RSNA®
Radiological Society of North America

820 Jorie Blvd
Oak Brook, IL 60523
TEL 1-630-571-2670
FAX 1-630-571-7837
RSNA.org

NEWS

RSNA Press Release

Alzheimer's Research Receives RSNA Margulis Award

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CHICAGO (Nov. 27, 2017) – The Radiological Society of North America (RSNA) presented its sixth Alexander R. Margulis Award for Scientific Excellence to Walter H. Backes, Ph.D., and colleagues, for the article, "Blood-Brain Barrier Leakage in Patients with Early Alzheimer Disease," published in November 2016.

Named for Alexander R. Margulis, M.D., a distinguished investigator and inspiring visionary in the science of radiology, this annual award recognizes the best original scientific article published in RSNA's peer-reviewed journal *Radiology*.

Alexander R. Margulis, M.D.

In the battle against Alzheimer's disease (AD), preclinical detection represents the holy grail of research. By the time patients exhibit symptoms of AD — the most common form of dementia — most have already experienced substantial brain degeneration, diminishing the hope for treatment. Detecting biomarkers of AD before the brain reaches a point where it can no longer overcome the damage is a critical goal of researchers.

The award-winning study identified a connection between leakage of the blood-brain barrier (BBB) and AD pathology, suggesting that increased BBB permeability may represent a key mechanism in the early stages of the disease.

The BBB is a collection of cells and subcellular structures in the cerebrovascular wall that separates the circulating blood from the brain and is essential to keeping brain tissue healthy. It also regulates the delivery of important nutrients and blocks neurotoxins and removes

surplus substances from the brain.

“Our results suggest that BBB impairment may be a contributing factor in the early pathophysiology of AD and might be part of a cascade of events eventually leading to cognitive decline and dementia,” said Dr. Backes, a professor of Medical Physics in the Department of Radiology at the Maastricht University Medical Center in Maastricht, the Netherlands.

In the study, Dr. Backes and colleagues used contrast-enhanced MRI to compare 16 early AD patients with 17 healthy age-matched controls. Researchers measured BBB leakage rates and generated a histogram to help determine the amount of leaking brain tissue.

The BBB leakage rate was significantly higher in AD patients compared with controls and the leakage was distributed throughout the cerebrum. AD patients had a significantly stronger leakage rate in the gray matter, including the cortex, the brain’s outer layer. The researchers also determined that measurements derived from the histogram showed very subtle BBB impairment in the brain’s white matter.

“Our research shows that the BBB breakdown in Alzheimer’s disease can now be investigated with medical imaging, in a noninvasive way, thus, without relying on postmortem tissue or spinal tap samples,” Dr. Backes said.

The key advantage of detecting BBB leakage with contrast MRI is that it can detect early microvascular changes in AD, even in cases where no directly visible cerebrovascular abnormalities can be observed.

The connection between BBB impairment and AD pathology was strengthened by the fact that the addition of diabetes and other non-cerebral vascular diseases to the analysis model did not change the results.

And because the clearance of amyloid-beta protein present in AD patients relies on a well-functioning BBB, leakage of the BBB may help to provide a biomarker for early diagnosis, or at least a marker indicating vulnerability for the development of dementia, Dr. Backes said.

The study breaks new ground in critical areas of Alzheimer’s research, according to *Radiology* editor Herbert Y. Kressel, M.D.

“We used to think that vascular dementia and Alzheimer’s disease were two totally distinct entities — one characterized by the accumulation of abnormal proteins and the other by vasculopathy,” Dr. Kressel said. “The study is important in that the method they developed to assess BBB leakage, previously felt to be a hallmark of vascular dementia, can be seen in patients with mild cognitive impairment due to Alzheimer’s, as well as those with advanced AD, but not in normal, healthy individuals.”

Dr. Backes, who has been at Maastricht University Medical Center for almost 19 years, primarily focuses his research on novel MRI techniques of brain function, vascular pathology and the vessel-brain interaction.

“The award is a strong stimulus for the particular topic we are working on and also for the further development and evaluation of such a new application of MRI to perform brain leakage measurements,” Dr. Backes said.

Along with his co-authors, Dr. Backes credits the collaboration between the Maastricht and Leiden University Medical Center in the Netherlands with aiding the integration of advanced MRI knowledge on brain microvascular imaging techniques. Alzheimer's centers that aided with the study were also pivotal to the research, he said.

Access the study at *RSNA.org/Radiology* (http://pubs.rsna.org/doi/full/10.1148/radiol.2016152244).

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Note: Copies of RSNA 2017 news releases and electronic images will be available online at *RSNA.org/press17* beginning Monday, Nov. 27.

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