ABSTRACTS

Neuro-Ophthalmic Literature Review

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OCT for the temporal arteries

Mollan SP, Keane PA, Denniston AK. The use of transdermal optical coherence tomography to image the superficial temporal arteries. *Eye (Lond)* 2017;31:157–160.

The gold standard for diagnosing giant cell arteritis (GCA) is temporal artery biopsy, but it is an invasive procedure. Can transdermal optical coherence tomography (OCT) be a non-invasive alternative? In this proof-of-concept case series, the authors used a commercially available dermatological OCT device (InVivoSight) to image the superficial temporal artery (STA) of eight patients: five with a clinical diagnosis of GCA (treated) and three healthy controls. The authors were able to identify the STA in all eight patients; however, the whole circumference of the artery was only demonstrated in two patients. There were OCT features that helped to distinguish artery from vein, but the authors did not comment on any differences between the OCT appearance of patients with GCA and those without. Further studies are required to see if this technique may aid GCA diagnosis in the future.

Carmen Chan

Optical coherence tomography of the optic nerve and macula: Pitfalls and how to avoid them

Chen JJ, Kardon RH. Avoiding clinical misinterpretation and artifacts of optical coherence tomography analysis of the optic nerve, retinal nerve fiber layer, and ganglion cell layer. *J Neuroophthalmol* 2016;36:417–438.

Optical coherence tomography (OCT) has become an indispensable tool for neuro-ophthalmologists in recent years. However, technical problems with

scan acquisition or segmentation software can lead to misinterpretations of the scan results. This is a comprehensive review of the most common artifacts associated with OCT examination of the optic nerve head and macular ganglion cell analysis, including practical advice on how to avoid them. The sources of error include patient's age, signal strength, media opacity, high refractive error, disc size, disc swelling, peripapillary atrophy, and macular pathology. There are many useful illustrations with examinations performed with spectral-domain OCT.

Carmen Chan

The optic nerve head deforms with adduction

Chang MY, Shin A, Park J, Nagiel A, Lalane RA, Schwartz SD, Demer JL. Deformation of optic nerve head and peripapillary tissues by horizontal duction. *Am J Ophthalmol* 2017;174:85–94.

The authors conducted a prospective experimental study evaluating optic nerve head changes with horizontal ductions in normal patients. They evaluated 23 eyes from 12 normal patients and measured the configuration of the optic nerve head and peripapillary tissues in central gaze and with 10, 20, and 30 degrees of adduction and abduction using optical coherence tomography (OCT). They found that adduction caused a posterior displacement of the temporal peripapillary retinal pigment epithelium and optic nerve cup displacement, most prominent at 30 degrees. There was also progressive optic nerve head tilting in adduction. Abduction did not cause a significant change in any of these variables. These OCT findings confirm the authors' previous work on magnetic resonance imaging (MRI) that showed that the optic nerve sheath becomes tethered in adduction, but

not in abduction. The authors propose that adduction imposes a strain on the optic nerve head and peripapillary tissue and may contribute to optic neuropathies, such as normal tension glaucoma.

John Chen

Retinal folds and treatment of idiopathic intracranial hypertension

Kupersmith MJ, Sibony PA, Feldon SE, Wang J-K, Garvin M, Kardon R. The effect of treatment of idiopathic intracranial hypertension on prevalence of retinal and choroidal folds. *Am J Ophthalmol* 2017;176:77–86.

The authors reviewed the data from the idiopathic intracranial hypertension treatment trial (IIHTT) and evaluated for changes in folds over time. Patients at baseline were evaluated for peripapillary wrinkles (Paton lines), retinal folds, choroidal folds, and creases. The acetazolamide-treated group had fewer wrinkles, retinal folds, and choroidal folds at 6 months compared with baseline, whereas the placebo group had no change in wrinkles or folds from baseline to 6 months. There was no difference in the percentage of patients with peripapillary wrinkles and choroidal folds between the acetazolamide-treated and placebo groups at 6 months. There was a delayed development of peripapillary wrinkles during resolution of some severe cases of papilloedema. Choroidal folds were the only type of fold associated with spinal fluid opening pressure, but there was no correlation between resolution of choroidal folds and improvement in papilloedema. Creases did not resolve in any patients but were only present in a small percentage at baseline. In summary, various types of folds can occur from the biomechanical changes with raised intracranial pressure. Most types of folds are not useful for monitoring papilloedema.

