context of an active medical legal environment with reimbursement to a greater extent being tied in to randomized clinical studies, this trial has the potential to undermine optimal patient care. Efforts such as the initiation of the Clinical Trials Advisory Committee by Dr. Bob Carter and Dr. Robert Friedlander are important in ensuring that we are more involved in designing clinical trials whose results will ultimately affect our clinical practice. For this technical forum, three perspectives are presented on the impact of ARUBA on clinical practice. The author perspectives are from Emory, New York University School of Medicine, and Stanford.

1. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. *Lancet*. 2014 Feb 15;383(9917):614-21.
2. Amin-Hanjani S, Albuquerque FC, Britz G, Connolly ES, Gunel M, Lavine SD, Lawton MT, MacDonald J, Ogilvy CS, Prestigiacomo CJ. "Commentary: Unruptured Brain Arteriovenous Malformations: What a Tangled Web They Weave." *Neurosurgery*, Aug;75(2): 195-92, 2014.
3. Bambakidis NC, Cockroft K, Connolly ES, Amin-Hanjani S, Morcos J, Meyers PM, Alexander MJ, Friedlander RM. "Preliminary results of the ARUBA study." *Neurosurgery*, Aug;73(2):E379-81, 2013.

ARUBA and Clinical Practice

Jonathon Grossberg, MD & C. Michael Cawley MD, FACS
Emory University, Atlanta GA

The results of "A Randomised Trial of Unruptured Brain Arteriovenous Malformations" (ARUBA) were recently published in *The Lancet* in February 2014.² The authors of the study concluded that medical management of patients with unruptured arteriovenous malformations (AVMs) is superior to surgical management for preventing major morbidity or mortality, such as stroke or death. While the study is technically a prospective, randomized, multi-center, intention-to-treat analysis, serious flaws in the

methodological details, including patient selection, prevent it from being the definitive study on the management of AVMs that it strives to be.

The first major limitation is the duration of patient follow-up. A mean follow-up period of 33 months is simply not adequate for study of this nature, which examines the complication rate of a one-time treatment for an otherwise life-long disease. The rationale for treating AVMs is that for the cost of a small, albeit real, upfront risk of a complication, the patient is provided with life-long protection against hemorrhage. Accordingly, any study of the risk-versus-benefit ratio of AVM treatment would not be expected to show a positive result for a number of years following treatment, much less during the 33-month follow-up period of the ARUBA study. For instance, although the surgical management group had a 20% (30.7% vs. 10.6%) absolute increase risk of stroke or death when compared to the medical group, the medical group still had a 2.2% annual rate of rupture. Accordingly, one would expect the medical management group to continue to have a 2.2% annual rate of rupture, which over ten plus years would likely surpass the risk of the surgical group.

The second major limitation is the number of patients enrolled. A total of 1740 patients were assessed for eligibility, but only 226 patients were actually enrolled and randomized. While 1014 patients did not meet the study's rigorous inclusion criteria, an additional 177 patients were treated outside of the study and 323 patients refused to provide consent for the study. Unfortunately, the study authors do not provide information on outcomes or AVM characteristics for these non-enrolled patients, who account for over two-thirds of the eligible patients for the study. It is difficult to make a sweeping statement regarding something as complex as AVM treatment from a study with a relatively small, and potentially biased, sample size.

The third major limitation is the type of treatment selected for the interventional arm of the study. Thirty of the 94 patients were treated with embolization alone, which, in our experience, likely exposed them to a higher risk of complications than treatment with neurosurgery, radiosurgery, or a combination thereof. Multiple studies have shown major complication rates between 8-11% for curative embolization.^{3,4} At our institution, which is similar to many other high volume institutions, we employ a multi-modality approach to brain AVMs; it is rare for brain AVMs to be treated by embolization alone. Accordingly, it is worrisome that nearly one-third of patients in the ARUBA study were treated with embolization alone. This observation brings further into question whether the study site inclusion criteria was too lax for the study. The study only required that sites self-report that their institution treated 10 AVMs per year in a multi-disciplinary team. There was no mention on whether all treatment modalities were commonly employed at all sites, and no mention of whether surgeon or proceduralist case logs or complication rates were examined by the study team. Albert Einstein once said: "Information is not knowledge." While the

ARUBA study does provide some additional information to the natural history of unruptured AVMs, it is dangerous to alter current treatment recommendations based on this flawed study. Unfortunately, as US health care gravitates toward evidence-based medicine, studies such as ARUBA will be doing patients a disservice by providing regulators with incorrect and potentially dangerous information. It falls upon the Neurosurgical community to conduct and publish rigorous studies, which prove the benefit of successful multi-modality AVM treatment.

1. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet. 2014 Feb 15;383(9917):614-21.
2. Katsaridis, Papagiannaki C, Aimar E. Curative embolization of cerebral arteriovenous malformations (AVMs) with Onyx in 101 patients. Neuroradiology. 2008 Jul;50(7):589-97.
3. Saatci I, Geyik S, Yavuz K, Cekirge HS. Endovascular treatment of brain arteriovenous malformations with prolonged intranidal Onyx injection technique: long-term results in 350 consecutive patients with completed endovascular treatment course. Journal of Neurosurgery. 2011 Jul;115(1):78-88.

ARUBA and practice impact regarding unruptured AVMs

Zumofen DW, Potts MP, Nossek E, Raz E, Shapiro M, Kondziolka D, Riina HA
New York University School of Medicine, New York, NY, USA

Unruptured arteriovenous malformations (AVMs) of the brain harbor an annual rupture risk of 2-4%.¹ Mortality after a first hemorrhage is over 10%,² and when left untreated, up to 30% of patients will suffer from a permanent neurologic deficit by 20 years.³ Given this perilous natural history, many neurosurgeons opt to treat unruptured AVMs, accepting the upfront risks of treatment in order to prevent future AVM-related morbidity. The individual complexity of AVMs and the multiple treatment modalities available, however, make it difficult to know just what the upfront risks of curative treatment vs. medical management are. While retrospective series of individual treatment modalities have shown excellent outcomes, especially with low Spetzler-Martin grade⁴ AVMs, treatment practices and experience vary widely.^{5,6} With this in mind, the ARUBA (A Randomized Trial of Unruptured Brain AVMs)⁷ trial sought to compare a strategy of medical management with or without surgical, radiosurgical, endovascular, or multimodal intervention for a composite outcome of death or symptomatic stroke (hemorrhagic or ischemic). This study was designed to test the superiority of medical management alone and was stopped early by the Data and Safety Monitoring Board when the

second planned interim analysis reached a statistically significant difference between the two treatment arms. At this point, with outcome data for 223 patients and a mean follow-up of 33 months, the primary outcome was reached in 10.1% of the medical management group and 30.7% of the intervention group.

Much publicity has surrounded the ARUBA trial and its results were awaited with anticipation by the cerebrovascular community. Since its publication last November, ARUBA has been a pervasive topic at our own institution's multidisciplinary weekly cerebrovascular conference, where the management decisions for unruptured AVM patients take place. In this multidisciplinary fashion, each unruptured AVM case is presented and discussed, and treatment recommendations are made based on balancing the perceived natural history risk of each individual AVM with the case-specific estimated risks of preventive intervention. While ARUBA sought to facilitate such a discussion, and indeed it did provide a more modern assessment of the short-term natural history of conservatively-treated unruptured AVMs, the shortcomings of the study have prevented us from applying its conclusions directly to our practice. We feel that the ARUBA trial failed in its very purpose, which was to guide our decision-making in those cases where both expectative observation and preventive intervention appear plausible. (**Fig. 1 and Fig. 2**). Instead, we continue to base our management decisions on the published risks of individual treatments, largely on our own group's personal experience and outcomes, and various patient-specific factors that are difficult to capture in a clinical trial.

In our opinion, the authors of ARUBA should be complimented for their inquisitiveness, but deserve critique for the study's following intrinsic limitations: *Enrollment bias*. ARUBA was originally designed to enroll 800 patients but after poor accrual was revised to a goal of 400 patients. Ultimately, only one-third of the 1740 screened patients were deemed eligible with an additional 323 refusing participation and 177 being treated outside of the randomization process. This resulted in less than one patient randomized per active center per year. While this number speaks to the rarity of unruptured cerebral AVMs, it also raises the concern of selection bias. The AVM characteristics and treatment modality of patients treated outside of the randomization process were not reported. It is therefore not known how well the ARUBA results can be generalized to the overall population of unruptured AVMs. *Treatment bias*. AVMs are a heterogeneous group of lesions with multiple factors known to affect the risk of both rupture and treatment.⁸ Similarly, the safety and efficacy of various AVM treatment modalities are heavily dependent upon operator experience as well as technological advancements.

