|  |  |  |  |
| --- | --- | --- | --- |
| **Center** | **OCT device** | **Number of subjects in final cohort** | |
| **Patients** | **Healthy controls** |
| Siriraj Hospital and Bumrungrad International Hospital, Bangkok, Thailand | Cirrus HD-OCT | 22 | 0 |
| Hospital Clinic of Barcelona-Institut d’Investigacions, Biomèdiques August Pi Sunyer, Barcelona, Spain | Spectralis SD-OCT | 8 | 12 |
| CIEM MS Research Center, University of Minas Gerais, Medical School, Belo Horizonte, Brazil | Spectralis SD-OCT | 26 | 0 |
| NeuroCure Clinical Research Center, Charité – Universitätsmedizin Berlin, Germany | Spectralis SD-OCT | 33 | 4 |
| Department of Neurology, Heinrich Heine University Düsseldorf, Germany | Spectralis SD-OCT | 10 | 28 |
| National Cancer Center Korea, Goyang-si, South Korea | Topcon 3D OCT-1 | 31 | 0 |
| Kashani MS Center, Isfahan University of Medical Sciences, Isfahan, Iran | Spectralis SD-OCT | 12 | 12 |
| Cerrahpasa Medical Faculty, Istanbul University, Turkey | Cirrus HD-OCT | 3 | 0 |
| The Walton Centre for Neurology and Neurosurgery, Liverpool, UK | Spectralis SD-OCT | 1 | 0 |
| Pierre Wertheimer Neurological Hospital, Hospices Civils de Lyon, France | Spectralis SD-OCT | 6 | 0 |
| Department of Neurology, KS Hegde Medical Academy, Nitte University, Mangalore, India | Spectralis SD-OCT | 19 | 16 |
| Department of Neurology, Hospital Clínico de Maracaibo, Maracaibo, Venezuela | No scans included in final anaysis | 0 | 0 |
| Department of Neurology, University of Michigan Medical School, Ann Arbor, MI, United States | Spectralis SD-OCT | 1 | 0 |
| Hospital San Raffaele and University Vita-Salute San Raffaele, Milan, Italy | Spectralis SD-OCT | 24 | 0 |
| Institute of Clinical Neuroimmunology, University Hospital, Ludwig-Maximilians Universitaet Muenchen, Munich, Germany | Spectralis SD-OCT | 5 | 0 |
| NYU Multiple Sclerosis Comprehensive Care Center, Department of Neurology, NYU School of Medicine, NY, USA | No scans included in final anaysis | 0 | 0 |
| Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark | Spectralis SD-OCT | 6 | 0 |
| Oxford University Hospitals, National Health Service Trust, Oxford, UK | Spectralis SD-OCT | 35 | 0 |
| Neuro-Ophthalmology Division, Department of Ophthalmology, Rabin Medical Center, Petah Tikva, Israel | Cirrus HD-OCT | 13 | 0 |
| Department of Neurology and Neurosurgery, Federal University of São Paulo, São Paulo, Brazil | Spectralis SD-OCT | 1 | 0 |
| Swedish Neuroscience Institute Neuro-Ophthalmology, Seattle, WA, USA | Cirrus HD-OCT | 17 | 0 |
| Neurology Service, University Hospital of Strasbourg, France | Spectralis SD-OCT | 10 | 0 |

## Table e-1: Participating centers with respective OCT device, number of AQP4-IgG seropositive NMOSD patients and healthy controls in final cohort

*Abbreviations:* AQP4-IgG: aquaporin-4 antibodies, NMOSD: Neuromyelitis optica spectrum disorders, OCT: optical coherence tomography

