SUPPLEMENTAL METHODS

Imaging Protocol

A T1-weighted MPRAGE was used for structural registration and obtained prior to SRS. with TR=1.7s, TE=2.36ms, TI=900ms, FA=8deg, GRAPPA = 2, receiver bandwidth = 200 Hz/Px, echo spacing 7.4ms, turbo factor = 176, in-plane resolution = 0.8 x 0.8mm, slice thickness = 1mm with scan time = 6:27 mins. At 3-month followup, MRI was repeated with T1-weighted post-contrast SPACE using TR=0.5s, TE=13ms, FA=120deg, GRAPPA = 2, receiver bandwidth = 465 Hz/Px, in-plane resolution = 0.9 x 0.9mm, slice thickness = 1mm.

SRS Procedure

A thermoplastic mask with an open face was molded to the patient's head, and a treatment planning CT having 0.8 to 1 mm slice thickness was acquired. The pre-treatment MPRAGE and fast gray matter acquisition T1 inversion recovery (FGATIR) MRI was rigidly registered to the treatment planning CT. The internal capsule, thalamus, and third ventricle were delineated on the treatment planning CT. Points marking the center of the anterior commissure (AC), center of the posterior commissure (PC), as well as a point in the mid-sagittal plane were placed on the CT to define the patient reference coordinate system.[1] The target point was the ventralis intermediate nucleus (VIM) located 1/4 of the AC–PC distance plus 1 mm anterior to the PC, 1/2 the width of the third ventricle plus 11 mm lateral to the AC–PC line, and 2.5 mm superior to the AC–PC line.[2] 67.5 Gy were prescribed to the 50% isodose line (D_{max} = 135Gy). The isocenter was moved away from the VIM the minimum distance required to keep the 26 Gy isodose line medial to the internal capsule. Plans were created using the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) and the dose calculated using either the AAA or AcurosXB algorithm with grid spacing 1 mm. Patients were treated using a Varian Edge™ (Palo Alto, CA) linear accelerator equipped with high-definition multi-leaf collimator and 10MV flattening-filter free beam using the virtual-cone technique.[3] Optical surface guidance was used to monitor the patient position during treatment.[4]

Image Normalization

The structural images, lesion connectivity maps, and lesion tract maps were then normalized into Montreal Neurological Institute (MNI) template space using the MNI_ICBM_2009b_NLIN_ASYM template—based on the MPRAGE images—with the SyN registration method in Advanced Normalization Tools.[5,6] A five-stage nonlinear transform was applied: two linear (rigid and affine) registrations, whole-brain nonlinear SyN-registration, and two nonlinear SyN-registrations with a focus on subcortical nuclei.[7] Next, an affine transform restricted to subcortical regions of interest was performed to ensure accurate subcortical registration.[8] The right hemisphere lesion connectivity maps and lesion tract maps were nonlinearly flipped to the left hemisphere for comparison across the cohort.

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