Unfortunately, ARUBA was not powered to stratify the risks of various AVM characteristics or treatment modalities. Furthermore, there were no treatment guidelines for participating centers to follow or even a credentialing process to ensure adequate experience with various treatments. It is therefore difficult to apply the ARUBA results to a given AVM type or treatment method. *Outcome bias.* The goal of preventative treatment for most AVMs is complete and permanent cure and the risk of AVM rupture after complete eradication can be reasonably estimated to be nearly zero. AVM cure must therefore be considered in the success of any intervention. Unfortunately, ARUBA did not report AVM cure rates in the interventional arm so it is not known if morbidity in that arm was related to treatment or simply the natural history of incompletely treated AVMs. *Follow-up bias.* Perhaps the most significant criticism with ARUBA is that the trial was halted early with only 33 months of follow-up. It is not surprising that the interventional arm had a higher short-term morbidity during this relatively brief follow-up time. The treatment of AVMs seeks to eliminate a lifetime of rupture risk and patients in the interventional arm were exposed to the upfront risk of treatment without sufficiently long follow-up to see a potential benefit. Conversely, patients in the medical arm were exposed to only a fraction of their lifetime rupture risk. *Management decision making bias.* Clinical trials are designed around their primary outcome. In ARUBA, patients were randomized to observation versus the treating teams' opinion as to what the optimal intervention might be for that person. In different parts of the world that opinion can vary widely. This concept was prominent at the recent 2nd World AVM Congress in Nancy, France. Until more consensus is reached regarding AVM management, outcomes will continue to vary widely, not just related to treatment technique, but also in function of management decision making. Here at the New York University School of Medicine, we believe that the lifetime rupture risk of an unruptured AVM warrants treatment in patients with more than 10 years of life expectancy. We typically recommend surgery for the treatment of low Spetzler-Martin grade⁴ AVMs while radiosurgery is reserved for higher grade, deep-seated, or eloquent lesions. Embolization is most commonly used as an adjunct to surgical resection, with rare instances when we believe an AVM can be completely cured with embolization alone.⁹ Finally, we do not as a rule recommend pre-radiosurgical embolization, but in certain circumstances have performed embolization following radiosurgical treatment.

In conclusion, it is important to acknowledge the great effort behind ARUBA. Few cerebrovascular conditions have had the benefit of a randomized trial to help guide management, and the

investigators should be commended for organizing such a complex and sizable trial. The critiques discussed here should not be considered a failure of the trial, but instead as potential lessons on how to better design future studies of AVM management. Given the complexity of AVMs and AVM management, we believe that future studies should focus on specific AVM subtypes (i.e., low-grade or eloquent) and be limited to a single interventional modality or treatment algorithm. Importantly, any study comparing conservative management to intervention must have long-term follow-up of at least 10 years in order to have a meaningful impact on AVM management. We feel that only in this way can the complexities of AVM management be better understood.

Figure annotations

Figure 1: (Illustrative case 1) This 63 year-old right-handed female underwent brain imaging for tremor. Axial T2 weighted MRI (A/B) revealed an AVM nidus in the left angular gyrus region. Left internal carotid artery angiogram in PA (C) and lateral projection (D) demonstrated arterial supply by a dilated branch of the left middle cerebral artery and venous drainage toward the superior sagittal sinus and inferiorly toward the Vein of Labbe. Therapeutic strategies include expectative observation as well as combinations of embolization, resection, and stereotactic irradiation.

Figure 2: (Illustrative case 2) This 33year-old right-handed male underwent brain imaging for headaches. Axial gadolinium enhanced T1 weighted MRI (A/B) revealed an AVM nidus in the left superior temporal sulcus region. Left internal carotid artery angiogram in PA (C) and lateral projection (D) demonstrated arterial supply by a dilated branch of the left middle cerebral artery and venous drainage superficially towards the vein of Trolard to the superior sagittal sinus and anteriorly inferiorly towards the Sylvian venous system. Therapeutic strategies include expectative observation as well as combinations of embolization, resection, and stereotactic irradiation.