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of eyes** | **Thickness**  **[µm, mean±SD]** | **Comparison to** | **Absolute difference**  **[µm, mean]** | | **Relative difference**  **[%, mean]** | | **B** | **SE** | **p-value** | **R2marg** | **R2cond** |
| **GCIP** | | | | | | | | | | | | |
| **NMOSD-ON** | 22 | 56.4 ± 7.3 | **NMOSD-NON**  (N=35,  75.1 ± 7.6 µm) | - 18.7 | | - 24.9 | | - 18.0 | 1.8 | **1.9e-13** | 0.654 | 0.849 |
| **NMOSD-1-ON** | 16 | 56.5 ± 8.5 | - 18.5 | | - 24.7 | | - 17.1 | 2.1 | **5.1e-10** | 0.628 | 0.834 |
| **NMOSD-2-ON** | 2 | 57.8 ± 2.4 | **NMOSD-1-ON** | 1.3 | | 2.3 | | - 6.8 | 0.8 | 0.064 | 0.416 | 0.996 |
| **NMOSD- ≥3-ON** | 4 | 55.0 ± 1.6 | **NMOSD-2-ON** | -2.8 | | -4.8 | | -3.6 | 1.9 | 0.307 | 0.655 | 0.781 |
| **NMO-NONcon** | 13 | 73.8 ± 6.9 | **NMOSD-NONnon**  (N=22,  75.8 ± 8.0 µm) | -2.0 | | - 2.7 | | - 1.2 | 3.0 | 0.688 | 0.111 | 0.701 |
| **NMOSD-NON1-con** | 11 | 75.0 ± 6.2 | - 0.8 | | - 1.0 | | - 0.2 | 3.1 | 0.959 | 0.102 | 0.689 |
| **pRNFL** | | | | | | | | | | | | |
| **NMOSD-ON** | 32 | 64.7 ± 13.5 | **NMOSD-NON**  (N=51;  105.6 ± 22.2 µm) | - 26.7 | | - 29.3 | | -27.8 | 2.6 | **7.6e-17** | 0.568 | 0.878 |
| **NMOSD-1-ON** | 20 | 68.6 ± 15.2 | - 22.8 | | -24.9 | | -25.2 | 2.9 | **7.9e-12** | 0.456 | 0.887 |
| **NMOSD-2-ON** | 5 | 58.8 ± 5.8 | **NMOSD-1-ON** | - 9.8 | | -14.3 | | -12.2 | 3.0 | **1.0e-2** | 0.125 | 0.938 |
| **NMOSD- ≥3-ON** | 7 | 57.6 ± 6.5 | **NMOSD-2-ON** | - 1.2 | | - 2.1 | | - 1.1 | 3.1 | 0.729 | 0.147 | 0.919 |
| **NMOSD-NONcon** | 20 | 88.8 ± 11.2 | **NMOSD-NONnon**  (N=31;  93.1 ± 10.1 µm) | -4.3 | | -4.8 | | -4.4 | 3.5 | 0.210 | 0.110 | 0.711 |
| **NMOSD-NON1-con** | 14 | 90.8 ± 8.6 | -2.3 | | -2.5 | | -0.2 | 3.1 | 0.958 | 0.266 | 0.666 |
| **INL** | | | | | | | | | | | | |
| **NMOSD-ON** | 22 | 41.7 ± 3.3 | **NMOSD-NON**  (N=35; 42.3 ± 3.9 µm**)** | - 0.6 | | - 1.4 | | 0.4 | 0.6 | 0.518 | 0.137 | 0.920 |
| **NMOSD-1-ON** | 16 | 41.5 ± 3.4 | - 0.8 | | - 2.0 | | 0.3 | 0.6 | 0.634 | 0.119 | 0.924 |
| **NMOSD-2-ON** | 2 | 41.9 ± 0.8 | **NMOSD-1-ON** | 0.4 | | 0.9 | | -2.3 | 0.9 | 0.220 | 0.161 | 0.971 |
| **NMOSD- ≥3-ON** | 4 | 42.5 ± 4.1 | **NMOSD-2-ON** | 0.6 | | 1.5 | | < 0.1 | 0.5 | > 0.999 | 0.986 | 0.991 |



