

## **An Imaging Study of Renal Angiomyolipoma in Patients with Tuberous Sclerosis Complex**

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**Introduction:** Tuberous sclerosis complex (TSC) is an autosomal dominant tumor suppressor syndrome afflicting one of every 6000 people. The disease is linked to mutations in the TSC1 or TSC2 genes. Angiomyolipomas (AMLs), tumors rich in fat, blood vessels and muscle, commonly found in TSC kidneys, increase in size with age and are a leading cause of TSC adult mortality. The extraordinarily high levels of NaCl and urea in the renal medulla versus the cortex are damaging to vulnerable DNA, interfere with DNA repair and thus possibly contribute to tumor growth.

**Purpose:** We performed a feasibility study of TSC patients to determine whether sufficient radiographic imaging exists to map the location of AMLs within different zones of the kidneys and to investigate if a pattern of tumor location is discernable. We expected to find a disproportionate number of AMLs in the renal medulla versus the cortex based on the hypothesis that the medulla's high osmolality facilitates tumor growth.

**Methods:** All patients, under the age of eighteen, were selected for this study from the Tuberous Sclerosis Clinic of Cincinnati Children's Hospital Medical Center, having fulfilled the clinical diagnostic criteria for TSC with abdominal or retroperitoneal imaging electronically accessible. AMLs larger than 4 mm and exclusively located within either a well-demarcated cortex or medulla were scored and measured for size, side, dimensional position and relative distance from papilla (if medullary).

**Results:** A total of 200 AMLs were identified from 33 patients, measured and mapped to one of six zones: upper and lower polar, anterior and posterior interpolar and medial and lateral interpolar. Ultrasound (n=26), magnetic resonance imaging (n=2) and computed tomography (n=5) imaging modalities were analyzed to score the 70 medullary and 130 cortical AMLs. Imaging studies of 100 patients met the inclusion criteria for analysis. Sixty-seven imaging studies did not contain scorable data commonly due to poor cortico-medullary demarcation or significantly distorted renal architecture.

**Conclusion:** A greater number of tumors were found in the renal medulla of TSC patients than were expected by comparison to the normal anatomic reference data of cortex to medulla size ratios. This discovery was consistent with the hypothesis that high osmolarity contributes to tumor growth. Our investigation has established the groundwork for association studies with age, gender, biomarkers and possible therapeutic approaches, including the pharmacologic modification of the medullary osmolar gradient.