SIGNIFICANT REDUCTION OF BETA-AMYLOID IN THE CNS FOLLOWING EXTERNAL RADIATION: IMPLICATIONS FOR TREATMENT IN ALZHEIMER’S DISEASE

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Purpose/objective(s): AD, the most frequent form of dementia, is characterized by extracellular beta-amyloid (AB) plaques and neurofibrillary tangles of Tau protein. In this preliminary pre-clinical study, we investigated if cranial X-irradiation could reduce the formation of AB plaques using a murine model of AD.

Materials/methods: B6.Cg-Tg (APPswe,PSEN1dE9)85Dbo/J (005864) transgenic mice develop early onset AD (005864, Jackson Laboratory, ME). 6 month old males were treated with a single dose of 5, 10 or 15 Gy to half of the brain and harvested at 2, 4 and 8 weeks post radiation. Coronal sections were cut and mounted for H&E and anti-beta-amyloid immunohistochemistry. The plaque number and size were compared between the shielded and irradiated halves of the brain.

Results: Treatments were well tolerated. Radiation treatment was associated with a statistically significant reduction in plaques throughout the brain in the irradiated side (paired t-test \(p=0.002\)). This effect was more significant when only the hippocampus region was considered (\(p=0.0004\)). There was significant differences between the observation times after radiation when all brain regions (\(p=0.002\)) or hippocampus (\(p=0.018\)) were analyzed with the greatest reduction at longer times post treatment. At 4 weeks post treatment 5, 10 and 15 Gy caused a 71+/-3%, 87+/-24%, 92+/-34% reduction in plaque incidence in the hippocampus.

Conclusion: We report for the first time that external beam irradiation produced a significant reduction in beta-amyloid plaques associated with AD. Further investigation into the mechanism and use of fractionated external irradiation are ongoing. We plan to translate this work into a Ph I / II Human Trial.