Brain Diffusion Imaging and Tractography to Distinguish Clinical Severity of Human *PLP1*-Related Disorders

Catherine Sarret, MD, PhD ; Jean-Jacques Lemaire, MD, PhD ; Anna Sontheimer, PhD student ; Jerome Coste, PhD ; Nadia Savy, MD, PhD student ; Bruno Pereira, PhD ; Bastien Roche, Odile Boespflug-Tanguy, MD, PhD.

Background: We performed quantitative diffusion tensor imaging and brain tractography to distinguish clinical severity in a series of 35 patients with hypomyelinating PLP1-related disorders classified using the Motor Developmental Score according to the best motor function acquired before the age of 5 years and the gross motor function measure (GMFM) at the time of magnetic resonance imaging acquisition.

Methods: We calculated fractional anisotropy and diffusivity values in 26 regions of interest and the numbers of fibers and volumes of hemisphere tractograms. Fiber bundles on tractograms were characterized according to 3 criteria: size, direction of main-stream fibers, and connectivity of bundles (extratelencephalic projections, commissural fibers, and intrahemispheric connections).

Results: Age-adjusted multivariate analysis in 3 severity groups revealed increased isotropic diffusion in the superior cerebellar peduncle and grey matter in the most severe group, and larger tractogram volumes and increased numbers of fibers in the least severely affected group. Tractogram patterns showed preserved extratelencephalic projections and a main anterior-posterior aspect of intrahemispheric fibers in most patients, whereas interhemispheric connectivity was variable. The most severely affected and intermediate patients had less intrahemispheric connectivity, with a frequent predominant anterior-posterior direction of main-stream fibers.

Conclusion: Diffusion tensor imaging and tractographic parameters can operate as biomarkers to distinguish clinical severity in PLP1-related disorders and could improve our understanding of hypomyelinating leukodystrophies.