



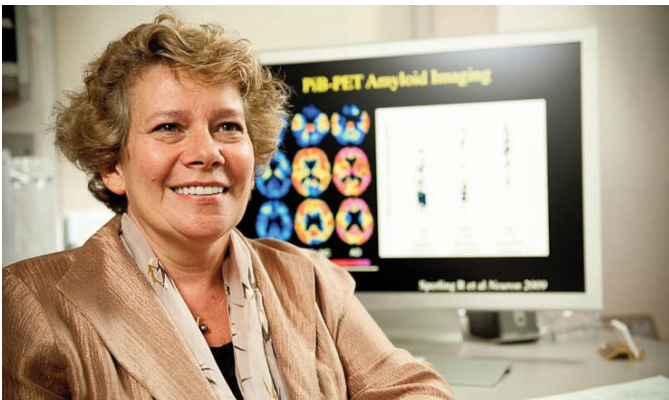
Neurology and Neurosurgery Advances

FALL 2014

Landmark Clinical Trial Evaluates Novel Approach to Alzheimer's Disease Prevention

Led by Principal Investigator Reisa Sperling, MD, Director of the Center for Alzheimer Research and Treatment at Brigham and Women's Hospital (BWH), the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) study is a landmark international clinical trial evaluating the efficacy of anti-amyloid treatment in preventing memory loss due to Alzheimer's disease among healthy older adults.

"This really is a novel study, where we are aiming to prevent or slow the onset of AD symptoms in healthy adults with amyloid-beta plaque by providing treatment much earlier in the disease process," said Dr. Sperling. "If the study shows a benefit in preventing or slowing cognitive decline in study



Reisa Sperling, MD, Director, Center for Alzheimer Research and Treatment

Contents

- Cover Landmark Clinical Trial Evaluates Novel Approach to Alzheimer's Disease Prevention
- Page 2 Advanced Minimally Invasive Options for Aneurysm and Stroke Patients
- Page 4 Brigham and Women's Hospital Launches the Ann Romney Center for Neurologic Diseases

participants, registration of a drug for preclinical AD could occur within the next five years."

Older individuals eligible for the A4 study have elevated levels of amyloid-beta plaque, as assessed by imaging, but currently are not exhibiting clinical signs of cognitive impairment or dementia. Participants in the study will be randomized to receive solanezumab, an investigational anti-amyloid agent, or a placebo.

Previous studies of solanezumab demonstrated some improvement in patients with mild symptoms of AD, however, no benefit was seen among patients with more advanced AD. The A4 study takes a very different approach aiming to reduce amyloid-beta buildup in the brain before symptoms appear.

A4 Study Participants

More than 60 sites in the United States, Canada, and Australia will screen more than 10,000 older individuals for the A4 study, which will ultimately enroll 1,000 participants. Supported by the National Institute on Aging – part of the National Institutes of Health – the A4 study is expected to last three years.

Healthy older men and women meeting the following criteria may be referred for evaluation for the A4 study:

- 65 to 85 years-of-age;
- Normal thinking and memory abilities;
- Spouse, family member, or friend who has weekly contact with the study participant and is willing to answer questions on a yearly basis.

Key Companion Study

A companion to the A4 study is the Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN) study. The LEARN study is a first of its kind study that will follow individuals who do not have elevated levels of amyloid-beta plaque

continued on page 3



Advanced Minimally-invasive Options for Aneurysm and Stroke Patients

Neuroendovascular surgeons at Brigham and Women's Hospital (BWH) are delivering newer catheter-based options and advanced hybrid approaches for patients with aneurysm and stroke.

"These procedures can typically be completed in a shorter period of time with less risk of complications and improved outcomes," said Ali Aziz-Sultan, MD, Section Chief of the BWH Center for Cerebrovascular Diseases and Section Chief of the Endovascular/Interventional Neuroradiology Service at BWH. "Using the hybrid operating suite, we also are able to combine minimally invasive endovascular and traditional neurosurgical approaches in one location to improve efficiency and reduce morbidity."

Several of the latest interventions offered include:

- **Flow-diverting stent** – Flow-diverting stents are placed across the aneurysm neck into the parent vessel, rather than the aneurysm sac. The stent impedes flow to the aneurysm, causing the aneurysm to shrink. This procedure can be completed much more rapidly than aneurysm clipping or coiling with less risk of complications in select cases. It also can be performed for select patients who are not eligible for clipping or coiling. Dr. Aziz-Sultan has performed more than 60 of these procedures throughout his career and has taught this approach across the country (see *Case Study One*);
- **Stent retrievers** – Mechanical embolectomy using the newest mesh stent retrievers in patients with acute ischemic stroke has seen recanalization rates as high as 90 percent, significantly greater than the rates seen with older devices. This is one of many options available to patients as part of comprehensive multimodality stroke care at BWH, which brings together neurosurgeons, stroke neurologists, and interventional neuroradiologists to evaluate and treat patients;
- **Hybrid approaches** – Dual-trained neurosurgeons with expertise in interventional neuroradiology and open vascular surgery at BWH use a hybrid operating suite to provide simultaneous multimodality treatment for stroke or aneurysm, including patients with intracranial hemorrhage and acute ischemic stroke (see *Case Study Two*).