## Table e-2: Group comparisons for Cirrus HD-OCT

*Abbreviations:* B: estimate, ON: optic neuritis episode, INL: inner nuclear layer, NMOSD: AQP4-IgG seropositive NMOSD, NMOSD-NON: AQP4-IgG seropositive NMOSD eyes without a history of ON, NMOSD-NONnon: AQP4-IgG seropositive NMOSD eyes without a history of ON or contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of one contralateral ON, NMOSD-ON: AQP4-IgG seropositive NMOSD eyes with a history of ON, NMOSD-1-ON: AQP4-IgG seropositive NMOSD eyes with a history of one ON, NMOSD-2-ON: AQP4-IgG seropositive NMOSD eyes with a history of two ONs, NMOSD-≥3-ON: AQP4-IgG seropositive NMOSD eyes with a history of three or more ONs, pRNFL: peripapillary retinal nerve fiber layer, Rcon: conditional R-squared, Rmarg: marginal R-squared, SD: standard deviation, SE: standard error.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of eyes** | **Thickness**  **[µm, mean±SD]** | **Comparison to** | **Absolute difference**  **[µm, mean]** | **Relative difference**  **[%, mean]** | **B** | **SE** | **p-value** | **R2marg** | **R2cond** |
| **GCIP** | | | | | | | | | | |
| **NMOSD-ON** | 30 | 63.8 ± 10.4 | **NMOSD-NON**  (N=9;  77.1 ± 6.0 µm) | - 13.3 | - 17.2 | - 13.2 | 3.9 | **1.7e-3** | 0.248 | 0.294 |
| **NMOSD-1-ON** | 22 | 65.6 ± 10.2 | - 11.5 | - 14.9 | - 12.7 | 4.0 | **3.9e-3** | 0.262 | 0.262 |
| **NMOSD-2-ON** | 5 | 64.0 ± 8.8 | **NMOSD-1-ON** | - 1.6 | - 2.5 | - 2.3 | 6.0 | 0.706 | 0.008 | 0.008 |
| **NMOSD- ≥3-ON** | 3 | 50.7 ± 1.6 | **NMOSD-2-ON** | - 13.3 | - 20.8 | 3.0 | 8.8 | 0.757 | 0.707 | 0.980 |
| **pRNFL** | | | | | | | | | | |
| **NMOSD-ON** | 43 | 72.8 ± 27.7 | **NMOSD-NON**  (N=11; 105.6 ± 22.2 µm) | -32.8 | -31.0 | -33.9 | 8.1 | **1.6e-4** | 0.228 | 0.615 |
| **NMOSD-1-ON** | 29 | 76.7 ± 26.6 | -28.8 | -27.3 | -30.6 | 9.3 | **2.4e-3** | 0.212 | 0.317 |
| **NMOSD-2-ON** | 8 | 75.8 ± 34.1 | **NMOSD-1-ON** | -1.0 | -1.3 | -1.1 | 13.0 | 0.935 | 0.001 | 0.497 |
| **NMOSD- ≥3-ON** | 6 | 49.8 ± 10.5 | **NMOSD-2-ON** | -25.9 | -34.2 | - 4.1 | 4.2 | 0.373 | 0.423 | 0.989 |
| **INL** | | | | | | | | | | |
| **NMOSD-ON** | 30 | 39.1 ± 2.9 | **NMOSD-NON**  (N=9; 36.5 ± 2.1 µm) | 2.6 | 7.1 | 1.7 | 0.6 | **0.013** | 0.258 | 0.880 |
| **NMOSD-1-ON** | 22 | 38.9 ± 3.1 | 2.4 | 6.5 | 1.6 | 0.6 | **0.023** | 0.267 | 0.895 |
| **NMOSD-2-ON** | 5 | 38.4 ± 2.3 | **NMOSD-1-ON** | -0.5 | -1.2 | 1.3 | 1.5 | 0.395 | 0.204 | 0.785 |
| **NMOSD- ≥3-ON** | 3 | 41.5 ± 1.2 | **NMOSD-2-ON** | 3.1 | 8.1 | 1.9 | 3.5 | 0.624 | 0.382 | 0.821 |

