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# Early Recognition of Chronic Traumatic Encephalopathy through FDDNP PET Imaging

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## ABSTRACT

The PET biomarker, F-FDDNP (2-(l-[6-[(2-[F-IS]fluoroethyl(methyl)amino]-2-naphthyl) ethyldiene] malononitrile) [FDDNP] has shown sensitivity for in vivo detection of tau in addition to 1 -sheet-containing brain amyloid neuroaggregates. Tau protein in a characteristic distribution is felt to be the cardinal pathologic feature of Chronic Traumatic Encephalopathy. This project will examine whether FDDNP PET imaging correlates with, and/or can predict, decline in cognitive function in those exposed to cumulative head trauma. All operational aspects of this study have been accomplished including local IRB approval, identification of potential subjects from the Professional Fighters Brain Health Study to rec uit, logistics of the study visit and PET FDDNP imaging, case report forms, and electronic data entry. Actual enrollment of subjects has been delayed awaiting approval from the Human Research Protection Office.

## Subject Terms

- Traumatic Brain Injury
- Positron Emission Tomography
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Introduction: Blast injuries and other head injuries sustained in battle have been associated with the development of chronic traumatic encephalopathy (CTE). Pathological series have indicated that a characteristic feature of CTE is accumulation of tau protein in the brain. Until very recently, there has been no reliable way of measuring tau deposition in the brain during life. One PET biomarker, F-FDDNP (2-(1-[6-[2-([F-18]fluoroethyl](methyl)amino)-2-naphthyl] ethyliden) malononitrile) [FDDNP] has shown sensitivity for in vivo detection of tau in addition to β-sheet-containing brain amyloid neuroaggregates. This project will examine whether FDDNP PET imaging correlates with, and/or can predict, decline in cognitive function in those exposed to cumulative head trauma.

Keywords: Traumatic Brain Injury, Chronic Traumatic Encephalopathy, PET imaging, Tau

Overall Project Summary: Preparation for enrollment of participants was completed including: the development of a Standard Operating Procedure manual, creation of case report forms, determination of procedures for transfer of FDDNP ligand from production at UCLA to delivery at the Cleveland Clinic, generation of a list of subjects from the Professional Fighters Brain Health Study that would be eligible for enrollment, and local IRB approval (including research monitoring plan).

Though we had initially projected that the tasks listed above would be completed within the first 6 months of the project start, we faced significant delays due to two factors. One delay was due to the time required to finalize the contractual service agreement between UCLA and Cleveland Clinic. The current point of stall is at the Human Research Protection Office. Our project has been under review by HRPO for close to 6 months; we have provided response to all their queries and are awaiting approval.

Once we obtain approval from HRPO, we anticipate enrolling the initial subjects within 6 weeks. However, in order to complete the 3 year follow up of subjects, we will need to extend the completion date accordingly. Once we begin enrollment of subjects, we do not anticipate any further delays in the conduct of the study.

Key Research Accomplishments: Not Applicable
Conclusion: There remains a need for biomarkers that can identify individuals at risk of CTE. Molecular imaging agents such as FDDNP hold promise as a means of revealing tau pathology and potentially could be included in a diagnostic algorithm.

Publications, Abstracts, Presentations: As enrollment and data collection has not occurred, we have had no publications/abstracts/presentations

Inventions, Patents, Licenses: Not applicable

Reportable Outcomes: None

Other Achievements: None

References – None

Appendices – None