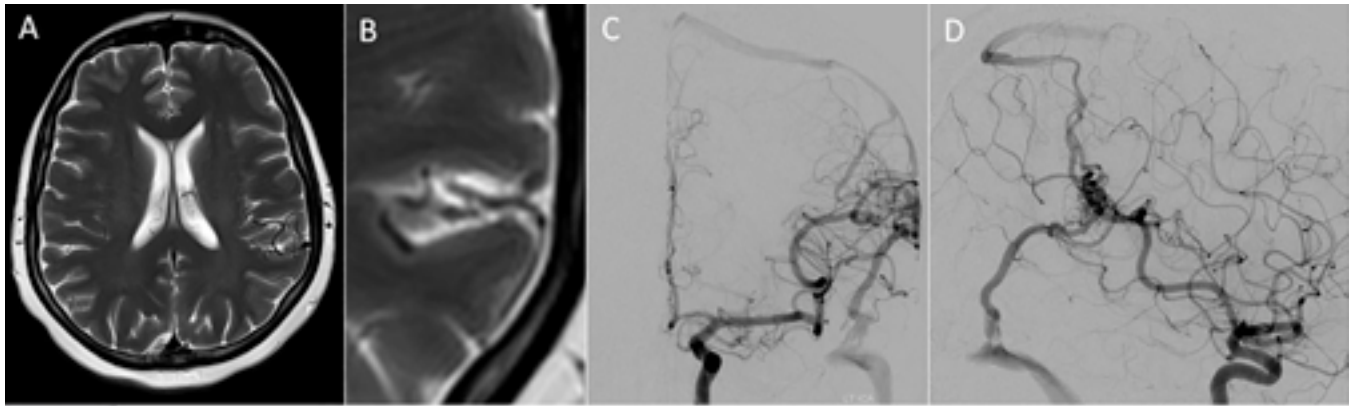


Figure 1

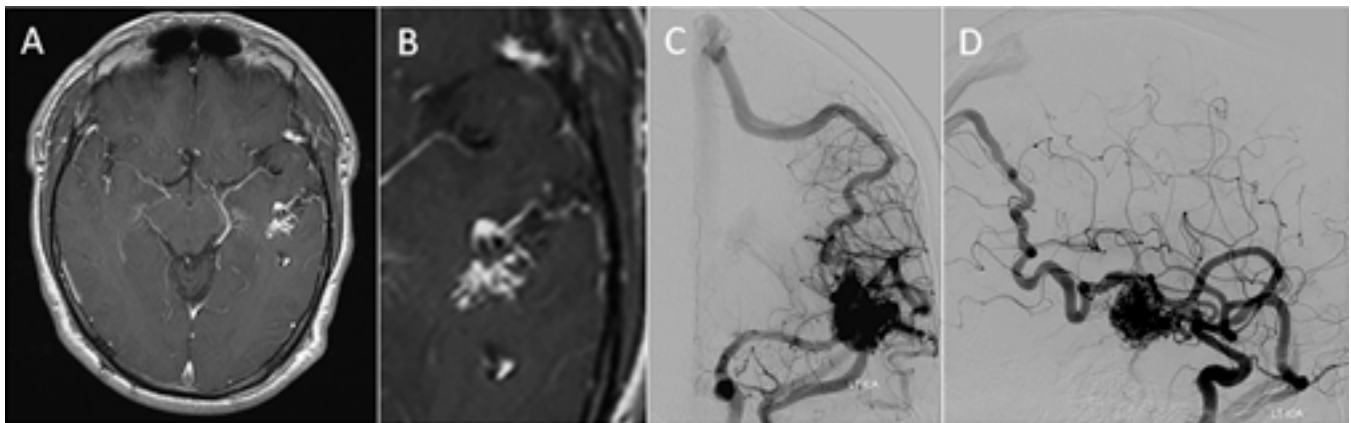


Figure 2

References

1. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. *Journal of neurosurgery*. Sep 1990;73(3):387-391.
2. ApSimon HT, Reef H, Phadke RV, Popovic EA. A population-based study of brain arteriovenous malformation: long-term treatment outcomes. *Stroke; a journal of cerebral circulation*. Dec 2002;33(12):2794-2800.
3. Crawford PM, West CR, Chadwick DW, Shaw MD. Arteriovenous malformations of the brain: natural history in unoperated patients. *Journal of neurology, neurosurgery, and psychiatry*. Jan 1986;49(1):1-10.
4. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. *Journal of neurosurgery*. Oct 1986;65(4):476-483.