Ali Aziz-Sultan, MD
Chief, Vascular/Endovascular Neurosurgery

Case Study One: Flow-diverting Stent for Aneurysm Embolization

Background:

A 53-year-old presented with ocular dryness and increased eye pressure. Magnetic resonance imaging revealed an incidental left-sided para clinoid aneurysm. Cerebral angiogram showed the aneurysm to be 7.2 mm (*Image 1*).

Approach:

The patient was taken to the neuro-angiographic suite at BWH. Frontal and lateral digital angiography was performed on the left carotid artery prior to deployment of the embolization device. The device was unsheathed and expanded to span from the distal ophthalmic segment of the internal carotid artery to the lacerum segment of the internal carotid artery, covering the aneurysm neck (*Image 2*). Repeat lateral digital angiography of the left internal carotid artery was performed during the embolization device deployment to confirm parent vessel patency and appropriate device sizing and placement. Flow within the aneurysm was notable for delayed, stagnant filling of the aneurysm. The patient tolerated the procedure and removal of the aneurysm without complications (*Image 3*).

Follow up:

The patient remained neurologically intact at baseline and was discharged on the second post-procedure day. She continues to be symptom free.

Image 1

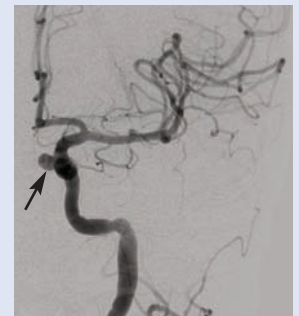


Image 2

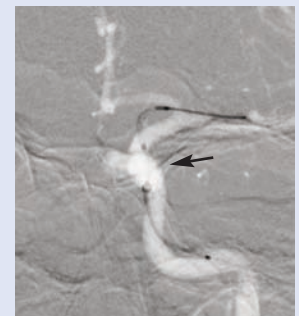
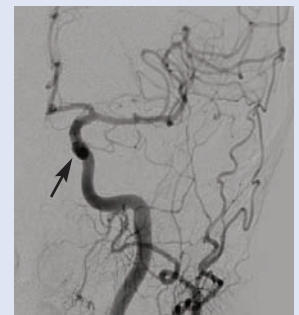


Image 3



Access and Information

For a consultation, more information on our neurology and neurosurgery services, or to refer a patient, please call our helpful and experienced Referral Coordinators at (617) 732-9894 or email bwhreferrals@partners.org.

Case Study Two: Hybrid Approach for Aneurysm Hemorrhage

Background:

A 27-year-old patient presented to a community hospital emergency room with a sudden severe headache and left-sided paralysis. Imaging showed a very large right-sided hemorrhage (*Image 1*) and a surgically difficult to access distal cerebral aneurysm (*Image 2*).

Approach: The patient was transferred to BWH, where he was rushed into the hybrid operating suite for emergent, life-saving treatment. Here, the patient underwent both coiling of the aneurysm (*Image 3*) and evacuation of the hematoma (*Image 4*). This treatment paradigm, which was specifically tailored to the patient, is traditionally completed in two separate environ-

ments – embolization in a radiology suite and hematoma evacuation in a traditional OR. Both procedures were completed in the hybrid operating suite in less than two hours. The reduced time to treatment prevented brain herniation and significant morbidity.

Follow up:

The patient's bleeding was controlled following obliteration of the aneurysm. Hematoma evacuation prevented a cerebral herniation. The patient has made a great recovery. He is able to move both sides of his body and ambulate. In addition, he is back to his communication baseline including following commands and home address recall.

Image 1

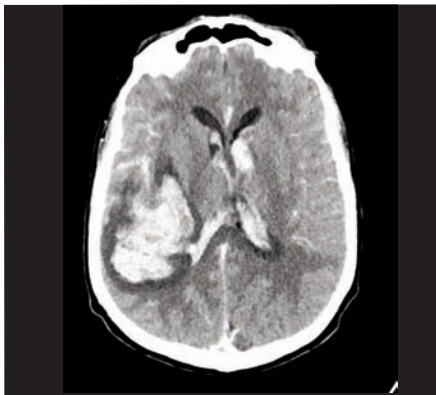


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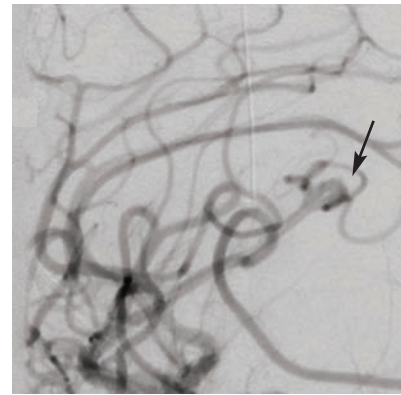


