



the compassion to care, the leadership to conquer

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**ALZHEIMER DISEASE PLAQUES SEEN WITH CONVENTIONAL MRI  
IN ANIMAL MODEL FOR THE FIRST TIME**

***- MRI and advanced computer analysis bring us closer to early identification of Alzheimer's -***

**Chicago, July 27, 2008** – For the first time, scientists have captured images of brain lesions similar to those found in Alzheimer's disease using clinical-grade MRI in an animal model of the disease, according to research reported today at the Alzheimer's Association's 2008 International Conference on Alzheimer's Disease (ICAD 2008), in Chicago.

These lesions, known as amyloid plaques, have been "imaged" previously using very high power MRI scanners that are only used on animals, and also with PET scans combined with specialized marker chemicals. This is the first time images of plaques were captured with conventional, clinical strength MRI.

Two other studies reported at ICAD 2008 use MRI and advanced computer analysis to bring us closer to early identification of Alzheimer's, perhaps even before symptoms are evident.

MRI technology is more widely distributed and relatively less expensive than other imaging technologies. In addition, it doesn't expose people to radiation, as do the "high energy" imaging approaches.

"As we get closer to the development of therapies that can slow or even stop the progression of Alzheimer's, earlier detection of the disease becomes crucial for early intervention," said William Thies, PhD, vice president of Medical and Scientific Relations at the Alzheimer's Association. "Early evaluation and diagnosis is also important because some Alzheimer's-like symptoms can be reversed if they are caused by treatable conditions, such as depression, drug interaction, or thyroid problems. If it is Alzheimer's, early diagnosis gives the person and their family an opportunity to build the right medical team, get access to existing medications, find helpful programs and services, and plan for the future. Plus, there is the opportunity to participate in studies of experimental drugs or other disease modifying treatments."

"As we search for ways to identify Alzheimer's early, these MRI studies show that researchers are moving closer to accurate early detection of the disease, and that we may soon be able to use this technology to determine who is at greater risk," Thies added.

**MRI Scans Show Images of Amyloid Plaques in Rabbit Model**

Definitive diagnosis of Alzheimer's currently happens at autopsy by demonstrating the presence of characteristic brain lesions, including amyloid plaques. The ability to non-invasively show amyloid plaque levels in living people could markedly improve the diagnosis and treatment of people with Alzheimer's.

John Ronald, a Ph.D. candidate in Medical Biophysics, along with Brian Rutt, PhD, and colleagues at the Robarts Research Institute and University of Western Ontario, London, Ontario, Canada, used clinical strength MRI scanners to take brain images from rabbits that had been fed a high cholesterol diet for more than two years. These animals form amyloid plaques in their brains.

According to the researchers, the MRI scans revealed distinct signal voids – black spots – in several brain areas including the hippocampus, which is very important for memory. Autopsy examination revealed that the void areas reflected the presence of small clusters of amyloid plaques. Each cluster had high levels of iron, which the researchers say caused the MRI signal voids; these signal voids were not found in animals fed a normal diet.

“Although some of the technology used to generate these images was designed specifically for rabbits, this preliminary discovery hints at the promise of using clinical MRI scanners to visualize plaques in people with Alzheimer’s,” Ronald said. “Extension of these technologies to living animals is practical, and should allow us to study the course of Alzheimer’s in animals over time.”

“We have customized this MRI scanner in very important ways for microimaging. Particularly, we have added special hardware that allows the scanner to clearly detect structures smaller than 50 microns (0.05 mm) and to more sensitively detect iron-containing structures than has been possible using clinical MRI in the past,” Ronald added.

### **Computer Analysis of MRI Scans Gives Alzheimer’s Disease Severity “Score”**

In addition to amyloid plaques, there is another brain lesion that is characteristic of Alzheimer’s – neurofibrillary tangles. The “gold standard” for post mortem measurement of Alzheimer’s tangle severity is known as Braak staging.

Prashanthi Vemuri, PhD, Clifford R. Jack, MD, and colleagues at the Mayo Clinic, Rochester, MN, sought to validate the ability of a new MRI analysis algorithm – known as the STructural Abnormality iNDex (STAND) score – to capture Alzheimer’s-related tangle severity. This was done by comparing the person’s STAND-score derived from an MRI scan taken before death with the person’s Braak stage calculated after death.

