**Supplement**

**Supplementary table 1: Participating centres**

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| **Centre** | **Device** | **MOGAD [N]** | **HC [N]** |
| Charité–Universitätsmedizin Berlin, Germany | Heidelberg Spectralis SD-OCT | 13 | 12 |
| Johns Hopkins University School of Medicine, USA | Cirrus HD-OCT | 11 | 36 |
| Ludwig-Maximilians Universität Munich, Germany | Heidelberg Spectralis SD-OCT | 12 | 10 |
| Nitte University, India | Heidelberg Spectralis SD-OCT | 10 | 0 |
| Université de Lille, France | Heidelberg Spectralis SD-OCT | 8 | 5 |
| Mayo Clinic, Rochester, USA | Cirrus HD-OCT | 3 | 0 |
| Medical University of Vienna, Austria | Heidelberg Spectralis SD-OCT | 6 | 0 |
| Heinrich Heine University Düsseldorf, Germany | Heidelberg Spectralis SD-OCT | 6 | 18 |
| Ruhr University Bochum, Germany | Heidelberg Spectralis SD-OCT | 4 | 0 |
| Technical University Munich, Germany | Heidelberg Spectralis SD-OCT | 4 | 17 |
| University of Southern Denmark, Denmark | Heidelberg Spectralis SD-OCT | 3 | 0 |
| Hospices Civils de Lyon, France | Heidelberg Spectralis SD-OCT | 1 | 0 |
| Hospital Clinic Barcelona-Institut d’Investigacions, Biomèdiques August Pi Sunyer, Spain | Heidelberg Spectralis SD-OCT | 0 | 41 |

**Supplementary table 2: Additional contributors of the CROCTINO study group**

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**Supplementary table 3: ON characteristics for 92 episodes in 41 patients**

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| --- | --- | --- |
| **ON characteristic** | | **N (%)** |
| Most affected segment | Orbit | 32 (35) |
| Canalicular segment | 1 (1) |
| Intracranial segment | 4 (4) |
| Chiasm | 2 (2) |
| Orbit and chiasm | 1 (1) |
| Optic nerve head swelling | Clearly seen | 23 (25) |
| Clearly not seen | 29 (32) |
| Orbit affection | Clearly seen | 33 (36) |
| Clearly not seen | 18 (20) |
| Canalicular segment affection | Clearly seen | 17 (18) |
| Clearly not seen | 28 (30) |
| Intracranial segment affection | Clearly seen | 10 (11) |
| Clearly not seen | 31 (34) |
| Chiasm affection | Clearly seen | 5 (5) |
| Clearly not seen | 34 (37) |

**Supplementary analysis 1: Excluding subclinical ON at baseline in non-ON eyes**

To exclude subclinical ON episodes at baseline, we collected VEP data of 26 eyes from 4 centers at baseline (Spectralis cohort): Fifteen eyes had a history of clinical ON and eleven eyes had no history of clinical ON. Out of these eleven eyes without clinical ON, eight (73%) had a VEP latency within normal limits and three eyes (27%) of two patients had a VEP latency above the center-specific threshold. The patient without any history of ON and bilateral VEP latency above the center-specific threshold had normal GCIPL volume (bilateral 0.66mm3) and pRNFL thickness (bilateral 113µm) suggesting a non-ON related cause of VEP latency delay. The patient with unilaterally prolonged VEP latency (124ms vs. 117ms contralaterally) also had no history of clinical ON and showed no significant side difference in GCIPL volume (0.56mm3 vs. 0.57mm3) or pRNFL thickness (98µm vs. 99µm). No VEP data were available for the Cirrus cohort.

As a second attempt to exclude subclinical ON episodes, we analyzed the inter-eye difference at baseline. According to Nolan et al. (DOI 10.1097/WNO.0000000000000629) a pRNFL difference of > 6µm is highly suggestive of a previous unilateral ON. None of the 22 patients without any history of ON (and bilateral pRNFL values at baseline) had an inter-eye difference exceeding this threshold (Spectralis: N=21, 1.9±1.6µm, maximum: 6µm for N=1, Cirrus: N=1, 3µm). Subclinical ON episodes with consequences for the retinal neuronal content seem therefore unlikely in this subset analysis of non-ON patients.

**Supplementary analysis 2: Additional longitudinal analyses in ON and non-ON eyes**

For the Spectralis cohort, longitudinal high-contrast visual acuity data (HCVA, in logMAR) were available for 52 eyes (16 ON-eyes and 36 non-ON eyes): HCVA did not change longitudinally in these eyes combined (B<0.01, SE<0.01, p=0.80) as well as in ON eyes (B<0.01, SE<0.01, p=0.61) and non-ON eyes (B<0.01, SE<0.01, p=0.62) separately. We also did not find significant VEP latency prolongation in a subset of eight eyes with longitudinal VEP data (B=-0.08, SE=0.09, p=0.35). Analyzing the complete dataset separated into ON and non-ON eyes, non-ON eyes (B=-0.14, SE=0.03, p<0.001) but not ON (B=-0.02, SE=0.02, p=0.463) underwent longitudinal pRNFL thinning. Neither non-ON eyes (B<0.01, SE<0.01, p=0.46) nor ON eyes (B<0.01, SE<0.01, p=0.15) underwent longitudinal GCIPL thinning.

For the Cirrus cohort, longitudinal HCVA was available for 22 eyes (17 ON eyes, 5 non-ON eyes): HCVA did not change longitudinally in these eyes combined (B<0.01, SE<0.01, p=0.98) as well as in ON eyes (B<0.01, SE<0.01, p=0.80) and non-ON eyes (B<0.01, SE<0.01, p>0.99) separately. Significant longitudinal pRNFL and GCIPL thinning was not seen in ON eyes (pRNFL: B=-0.33, SE=0.28, p=0.25, GCIPL: B=-0.24, SE=0.24, p=0.34) and non-ON eyes separately (pRNFL: B=0.17, SE=0.20, p=0.41, GCIPL: B=-0.12, SE=0.28, p=0.72).