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MRI-BASED ALZHEIMER'S DISEASE BIOMARKERS FOR EARLY DIAGNOSIS AND CLINICAL TRIALS

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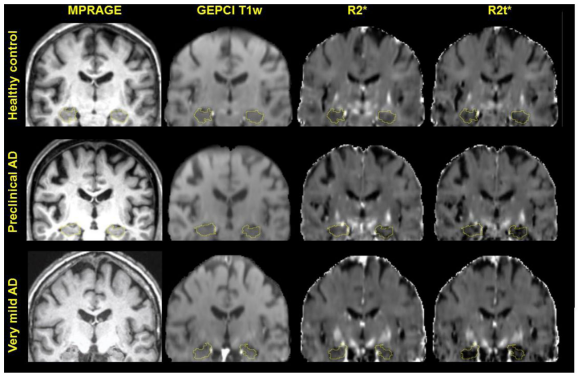
Technology Description

Researchers in Prof. Dmitriy Yablonskiy's laboratory have developed patented neuroimaging techniques to identify pre-clinical and early stage Alzheimer's disease (AD) using MRI-based biomarkers of amyloid accumulation and other pathological changes in the brain. These quantitative parameters from Gradient Echo Plural Contrast Imaging (GEPCI) could offer a safer and more widely-available alternative to PET for non-invasive diagnosis or as a surrogate marker in clinical trials of AD drug candidates.

If patients with AD could be easily identified early, before they develop cognitive symptoms, then it may be possible to offer therapies that prevent the disease before significant and irreversible neuronal loss occurs. To address this challenge, these GEPCI image acquisition and analysis techniques offer a quantitative assessment of brain tissue structure and function with the potential to detect biomarkers of Alzheimer's brain pathology and the accumulation of amyloid beta during the critical preclinical stage. The methods provide a measure of brain tissue cellular damage that is highly correlated to both cognitive performance and conventional PET measurements of amyloid beta (the current gold standard for non-invasive testing). Because MRI is much more widely available than PET and does not require any radioactive agents, this technology could potentially offer a viable option for diagnosis to improve to improve patient outcomes. In addition, it could be utilized as a screening tool, providing a surrogate marker in clinical trials of new drugs to treat and prevent AD.



Sample images of three patients: *a healthy control, a patient with preclinical AD, and a patient mild AD (CDR = 0.5) In all cases, MPRAGE and GEPCI T1w images show small atrophy progressing from healthy to AD group. Gradually decreased GEPCI R2t* suggest altered tissue integrity even in the areas without atrophy.*

Stage of Research

Using a cohort of 34 patients participating in a survey of aging and dementia, the inventors demonstrated proof of concept that GEPCI measurements are good correlates of beta-amyloid accumulation and neurodegeneration. These metrics can distinguish normal, preclinical and mild Alzheimer's disease with a strong correlation between GEPCI and beta-amyloid burden defined by PET imaging. (Publication)

Applications

- **Neuroimaging** with end-user applications in:
  - **diagnostics/screening** to identify at-risk patients who are developing Alzheimer's disease
  - **surrogate marker for clinical trials** – especially for trials of preventative therapy in pre-symptomatic patients

Key Advantages

- **Early/preclinical non-invasive detection**:
  - sensitive to pathological changes in brain tissue before neurocognitive changes
  - distinguishes normal individuals from both asymptomatic and early symptomatic Alzheimer's disease
- **More widely available and safer than PET** (the in vivo gold standard for amyloid detection)
  - based on MRI sequence that is available from most manufacturers
  - no radioactive imaging agents
  - faster than PET
- **Standard, quantitative measurements**:
  - high resolution 3D measurements
  - parameters are reproducible and independent of MRI scanner, enabling **multi-center applications**

Publications

- Kothapalli SV, Benzinger TL, Aschenbrenner AJ, Perrin RJ, Hildebolt CF, Goyal MS, Fagan AM, Raichle ME, Morris JC, Yablonskiy DA. Quantitative gradient echo MRI identifies dark matter as a new imaging biomarker of neurodegeneration that precedes tissue atrophy in early Alzheimer's Disease. *Journal of Alzheimer's Disease.* 2022 Jan 18;85(2):905-924.
- Zhao Y, Raichle ME, Wen J, Benzinger TL, Fagan AM, Hassenstab J, Vlassenko AG, Luo J, Cairns NJ, Christensen JJ, Morris JC, Yablonskiy DA. In vivo detection of microstructural correlates of brain pathology in preclinical and early Alzheimer Disease with magnetic resonance imaging. *Neuroimage*. 2017 Mar 1;148:296-304
- Everding G. Damage early in Alzheimer's disease ID'd via novel MRI approach. *Washington University School of Medicine in St. Louis.* 2022 Mar 2.

Patents: MRI method for in vivo detection of amyloid and pathology in the Alzheimer brain (U.S. Patent No. 10,779,762)

Related Web Links: Yablonskiy Profile