**Diffusional Kurtosis Imaging Assessment of Tuberous Sclerosis Complex**

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**INTRODUCTION:**

Tuberous sclerosis complex (TSC) is a rare, multi-system genetic disease that, as a result of dominant mutations of TSC1 and TSC2 genes, causes tumors/lesions to grow in various organs. In the central nervous system, TSC is predominantly characterized by cortical/subcortical tubers which are responsible for the seizures (90%) and mild to severe developmental delays found in TSC [1]. Although tuber lesions are presumed to contribute to epileptogenesis in TSC, a few studies have identified “silent” tubers with active surrounding perilesion tissue that appear normal on conventional MRI images [2, 3]. In this preliminary study, we aim to quantitatively characterize the in-vivo microstructure of tuber lesions (L) as compared to perilesion (P) tissue and normal appearing contralateral (C) perilesion tissue using metrics derived from Diffusional Kurtosis Imaging (DKI) [4, 5]. To our knowledge, this is the first study to apply DKI in TSC. Investigation of DKI in this cohort provides an additional incentive as there is extensive literature on the histology of resected TSC tuber lesions and perilesion tissue, thus allowing in-vivo DKI metric values to be directly associated with morphological human cell properties in-vitro.

**METHODS:**

This study involved 6 participants with TSC (3 males) with a mean age of 6.03 years (range: 2.23-10.17 years) and 6 age-matched controls (6 males) with a mean age of 6.18 years (range: 2.67-10.22 years). All subjects were recruited from the NYU Langone Medical Center by a pediatric neurosurgeon (HW) and pediatric neuroradiologist (SM) with approval from the NYU IRB. Subjects were either TSC patients that required MRI for clinical purposes or controls who received MRIs for clinical issues not due to significant neurological symptoms and were cleared by an experienced pediatric neurosurgeon (JH) and a pediatric neuroradiologist (SM). The TSC group included 3 males and 3 females with a mean age of 6.03 years (range: 2.23-10.17 years). All subjects were recruited from the NYU Langone Medical Center by a pediatric neurosurgeon (HW) and pediatric neuroradiologist (SM) with approval from the NYU IRB. Subjects were either TSC patients that required MRI for clinical purposes or controls who received MRIs for clinical issues not due to significant neurological symptoms and were cleared by an experienced pediatric neurosurgeon (JH) and a pediatric neuroradiologist (SM). The TSC group included 3 males and 3 females with a mean age of 6.03 years (range: 2.23-10.17 years). The TSC group included 3 males and 3 females with a mean age of 6.03 years (range: 2.23-10.17 years). The TSC group included 3 males and 3 females with a mean age of 6.03 years (range: 2.23-10.17 years).

**RESULTS and DISCUSSION:**

Two-sample t-tests (two-tailed) of regions within the TSC group revealed MK, AK, and RK means for the L to be significantly lower than the means for the P (L vs. P: MK < 0.001, AK < 0.01, RK < 0.01) and C (L vs. C: MK = 0.003, AK = 0.04, RK = 0.15). MD, AD, and RD means for the L were significantly higher than the means for the P (L vs. P: MD < 0.001, AD < 0.01, RD < 0.01) and C (L vs. C: MD < 0.01, AD < 0.01, RD < 0.01). FA means for the L were lower but not significantly different from the P and C means. For all metrics, the P means did not significantly differ from the C means (Figure 2). The MD and FA results are similar to findings of a previous DTI study of TSC [7]. These results suggest that the microstructure of the lesion is compromised equally in radial and axial directions whereas perilesion tissue does not seem to differ from normal appearing contralateral tissue. The TSC and control group did not statistically differ in age (p = 0.94, two-tailed). Comparison between both groups’ L, P, and C means also replicate the regional trends within the TSC group and verify that only the lesion differs in microstructure when compared to normal tissue (Figure 3). C means were not significantly different between the TSC and control group thus validating the use of contralateral perilesion tissue as a within subject control (Figure 3C). As expected, the L, P, and C means within the control group were not significantly different. Given the very small cohort, interpretation of these results should be made with caution. Nonetheless, these findings suggest that lesions are associated with a substantial increase in diffusivity (as indicated by MD, AD, and RD) and a substantial decrease in diffusional heterogeneity (as indicated by MK, AK, and RK). Future analysis will include more subjects, as well as to compare tuber and perilesion values of TSC patients with and without seizures and correlate the observed diffusional changes with histological observations of abnormal dysplastic neurons.

**REFERENCES:**