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TITLE: Early Recognition of Chronic Traumatic Encephalopathy Through FDDNP
PET Imaging

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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} ethylidene) 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:

Upon receiving approval from the Human Research Protection Office, enrollment of participants began in March, 2015. We have completed 19 PET FDDNP studies, with 9 additional subjects scheduled within the next 6 weeks. Recruitment progress is reflected in the following grid:

| Type of Fighter | Scheduled | | Completed | | Completed/Total |
|---------------------|-----------|-----|-----------|-----|-----------------|
| | Boxer | MMA | Boxer | MMA | |
| Normal | 2 | | 3 | | 3/20 |
| Active, Unimpaired | 3 | 0 | 4 | 5 | 9 / 12 |
| Active, Impaired | 0 | 0 | 4 | 1 | 5 / 12 |
| Retired, Unimpaired | 1 | 0 | 0 | 0 | 0 / 12 |
| Retired, Impaired | 3 | 0 | 2 | 0 | 2 / 12 |
| TOTAL: | 9 | | 19 | | 19 / 68 |

Though we are awaiting completion of 50% of the scans before we began preliminary quantitative analyses, the scan quality has been excellent and from a qualitative perspective, distinct patterns seem to be emerging, similar to those reported in prior studies of retired NFL players (example of normal control in figure 1 and an impaired subject with increased FDDNP uptake in figure 2).

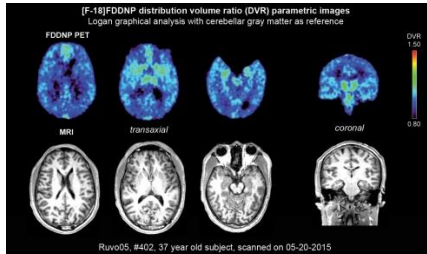


Figure 1

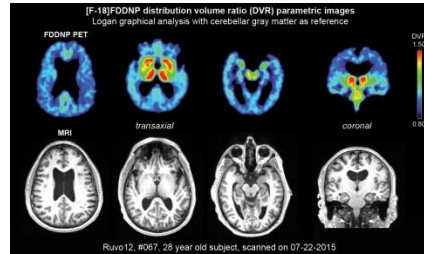


Figure 2

It was initially anticipated that we would be able to complete enrollment within 6 months but several factors have delayed achieving that goal. The FDDNP tracer can only be produced at UCLA on Wednesday, which limits enrollment to 2 subjects per week (instead of the projected 3). Moreover, key personnel (PET technician, study coordinator) were on vacation at times during the summer which resulted in several weeks where enrollment was held. Moreover, we had one occasion of a subject missing their appointment, one dose failure, and one week where the UCLA cyclotron was out of service for inspection.

Barring other unexpected issues, we plan to enroll approximately 5 subjects per month which would allow us to reach our complete enrollment by summer, 2016. We have several initiatives now in place including the hiring of a dedicated recruitment specialist for the Cleveland Clinic research team, as well as outreach to major organizations in the fight industry (UFC, Top Rank Promotions, Haymon Boxing, California Athletic Commission, Nevada Athletic Commission, and Ring 10) to assist in recruitment of retired fighters.

In order to complete the 3 year follow up of subjects, we will need to extend the completion date accordingly.

The only other change made in the conduct of the study involves modification of the monitoring plan. Instead of all the monitoring visits being done remotely, our monitor will now perform one monitoring visit per year at the Las Vegas site, with the other quarterly reviews being completed remotely from Cleveland. The primary reason for this change was to allow thorough scrutiny of the regulatory documents on site that are too voluminous to be scanned and placed on line; complete records of the individual subjects are placed on a shared, password protected drive that can be reviewed remotely.

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 data collection is still accruing, we have not yet had publications/abstracts/presentations

Inventions, Patents, Licenses: Not applicable

Reportable Outcomes: None

Other Achievements: None

References – None

Appendices – None