The researchers developed an algorithm that extracts atrophy information from an individual patient’s three-dimensional MRI scan. A STAND-score is assigned based on comparing the degree of atrophy in the person’s brain to atrophy patterns extracted from a large library of 160 Alzheimer’s and 160 cognitively normal subjects’ MRI scans. The STAND score is positive if the brain looks more Alzheimer’s-like and negative if the scan looks normal, and can be adjusted for demographics. According to the researchers, STAND-scores have 90 percent accuracy in distinguishing the MRI scans of people with Alzheimer’s from normal MRI scans.

In order to verify the adjusted STAND scores against Braak staging, the researchers identified 101 patients who had an MRI scan within four years of the time of death as well as postmortem Braak staging. They compared the two and, on a scale of 0 to 1, found the strength of association between the STAND-score and Braak stage to be 0.63 ( $p < 0.0001$ ).

“This study shows that information extracted from MRI scans can accurately capture the severity of Alzheimer’s tangle pathology,” said Vemuri. “While this work needs to be replicated and confirmed, because there is evidence indicating that structural changes in the brain precede cognitive symptoms, STAND scores may also prove to be useful for early identification of Alzheimer’s.”

### **MRI Used to Measure Alzheimer-like Patterns of Brain Atrophy in Normal Elderly**

In previously reported research, Christos Davatzikos, PhD, of the Department of Radiology at the University of Pennsylvania, Philadelphia; Susan Resnick, PhD, of the National Institute on Aging, Bethesda, MD; and colleagues used a new computer-based image analysis technique (advanced high-dimensional pattern classification) to analyze MRI scans from participants in the Alzheimer's Disease Neuroimaging Initiative (ADNI) and to derive an index of Alzheimer-like brain abnormality.

In a new study reported at ICAD 2008, they examined the presence and progression of such patterns in elderly individuals who are cognitively normal, and a small group with mild cognitive impairment (MCI), from the Baltimore Longitudinal Study of Aging (BLSA).

One hundred nine (109) healthy elderly participants from the BLSA were analyzed over periods of up to nine years. The researchers found that Alzheimer's-like patterns of brain atrophy were increasingly present in participants over age 80. The rate of progression of the index of Alzheimer-like patterns over time also was higher in the older participants. Memory performance of healthy elderly and those with MCI who displayed Alzheimer-like brain atrophy patterns, as measured using standard neuropsychological batteries, was lower compared to people that didn't display these patterns and had lower Alzheimer-like index values.

“Although the clinical significance of these Alzheimer's-like patterns of brain atrophy must be further evaluated, we are very hopeful that these pattern analysis tools will provide early indicators of brain changes that resemble those seen in people with Alzheimer's, years before memory problems are recognized clinically,” said Davatzikos.

### **About the Alzheimer's Association**

The Alzheimer's Association is the leading voluntary health organization in Alzheimer's research, care and support. Our mission is to eliminate Alzheimer's disease through the advancement of research, provide and enhance care and support for all affected, and reduce the risk of dementia through the promotion of brain health. Our vision is a world without Alzheimer's. For more information, visit [www.alz.org](http://www.alz.org).

### **About ICAD**

The Alzheimer's Association 2008 International Conference on Alzheimer's Disease (ICAD 2008) is the largest gathering of Alzheimer researchers in history. At ICAD 2008, more than 5,000 researchers will share groundbreaking information and resources on the cause, diagnosis, treatment and prevention of Alzheimer's and related disorders. As a part of the Association's research program, ICAD serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.

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- John Ronald – “Direct visualization of  $\beta$ -amyloid plaques in hypercholesterolemic rabbits using clinical field-strength MRI.” (Funders: Heart and Stroke Foundation of Canada, Canadian Institutes for Health Research, National Institutes of Health (NHLBI))
- Prashanthi Vemuri – “Antemortem MRI based structural abnormality index (STAND)-scores correlate with postmortem Alzheimer disease Braak stages.” (Funders: National Institute on Aging, Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program, Alexander Family Professorship of the Mayo Foundation)
- Christos Davatzikos, Susan Resnick – “Longitudinal progression of Alzheimer' disease-like patterns of brain atrophy in normal elderly MCI diagnosis.” (Funders: National Institute on Aging, Institute for the Study of Aging)