5. Kano H, Lunsford LD, Flickinger JC, et al. Stereotactic radiosurgery for arteriovenous malformations, Part 1: management of Spetzler-Martin Grade I and II arteriovenous malformations. *Journal of neurosurgery*. Jan 2012;116(1):11-20.
6. Morgan MK, Rochford AM, Tsahtsarlis A, Little N, Faulder KC. Surgical risks associated with the management of Grade I and II brain arteriovenous malformations. *Neurosurgery*. Apr 2004;54(4):832-837; discussion 837-839.
7. Mohr JP, Parides MK, Stapf C, et al. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. *Lancet*. Feb 15 2014;383(9917):614-621.
8. Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D. Factors that predict the bleeding risk of cerebral arteriovenous malformations. *Stroke; a journal of cerebral circulation*. Jan 1996;27(1):1-6.
9. Sahlein DH, Mora P, Becske T, Nelson PK. Nidal embolization of brain arteriovenous malformations: rates of cure, partial embolization, and clinical outcome. *Journal of neurosurgery*. Jul 2012;117(1):65-77.

ARUBA and Clinical Practice

Robert L. Dodd, MD, PhD, Michael P. Marks MD, Gary K. Steinberg MD, PhD

Stanford University, Stanford, CA

Considerable controversy exists surrounding the best treatment for unruptured brain arteriovenous malformation (AVMs). Whether a patient harboring such a lesion should undergo open microsurgery, stereotactic radiosurgery, endovascular embolization, a combination of these, or conservative observation, currently depends on the evaluating physician, specific center expertise, morphologic characteristics of the lesion, and patient preference. Such variability in treatment algorithms may afford an excellent opportunity for a prospective, multicenter, randomized trial to evaluate outcomes. The ARUBA trial was the first and only such attempt to examine this disease in this manner; and since the recent publication of the trial results⁴, there has been and will likely continue to be, debate about how to interpret the results, and what insights the results add. The ARUBA authors concluded that the trial demonstrates superiority of conservative medical management over any intervention for unruptured brain AVMs in the short term. Others assert that the trial was poorly designed, unpowered, and provides little evidence that would alter current practice patterns in North America. Indeed, while all seem to agree that an evidence-based approach is needed for this clinical challenge, significant discrepancies exist regarding the degree of clinical equipoise to support patient randomization⁵, or how that randomization should be performed. Furthermore, it is unclear what effect the ARUBA trial will have on the current medico-legal environment, and if any such effect will change sentiments regarding equipoise.

IMPETUS

The fundamental question raised by the ARUBA trialists, was whether the natural history of hemorrhage for previously unruptured brain AVMs, exceeds the known risk of complications related to their treatment. For at least two reasons evident in the ARUBA trial, this remains a difficult hypothesis to test. The first relates to the heterogeneity of the disease. Typically found in young adults, brain AVMs are uncommon congenital lesions consisting of thin-walled dysplastic blood vessels shunting arterialized blood into draining veins without an interposed capillary bed. Though they may share common aspects of biology, their phenotype is variable, dependent in part on lesion size, location, and morphological characteristics. With prevalence in the general population estimated at 0.01%¹⁵⁻¹⁷, these lesions can lie dormant without symptoms, cause seizures, ischemia, headaches or rupture. Indeed intracranial hemorrhage from brain AVMs accounts for 2% of all strokes¹⁵⁻¹⁷, and a much higher percentage in young people in whom other stroke risks factors are often absent.

Natural history data from both prospective and retrospective observational studies of unruptured brain AVMs estimate hemorrhage rates that range from 1% to 4% per year, with a combined severe neurological disability and death rate between 10-34% for each hemorrhage^{1,2}. In addition, the actual risk in certain patient subgroups maybe increased by risk factors such as size, location, intranidal aneurysms, venous outlet stenosis, age, and pregnancy. While this alone infers impetus for potential therapy of unruptured brain AVMs, some acknowledging this heterogeneity suggested that certain AVM subgroups may also have a more benign natural history; and cautioned against the hazards of treatment^{2,3}.