## Table e-3: Group comparisons for Topcon 3D-OCT1

*Abbreviations:* B: estimate, ON: optic neuritis episode, INL: inner nuclear layer, NMOSD: AQP4-IgG seropositive NMOSD, NMOSD-NON: AQP4-IgG seropositive NMOSD eyes without a history of ON, NMOSD-NONnon: AQP4-IgG seropositive NMOSD eyes without a history of ON or contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of one contralateral ON, NMOSD-ON: AQP4-IgG seropositive NMOSD eyes with a history of ON, NMOSD-1-ON: AQP4-IgG seropositive NMO eyes with a history of one ON, NMOSD-2-ON: AQP4-IgG seropositive NMOSD eyes with a history of two ONs, NMOSD-≥3-ON: AQP4-IgG seropositive NMOSD eyes with a history of three or more ONs, pRNFL: peripapillary retinal nerve fiber layer, Rcon: conditional R-squared, Rmarg: marginal R-squared, SD: standard deviation, SE: standard error.

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Number of eyes** | **Thickness**  **[µm, mean±SD]** | **Comparison to** | **Absolute difference**  **[µm, mean]** | **Relative difference**  **[%, mean]** | **B** | **SE** | **p-value** | **R2marg** | **R2cond** | **Combined p-value** |
| **NMOSD** | 268 | 39.4 ± 3.5 | **HCs** | < 0.1 | < 0.1 | -0.4 | 0.5 | 0.489 | 0.015 | 0.062 | . |
| **NMOSD-ON** | 124 | 40.3 ± 3.9 | -0.9 | -2.3 | -1.0 | 0.6 | 0.109 | 0.065 | 0.899 | . |
| **NMOSD-NON** | 144 | 38.6 ± 3.9 | 0.8 | 2.1 | 0.5 | 0.5 | 0.309 | 0.065 | 0.899 | . |
| **NMOSD-ON** | 124 | 40.3 ± 3.9 | **NMOSD-NON** | 1.7 | 4.4 | 1.9 | 0.3 | **1.9e-8** | 0.131 | 0.824 | **3.7e-8** |
| **NMOSD-1-ON** | 76 | 40.3 ± 4.1 | 1.6 | 4.2 | 1.9 | 0.3 | **5.7e-8** | 0.146 | 0.847 | **2.0e-7** |
| **NMOSD-2-ON** | 28 | 41.2 ± 4.1 | **NMOSD-1-ON** | 1.0 | 2.4 | 1.4 | 0.9 | 0.108 | 0.096 | 0.837 | 0.156 |
| **NMOSD-≥3-ON** | 20 | 39.4 ± 2.4 | **NMOSD-2-ON** | -1.8 | -4.3 | -1.6 | 0.8 | 0.069 | 0.173 | 0.841 | 0.390 |

**Table e-4:** **Group comparisons of INL thickness for Heidelberg SD-OCT**

*Abbreviations:* B: estimate, ON: optic neuritis episode, NMOSD: AQP4-IgG seropositive NMOSD, NMOSD-NON: AQP4-IgG seropositive NMOSD eyes without a history of ON, NMOSD-NONnon: AQP4-IgG seropositive NMOSD eyes without a history of ON or contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of contralateral ON, NMOSD-NONcon: AQP4-IgG seropositive NMOSD eyes without a history of ON but with a history of one contralateral ON, NMOSD-ON: AQP4-IgG seropositive NMOSD eyes with a history of ON, NMOSD-1-ON: AQP4-IgG seropositive NMOSD eyes with a history of one ON, NMOSD-2-ON: AQP4-IgG seropositive NMOSD eyes with a history of two ONs, NMOSD-≥3-ON: AQP4-IgG seropositive NMOSD eyes with a history of three or more ONs, Rcon: conditional R-squared, Rmarg: marginal R-squared, SD: standard deviation, SE: standard error.