

Dear NMOSD Colleagues,

We hope you all had a wonderful summer! Many members of the NMOSD community came together at the GJCF roundtable and ICC meetings at ECTRIMS congress in London. The CROCTINO/PAMRINO Study Team had the opportunity of presenting a status update on our progress, and we are happy to inform you about our two retrospective imaging studies:

**CROCTINO:** Collaborative Retrospective Study on Retinal OCT in Neuromyelitis Optica

**PAMRINO:** Parallel Study on MRI in Neuromyelitis Optica

In the last report, we had invited the GJCF-ICC members to give feedback on the suggested eCRFs for CROCTINO. Thank you all for your excellent input; following your suggestions, we implemented a longitudinal study design and additional visual function assessments. Furthermore, since many of you agreed on sharing MRI data along with the OCT data, we decided to assess both studies in the same database. That way, participants do not need to enter demographic, clinical or functional data twice.

In the last report, we detailed the CROCTINO objectives and design so we want to use this volume to introduce its MRI companion project, PAMRINO, to you.

## **PAMRINO**

### Background & Objectives

Almost all NMOSD-related studies, including MRI studies in this field, suffer from low sample sizes, and thus hardly allow for proper analyses of results. Partly conflicting findings might be a result of cohort heterogeneity in terms of diagnosis, scanning protocols and analysis methods. PAMRINO's goal is to investigate optimal MRI protocols and analysis methods for the elucidation of imaging biomarkers in NMOSD and related disorders in a large multicenter cohort.

### Methodology

Within the PAMRINO study we will collect a broad range of MRI data that were acquired during normal clinical visits of NMOSD patients. This dataset consequently will be representative of real world sample MRI data with broad heterogeneity in terms of MR scanners, MR sequences and data quality. Our main goal for PAMRINO is to investigate this real world data to give an overview of what MRI data are acquired in everyday practices. This assessment will inform the research community of the extent of heterogeneity in MRI protocols that are applied in the diagnostic workup of NMOSD patients. With this information, optimization of protocols and standard methods may be introduced in prospective clinical and everyday practices in MRI scanning for NMOSD studies. This would ultimately allow for large-scale standardized analyses of MRI data to elucidate comparable differences in the brain and spinal cord of NMOSD patients.

We will evaluate these protocols with respect to the fulfillment of international recommendations for imaging protocols in terms of completeness and data quality.

This will be performed

- 1) on a quantitative level e.g. sequence parameters, slice thickness, and voxel sizes.
- 2) on a qualitative level i.e. image quality, movement or pulsation artifacts.

In a second step, after assessing this heterogeneity we will perform quantitative structural analysis on a subset of the data. The subset needs to be suitable for the analysis, as detailed below, and share a minimum comparability across the included datasets.

The analyses will include:

- 1) T2- lesion load measurements (count and volume) on FLAIR/T2/PDw images (min. 3 mm slice thickness)

- 2) Cerebral atrophy (if non-enhanced MPRAGE is available)
- 3) Cervical myelon atrophy (if MPRAGE including cervical spine is available)
- 4) Total myelon atrophy (if full spine imaging is available)

## Current CROCTINO/PAMRINO project status

The IT infrastructure (REDCap archive) for sharing demographic, clinical and visual function data is fully operational. An embedded link to XNAT allows convenient upload of OCT image data for each subject. An additional upload link for MRI images will be included in the next few weeks.

To date, 24 academic centers from Asia, Europe, and North & South America have agreed to contribute OCT images and related data to CROCTINO. Thus, we hope to meet the goal of obtaining, curating, and uploading 350 OCT datasets from NMOSD patients, and 100 matched healthy control subjects by July 1, 2017. We are currently recruiting centers for contribution of MRI datasets for PAMRINO. It is possible to participate in either study, PAMRINO and CROCTINO, independently of each other. We are happy to have your participation in either study or both, depending on the data that is available for you to share with us.

## Next steps

If you have already agreed on participating in CROCTINO, the Study team is going to contact you shortly. Other centers please contact the CROCTINO/PAMRINO Study team when you are interested in contributing MRI and/or OCT data! If you have scientific questions or suggestions for further scientific analyses, please contact us!

## CROCTINO/PAMRINO Study Team

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On behalf of NMOSD patients and families, we thank you for your time and effort in joining us in this exciting new projects!