The second reason the above hypothesis is difficult to test relates to variability in treatment. Just as the hemorrhage risk varies for different brain AVMs, so do the risks of treatment. Treatment for brain AVMs is primarily aimed at the complete eradication of the vascular nidus, and includes open microsurgery, stereotactic radiosurgery, and endovascular embolization. The efficacy and risk profile of therapy varies with the AVM location, size and morphology. In addition efficacy and risk may vary with each treatment modality, as well as with specific treatments within a given modality (e.g., embolization with PVA, nBCA, or Onyx)¹³. Small superficial AVMs in the nondominant frontal lobe can be completely excised with low risk providing an effective cure, yielding a future hemorrhage rate of zero. Conversely, a small deep AVM in the pons can be treated with effectively with radiosurgery, but may take 3 years to obliterate, having the same bleed risk of an untreated lesion for the duration of time until cure. A moderate sized left temporal lobe AVM with deep venous drainage and intranidal aneurysms may have a greater hemorrhage risk than either of the two prior lesions, however the treatment risk are also increased.

THE ARUBA TRIAL

The trial was conducted by 39 centers in nine countries and screened 1740 patients between April 2007 and April 2013, comparing the effectiveness of medical management plus interventional therapy (neurosurgery, radiosurgery, or endovascular embolization) to medical management alone⁴. Of the 726 patients with unruptured brain AVMs that were deemed eligible, 226 were randomized to either medical management (n=110) or some form of interventional treatment at the discretion of the treating institution

(n=116). The primary endpoint was death or stroke, and the secondary endpoint was death or disability at 5 years. Enrollment was halted at 33 months after a planned interim analysis, when data from 223 patients was available demonstrating better outcomes in the medically managed group compared to those who underwent interventional therapy⁴.

THE INTERPRETATION

With sponsorship from the NIH/NINDS, publication in the Lancet⁴, and being the first of its kind study for brain AVMs, the results of the ARUBA have been widely disseminated, and have led many clinicians to conclude that observation of unruptured AVMs is superior to all forms of intervention including microsurgical excision¹⁴. For many reasons this interpretation exaggerates the trial results. As detailed above, brain AVMs despite common biology, vary considerable in their clinical presentation, degree of symptoms, and risk of hemorrhage. Just as varied are the efficacy and risk of different therapies. To conclude intervention is inferior to conservative management for unruptured AVMs based on the 91 patients in the ARUBA intervention group who actually received therapy with 4 different AVM grades (SMG I-IV), and 6 different combinations of treatments, seems premature. Indeed the initially planned enrollment of 800 patients was revised to 400 after poor recruitment, and having the trial stopped prematurely with only having 91 patients to initiate interventional treatment, means the study's sample size is severely underpowered to address any significant question concerning interventions.

Most Spetzler Martin grade I AVMs and many grade II AVMs can be safely cured with surgery alone with very low risk by surgeons with experience^{18,19}. Only 5% of the ARUBA interventional group received this therapy at the time of publication (n=5). One ARUBA author suggested the trial results were mainly influenced by the event rates in grades II and III AVMs³, the majority of which occurred in the first 6 months⁴, a time period unlikely related to radiosurgical intervention. While not presented, this likely reflects a 15-30 fold higher rate of endovascular embolization complications than previously published retrospective analysis from experienced centers¹³. Variability also exists in the agent used for embolization, some of which require exceptional expertise, rarely achieve complete obliteration, and may risk hemorrhage if venous outflow is obstructed or blood flow is shunted to a more fragile nidus area.

While no trial is perfect⁶, particularly when studying rare conditions, there are several possible sources of systematic selection bias in the ARUBA trial, potentially favoring conservative management. First, only 31% (226 of 726) of the initially screened eligible patients were randomized in the trial. The remainder, either refused participation (45%) or were treated outside of the trial (24%), both with unknown results. Second, the short follow up interval biases outcome as the stroke risk plateaus after two years following intervention, but continues to increase with time following medical management. Third, nonsurgical intervention does not offer short-term cure of brain AVMs. Therefore comparing embolization or radiosurgery alone in the less than 36 month follow-up period of this trial would likely only result in a hazard ratio that favored conservative treatment, as any event in the interventional group adds to the natural history of the incompletely treated AVM nidus. Fourth, the definition of a stroke defined as "any new focal neurological deficit, seizure, or new onset-headache" associated with imaging findings⁴; overestimates treatment morbidity. Better outcome measures would have been evidence of

bleeding or infarct associated with a new neurological deficit, and with the resultant disability graded using standard measures employed in stroke trials.

