

# Low-dose whole brain radiation therapy for Alzheimer's dementia: Early results from a phase IIa Trial in human subjects



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## Biography

Leland Rogers is a radiation oncologist and professor of radiation oncology at Barrow Neurological Institute. He is board certified in radiation oncology by the American Board of Radiology. His expertise includes the treatment of central nervous system tumors using radiation therapy and brachytherapy. He is a fellow of the American College of Radiation Oncology, the American College of Radiology, and the American Society for Radiation Oncology. He is a member of the American Brachytherapy Society, the American Medical Association, NRG Oncology, and the Society for Neuro-Oncology. He earned his medical degree from the University of Kentucky College of Medicine. He completed his residency in radiation oncology at the University of North Carolina at Chapel Hill and a clinical fellowship in radiation oncology at the American Cancer Society. His research focuses on meningioma, ependymoma, and other brain and spinal tumors; trigeminal neuralgia; and Alzheimer's disease. He also studies brachytherapy in all its applications.



## Abstract

**Purpose:** To report initial neurocognitive results, imaging outcomes, ophthalmologic findings, and safety from lowdose whole brain radiation therapy (LD-WBRT) for patients with early Alzheimer's dementia (AD) treated on a phase IIa trial and with minimum 1-year follow-up, having completed the full measure of study assessment. **Patients and Methods:** Based upon favorable reductions in amyloid burden and improvements in neuro-cognition following low-dose brain irradiation in a murine model by the ROAD (Radiation Oncology in Alzheimer's Dementia) consortium, we launched a phase II trial for human subjects, administered at Virginia Commonwealth University (VCU) and Barrow Neurological Institute (BNI). Subjects with early AD are eligible for enrollment provided they are at least 55 years of age meet the definition of AD based on NINCDSADRDA criteria, have confirmatory FDG and Florbetapir PET findings, have the capacity to complete neurocognitive function (NCF), psychological function (PF), and quality of life (QOL) assessments, have a Rosen Modified Hachinski Score <4 and estimated survival >12 months. If taking AD medications at protocol entry, these must have been at a stable dose for >60 days. Screening NCF testing includes WTAR, MMSE-2, HVLT-R, BVMT-R, WAIS-IV Digit Span and Coding subsets, Trailmaking Tests, Controlled Oral Word Association Test, Semantic Fluency Test, and Pegboard Test. PF assessments include PHQ-9 and GAD-7. QOL assessments are QOL-AD and QUALID. Participant and informant ratings of participant cognition consist of Ecog questionnaires. All participants who meet screening criteria additionally undergo pretreatment NCF testing as well as PF and QOL assessments at least 30 days post screen, with additional tests BNT and JLO, which are only administered pre-treatment and 12-month post-treatment to minimize familiarity with the tests and fatigue. Subjects are evaluated with baseline, 6-week, 3-month, and 9-month, and 12-month physical examination, toxicity evaluation, and NCF, PF, and QOL assessments; baseline and 6-month FDG and Florbetapir PET, and with baseline and 9-month ocular examinations to evaluate for supranuclear cataracts, which have been reported in AD patients. Thirty patients are to be enrolled and treated with LD-WBRT in 2 sequential cohorts: the first 15 subjects 2Gy x 5, the remainder 2Gy x 10. **Results:** Six subjects have been enrolled to date, with 1 screen failure (not meeting criteria for early dementia). Five have been treated with LD-WBRT (2Gy x 5). Mean age is 73.2 years (range 69-77). Three subjects are female and 2 male. MMSE-2 results were defined as improved if numerically increased > 2, stable if increased or decreased <2, worsened if decreased > 2. Four of 5 patients experienced improvement or stability in MMSE-2 T-scores comparing pre-treatment baseline and 12-month post-treatment scores. Three improved; 1 from 37 to 50, one from 34 to 54, and another from 38 to 42, notably each with post-treatment scores in the average range for their respective ages. One remained stable over the same interval with MMSE-2 T-scores 26 and 24, scores which are moderately and severely impaired for age. One subject who met the low end of our inclusion criteria, and who was our eldest participant at 77, experienced a considerable decline in MMSE T-score from 39 pre-treatment to <1 at 12 months. Results were reviewed by the Data. Safety monitoring committee, and no safety issues were encountered. We will discuss additional NCF, PF, and QOL findings. Imaging results are presently under expert review.

## Publication:

1. High-risk Meningioma: Initial Outcomes From NRG Oncology/RTOG 0539.
2. Regarding Kelvin and Moore-Higgs, IJROBP 1999; 45:163-169; and Kelvin et al; IJROBP 1999;45:255-263
3. Gamma knife radiosurgery for trigeminal neuralgia associated with multiple sclerosis

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