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Radiation Oncology for Alzheimer's disease: Mechanisms of Action

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Abstract

Alzheimer's disease (AD) is a chronic progressive, fatal neurodegenerative disease which is the most common form of dementia among the elderly affecting over 5.8 million patients in the United States (US) and 36 million worldwide. Currently there is no effective treatment. Based on the observation that radiation therapy (RT) has been used to successfully treat systemic amyloidosis for over 2 decades our group hypothesized that RT could be used to treat AD. We have published preclinical data which supports this hypothesis using a transgenic murine model of AD.

Our experiments point to several molecular and cellular changes in AD which, alone or in combination, could be favorably impacted by RT. Each of these potential mechanisms require further investigation. We have shown RT reduces amyloid & tau possibly by increasing clearance of these molecules. RT is known to cause cell death, but the field of radiation genomics has shown RT can induce widespread changes in gene expression. Using microarray analysis we have shown expression changes in 84 genes thought to be related to AD including BACE2, presenilin 1 and Apo ε3.

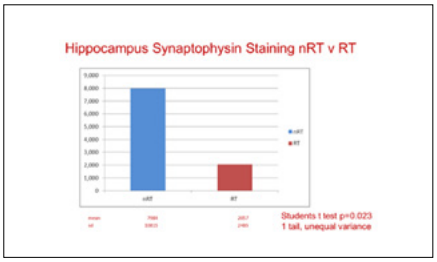
Other beneficial RT mechanisms may include alteration of immune responses. We have shown several changes in cytokine expression and microglia activation in the hemi-irradiated model. RT effects on vascular changes, heat shock protein expression and epigenetic changes are planned.

RT may reduce maladaptive neuroplasticity in the AD hippocampus, thus improving memory. Preliminary studies in our lab suggest synaptophysin is reduced in radiated versus un-radiated hippocampi supporting this theory (see Figure1).

We are currently investigating the sex differences in onset of amyloid deposition and response to RT in our model based on clinical observations of AD onset, severity and response to therapy in men and women.

Biography

Michael is currently Professor and Founding Residency Director, Department of Neurosurgery, Oakland University William Beaumont School of Medicine, Beaumont Health and a Director of the Michigan Head and Spine Institute. He is Past Chairman of the AANS/CNS Section on Neurotrauma and Critical Care for 2016-2018. He received his MD from Wayne State University School of Medicine where he also earned a PhD in anatomy and cell biology. He became Chief of Neurosurgery at Detroit Receiving Hospital. He served in the US Army reserves 1999-2009 and was mobilized to active duty in 2007. He served as President of the Michigan State Medical Society 2010-2011. He has published clinical and basic science research in neurotrauma and co-authored some of the earliest work demonstrating altered gene expression in human brain following traumatic brain injury. His current research focuses on a novel use of external radiation for the treatment of Alzheimer's disease.



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