One clear result from ARUBA is that the annualized hemorrhage rate of patients with AVMs followed without intervention was 2.2% (95% CI 0.9–4.5) overall⁴, consistent with prior estimates. This however, does not take into account possible increased risks in particular subgroups.

Since 1987 we have treated at Stanford more than 1150 patients with intracranial AVMs. Currently at our institution this trial has affected our practice predominantly in the additional time it takes to review treatment options with patients, at which time we provide our published retrospective analysis of outcomes and adverse events at our center^{7-13, 21}. In general for patients under 60 with unruptured Spetzler Martin grade I AVMs, who are good surgical candidates, microsurgical resection is offered. For grade II AVMs either microsurgery or radiosurgery maybe offered depending on the eloquence or deep location of the nidus. Spetzler Martin grade III AVMs require more thought based upon patient and AVM specific characteristics. While symptomatic patients are typically offered multi-modality therapy including adjuvant endovascular embolization, some asymptomatic patients are counseled to have conservative observation. Grade IV and V unruptured AVMs are challenging to manage regardless of the choice, and many more patients in this group are followed conservatively. Those that undertake intervention (primarily young patients), typically have a combination of treatments and it is understood that it may take many years to successfully obliterate these AVMs. Endovascular intervention is directed towards intranidal aneurysms or difficult to access areas of the AVM nidus, with the goal to reduce the size of the lesion for definitive therapy.

The ARUBA trial poses similar discussions such as those had by neurointerventionalists following the early termination of the IMS III trial²⁰. Most endovascular specialists doubted there was equipoise to randomize acute ischemic stroke patients to mechanical thrombectomy versus medical management with IV tPA, because of the benefits of vessel recanalization from prospective studies with historical controls. Now that the climate has changed, with some large insurance companies questioning the efficacy of treatment, demanding level I evidence, there is a growing shift in the balance of clinical equipoise. These same issues may affect the interventional management of unruptured brain AVMs. We hope that medical-legal and reimbursement considerations do not adversely influence our judgment in offering the best treatment for our AVM patients.

REFERENCES:

1. Ondra SL, Troupp H, George ED, Schwab K. The natural history of symptomatic arteriovenous malformations of the brain: a 24-year follow-up assessment. J Neurosurg. 1990 Sep;73(3):387-91.
2. Stapf C, Mast H, Sciacca RR, Choi JH, Khaw AV, Connolly ES, Pile-Spellman J, Mohr JP. Predictors of hemorrhage in patients with untreated brain arteriovenous malformation. Neurology. 2006 May 9;66(9):1350-5.
3. Mohr JP. Results of ARUBA are applicable to most patients with nonruptured arteriovenous malformations. Stroke. 2014 May;45(5):1541-2.

