Diffusion Tractography Guided Staged Bilateral Gamma Knife Radiosurgical Thalamotomy for Refractory Essential Tremors

Pavnesh Kumar, MD - The Ohio State University; Rituraj Upadhyay, MD - The Ohio State University; Erik H. Middlebrooks, MD - Mayo Clinic; Zachary Zordan, MD - The Ohio State University; Joshua D. Palmer, MD - The Ohio State University; Brian Dalm, MD - Ohio State University; Evan Thomas, MD, PhD - The Ohio State University

Objectives: Gamma Knife thalamotomy (GKT) targeting Ventral Intermediate Nucleus (VIM) is a well-established treatment for refractory tremor and staged bilateral GKT has been shown to be effective and safe for bilateral tremor. Traditionally atlas or coordinates-based localization of the VIM was used which may not correlate with individual patient's functional anatomy. Tractography based delineation of VIM complemented by tracking of dentato-rubro-thalamic tract (DRTT) which is considered relevant pathway for tremor alleviation has been shown to be effective with an improved side effect profile for both direct deep brain stimulation (DBS) as well as noninvasive thalamotomy procedures. We report the first clinical use of diffusion tractography for staged bilateral thalamotomy with gamma knife stereotactic radiosurgery in patients with refractory essential tremor.

Methods: Two patients with refractory essential tremor underwent staged bilateral GKT, utilizing diffusion tractography for DRTT delineation and MRI based landmarks for VIM target mapping, after failing medical management and being intolerant to focused ultrasound thalamotomy (FU-T).

On the day of treatment after attaching the Leksell G-headframe, a stereotactic planning CT scan was obtained and imported into Leksell Gamma Plan planning system. FGAITER, MPRAGE and Diffusion Tensor Imaging data was imported in Brainlab and used to segment the DRTT connecting contralateral dentate nucleus, cerebellar peduncle and ipsilateral VIM, motor cortex. Discrepancy between the coordinate predicted target and the modified individual patient functional anatomy based target was quantified. Shot isocenter was placed withing DTI determined tatget and if necessary shifted to avoid overlap of 26 Gy isodose line with the posterior limb of internal capsule which was contoured as avoidance structure. A single lesion was made during each GKT procedure in VIM using one 4-mm collimator with 65-67.5 Gy prescribed to 50% isodose lines. Both patients were treated on Leksell Gamma Knife Ikon model. Post procedure patients were evaluated at multiple time points to assess treatment response and side effects. The Fahn-Tolosa-Marin (FTM) tremor rating scale was used to score tremor response while Karnofsky Performance Status (KPS) was used to assess quality of life before and after each GKT.

Results: Patient 1: A 78-year-old right-handed female with medically refractory essential tremor affecting bilateral upper extremities, presented after failing to tolerate FUS-T. At the time of presentation, she had KPS of 70 and FTM score of 40. She underwent left VIM GKT for tremor affecting her right upper extremity (RUE). DTI tractography based left VIM target was located at 1.6 mm, 26.5˚θ and 120.6˚ø from traditional cordinate based target. At the first follow up 2 months post procedure she reported improvement in her RUE tremor with better functional ability with total FTM and KPS scores of 31 and 90, respectively. Subsequent follow-up at 7 months post procedure indicated continued improvement in her RUE tremor without any radiologic or physical signs of

toxicity. However, left upper extremity (LUE) continues to be bothersome and refractory to medical treatment. She underwent right VIM GKT 13 months after the first procedure with DTI tractography segmented right VIM being 3.4 mm, 29.7˚θ and 108.5˚ ø away from the conventional target. On post treatment check she was doing well without any side effects. She will be monitored further for response and toxicity assessment.

Patient 2: A 57-year-old right-handed male with medically refractory essential tremor since childhood involving bilateral upper, lower extremities, head and voice presented following an inability to tolerate FUS-T. He had KPS 70 and FTM score 60 at baseline. He initially underwent left VIM GKT for right upper extremity (RUE) tremor. VIM delineated with DTI differed 0.8 mm, 147.5˚θ and 104.5˚ø from coordinates-based target. At 3 month and subsequent follow ups significant improvement was noted in RUE tremor with enhanced functional capability. At 6-month follow-up, the FTM score improved to 29, and approximately 70% subjective improvement in right upper extremity (RUE) tremor, with no toxicity or side effects reported. Given excellent treatment response with no noticeable toxicity, he decided to proceed with right VIM GKT for LUE tremor and underwent treatment 6 months after the initial procedure with tractography based right VIM target at 1.9 mm, 99.0˚θ and 58.0˚ø from the traditional coordinates. He had a significant reduction in LUE tremor at 4 months follow up with continuing improvement on both sides with no noticeable toxicity.

Conclusion(s): Stereotactic radiosurgery (SRS) for staged bilateral thalamotomy demonstrated a particularly good initial response in patients with medically refractory bilateral tremor, without any treatment related neurological complications in the short term. The integration of tractography utilizing patient-specific connectivity patterns can refine target mapping and may enhance neuromodulatory effects, efficacy, and safety of this procedure. Further large cohort studies employing tractography for SRS thalamotomy in tremor management, with extended follow-up, are necessary to compare this targeting approach with standard methods.