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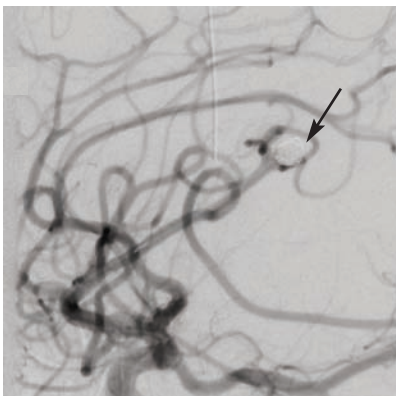
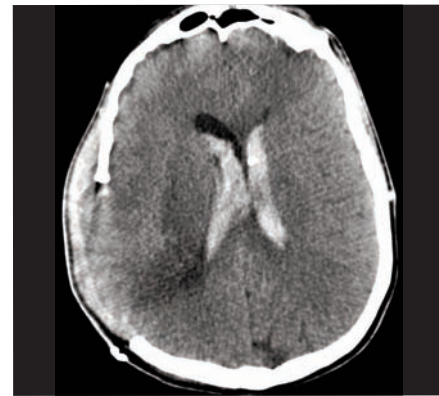


Image 4



Landmark Clinical Trial Evaluates Novel Approach to Alzheimer's Disease Prevention . . . continued from front cover

in order to identify other biological changes related to cognitive decline. Information from the study may help to ultimately develop a risk profile to distinguish individuals with normal cognition in the general population who are at risk of eventually developing Alzheimer's disease. In addition, a subset of participants in the LEARN study will undergo imaging to detect tau protein. Insights gleaned from the LEARN study are expected to help elucidate the findings from the A4 study.

For More on Our Alzheimer's Research

- Visit a4study.org to learn more about the A4 study and patient eligibility.
- For information on current trials and latest Alzheimer's disease research, visit our Center for Alzheimer Research and Treatment at brighamandwomens.org/CART or call (617) 732-8085.



Reisa Sperling, MD
 Director, Center for Alzheimer Research and Treatment,
 Department of Neurology

Brigham and Women's Hospital Launches the Ann Romney Center for Neurologic Diseases

In October, Brigham and Women's Hospital announced the launch of the Ann Romney Center for Neurologic Diseases. Through the Center, BWH will convene and lead a global collaboration in medical research to accelerate treatment, prevention and cures for five of the world's most complex neurologic diseases, multiple sclerosis, Alzheimer's disease, Lou Gehrig's ALS, Parkinson's disease and brain tumors.

The Ann Romney Center for Neurologic Diseases will create fertile ground for discovering breakthroughs and applications for scientific research by bringing together researchers and scientists working worldwide across each of the five disease states. Ann Romney, who is living with multiple sclerosis, will serve as a global ambassador to champion the Center's mission to transform the future of medicine.

"I know firsthand how terrifying and devastating these neurologic diseases can be, and I want to do everything in my power to help change outcomes for future generations," said Romney. "The team at Brigham and Women's Hospital gave me the gift of enduring hope and that is what this center is about – improving and saving the lives of the 50 million people facing a heart-breaking diagnosis. I hope everyone who shares this vision will join our effort."

The Ann Romney Center for Neurologic Diseases will be led by Howard L. Weiner, MD, Director, Multiple Sclerosis Program, and Dennis J. Selkoe, MD, Co-director, Center for Neurologic Diseases. For 30 years, Dr. Weiner and Dr. Selkoe have helped train the next generation of leaders in the field of neurologic diseases globally. Leveraging this deep relationship network, the Ann Romney Center for Neurologic Diseases will act as a catalyst, fueling collaboration among the global medical and scientific communities in pursuit of faster treatments and cures.



Howard L. Weiner, MD, Dennis J. Selkoe, MD, and Ann Romney

"We've proven that promising advances in neurologic diseases occur when research in one disease state is applied to other disease states," said Dr. Weiner. "What makes this Center different is the integration which allows us to discover connections between diseases that otherwise would not have been realized if the research remained in silos. The Ann Romney Center for Neurologic Diseases gives us a platform to take it to the next level."

By combining the unique assets of Brigham and Women's Hospital with the world's most advanced resources and minds, the Center will accelerate life-giving breakthroughs," said Elizabeth G. Nabel, MD, President of Brigham and Women's Hospital.

For more information, visit BWHAnnRomneyCenter.org.

Access to our Neurology and Neurosurgery Services

At Brigham and Women's Hospital, our neurologists and neurosurgeons are available for timely consultations and will work with you to develop a treatment plan.

Our Physician Liaison Tom Anderson can provide direct assistance with patient referrals and consultations. Tom can be reached at (617) 582-4760 or via email at tanderson0@partners.org.



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