4. Mohr JP, Parides MK, Stapf C, Moquete E, Moy CS, Overbey JR, Al-Shahi Salman R, Vicaut E, Young WL, Houdart E, Cordonnier C, Stefani MA, Hartmann A, von Kummer R, Biondi A, Berkefeld J, Klijn CJ, Harkness K, Libman R, Barreau X, Moskowitz AJ; international ARUBA investigators. Medical management with or without interventional therapy for unruptured brain arteriovenous malformations (ARUBA): a multicentre, non-blinded, randomised trial. Lancet. 2014 Feb 15;383(9917):614-21
5. Cockroft KM, Chang KE, Lehman EB, Harbaugh RE. AVM Management Equipoise Survey: physician opinions regarding the management of brain arteriovenous malformations. J Neurointerv Surg. 2013 Dec 6.
6. Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?" Lancet. 2005 Jan 1-7;365(9453):82-93.
7. Pandey P, Marks MP, Harraher CD, Westbrook EM, Chang SD, Do HM, Levy RP, Dodd RL, Steinberg GK. Multimodality management of Spetzler-Martin Grade III arteriovenous malformations. J Neurosurg. 2012 Jun;116(6):1279-88.
8. Darsaut TE, Guzman R, Marcellus ML, Edwards MS, Tian L, Do HM, Chang SD, Levy RP, Adler JR, Marks MP, Steinberg GK. Management of pediatric intracranial arteriovenous malformations: experience with multimodality therapy. Neurosurgery. 2011 Sep;69(3):540-56;
9. Chang SD, Marcellus ML, Marks MP, Levy RP, Do HM, Steinberg GK. Multimodality treatment of giant intracranial arteriovenous malformations. Neurosurgery. 2007 Jul;61(1 Suppl):432-42
10. Kelly ME, Guzman R, Sinclair J, Bell-Stephens TE, Bower R, Hamilton S, Marks MP, Do HM, Chang SD, Adler JR, Levy RP, Steinberg GK. Multimodality treatment of posterior fossa arteriovenous malformations. J Neurosurg. 2008 Jun;108(6):1152-61.
11. Jayaraman MV, Marcellus ML, Do HM, Chang SD, Rosenberg JK, Steinberg GK, Marks MP. Hemorrhage rate in patients with Spetzler-Martin grades IV and V arteriovenous malformations: is treatment justified? Stroke. 2007 Feb;38(2):325-9.
12. Fleetwood IG, Marcellus ML, Levy RP, Marks MP, Steinberg GK. Deep arteriovenous malformations of the basal ganglia and thalamus: natural history. J Neurosurg. 2003 Apr;98(4):747-50.
13. Jayaraman MV, Marcellus ML, Hamilton S, Do HM, Campbell D, Chang SD, Steinberg GK, Marks MP. Neurologic complications of arteriovenous malformation embolization using liquid embolic agents. AJNR Am J Neuroradiol. 2008 Feb;29(2):242-6.
14. Kamel H. Intervention for unruptured brain AVMs proves very harmful in the short term. <http://www.jwatch.org>
15. Brown RD Jr, Wiebers DO, Torner JC, O'Fallon WM. Frequency of intracranial hemorrhage as a presenting symptom and subtype analysis: a population-based study of intracranial vascular malformations in Olmsted County, Minnesota. J Neurosurg. 1996 Jul;85(1):29-32.
16. Brown RD Jr, Wiebers DO, Forbes G, O'Fallon WM, Piepgras DG, Marsh WR, Maciunas RJ. The natural history of unruptured intracranial arteriovenous malformations. J Neurosurg. 1988 Mar;68(3):352-7.

17. Hofmeister C, Stapf C, Hartmann A, Sciacca RR, Mansmann U, terBrugge K, Lasjaunias P, Mohr JP, Mast H, Meisel J. Demographic, morphological, and clinical characteristics of 1289 patients with brain arteriovenous malformation. Stroke. 2000 Jun;31(6):1307-10.
18. Pik JH, Morgan MK. Microsurgery for small arteriovenous malformations of the brain: results in 110 consecutive patients. Neurosurgery. 2000 Sep;47(3):571-5
19. Heros RC, Korosue K, Diebold PM. Surgical excision of cerebral arteriovenous malformations: late results. Neurosurgery. 1990 Apr;26(4):570-7;
20. Broderick JP, Palesch YY, Demchuk AM, Yeatts SD, Khatri P, Hill MD, et al; Interventional Management of Stroke (IMS) III Investigators. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke. N Engl J Med. 2013;368:893–903.
21. Sinclair J, Marks MP, Levy RP, Adler JR, Chang SD, Lopez JR, Do HM, Bell–Stephens TE, Lim M, Steinberg GK: Visual field preservation following curative multi-modality treatment of occipital lobe arteriovenous malformations. Neurosurgery 57:655–667, 2005.

OPPORTUNITIES FOR FUNDING

AANS FELLOWSHIP/GRANTS

<http://www.aans.org/Grants%20and%20Fellowships.aspx>

CNS FELLOWSHIP/GRANTS

<http://w3.cns.org/education/grants2.asp>

AMERICAN HEART ASSOCIATION

http://my.americanheart.org/professional/Research/FundingOpportunities/Funding-Opportunities_UCM_316909_SubHomePage.jsp

BRAIN ANEURYSM FOUNDATION

<http://www.bafound.org/applying-research-grant>

THE ANEURYSM AND AVM FOUNDATION

http://www.taafonline.org/pr_grants.html

Calendar

October 18-22, 2014

CNS Annual Meeting
Boston, MA

February 9-10, 2015

Cerebrovascular Section Meeting
Nashville, Tennessee

February 11-13, 2015

International Stroke Conference
Nashville, Tennessee

May 2-6, 2015

AANS Annual Meeting
Washington, D.C.