John Chen

Quality of life and neuromyelitis optica spectrum disorders

Schmidta F, Zimmermanna H, Mikolajczaka J, Oertela FC, Pachec F, Weinholda M, Schinzela J, Bellmann-Strobla J, Ruprecht K, Paula F, Brandta AU. Severe structural and functional visual system damage leads to profound loss of vision-related

quality of life in patients with neuromyelitis optica spectrum disorders. *Mult Scler Relat Disord* 2017;11:45–50.

The authors addressed the question of vision-related quality of life in patients with neuromyelitis optica spectrum disorders (NMOSDs). This was a cross-sectional study of 31 NMOSD patients of different serologic status matched with age and gender to 31 multiple sclerosis (MS) patients. National Eye Institute Visual Function Questionnaire (NEI-VFQ) in the validated German translation, optical coherence tomography (OCT), and visual function testing tools were used to correlate vision-related quality of life to structural damage and dysfunction of the visual system. Results showed that the NEI-VFQ composite score was significantly lower in NMOSD patients (77.4 ± 19.2) compared with MS patients (86.6 ± 6.7 , $p = 0.01$). Unilateral optic neuritis had only a minor effect on vision-related quality of life, both in NMOSD and MS patients. There was an association between low NEI-VFQ scores and worse OCT with visual function measurements. No significant difference in any OCT, visual function, or vision-related quality-of-life parameter between aquaporin-4 and myelin oligodendrocyte glycoprotein (MOG) immunoglobulin G (IgG)-positive patients was found. The authors suggest implementing the NEI-VFQ in longitudinal clinical studies of NMOSD patients to assess the efficacy of treatment on vision-related quality of life.

Rauan Kaiyrzhanov

Thyroid ophthalmopathy and retinal nerve fibre thickness

Mugdha K, Kaur A, Sinha N, Saxena S. Evaluation of retinal nerve fiber layer thickness profile in thyroid ophthalmopathy without optic nerve dysfunction. *Int J Ophthalmol* 2016;9:1634–1637.

This was a prospective, case-control, observation study conducted in a tertiary care center to evaluate retinal nerve fibre layer (RNFL) thickness, which may show optic nerve structural changes before functional impairment occurs. Patients were included if they had eyelid retraction with biochemical thyroid dysfunction, exophthalmos,

or extraocular muscle involvement, or if they had thyroid dysfunction with either exophthalmos or extra-ocular muscle involvement, or clinical activity score (CAS) $>3/7$. Patients were excluded if they had evidence of optic neuropathy, including vision less than 20/30, abnormal pupillary reaction, abnormal colour vision, abnormal contrast sensitivity, or visual field defects, or if they had a condition known to affect RNFL thickness.

Forty eyes with thyroid orbitopathy and 40 controls were studied. Eighteen were male, with mean age 38.75 years. Patients were evaluated at entry into study and after 6 months. Investigators found RNFL thinning in all four quadrants at initial evaluation in orbitopathy patients compared with controls. After 6 months, there was further thinning of the inferior quadrant, signifying damage in these patients even with a clinically normal optic nerve. Mean CAS at visit 1 was 1.95 and at visit 2 0.68. There was no correlation between CAS and RNFL thickness. The study did not discuss duration of thyroid eye disease, and it would be interesting to see if this correlates with RNFL thinning.

Peter MacIntosh

Ophthalmological findings in mitochondrial disease

Zhu C, Traboulsi E, Pariky S. Ophthalmological findings in 74 patients with mitochondrial disease. *Ophthalmic Genet* 2017;38:67–69.

The authors describe a retrospective review of 74 patients with confirmed mitochondrial disorders, including Leigh disease, chronic progressive external ophthalmoplegia, Pearson/Kearns-Sayre syndrome, and Leber hereditary optic neuropathy. The association of visual complications with mitochondrial disorders stems from the fact that the visual system has a high energy demand, and mitochondria are important for supplying that energy. The study found that 35% of patients had one or more ophthalmological abnormalities, with retinal pigmentary changes being the most common in 16% of patients, followed by partial or total optic atrophy in 10% and decreased extra-ocular movements in 8%. Other findings included macular atrophy, macular dystrophy, ptosis, and visual field defects. It is important to identify

ophthalmic complications from mitochondrial disease. Some of these complications, such as ptosis and extraocular motility changes, can be surgically corrected to improve patient quality of life.

Peter MacIntosh

Transient smartphone blindness

Sathiamoorthi S, Wingerchuk DM. Transient smartphone blindness: relevance to misdiagnosis in neurologic practice. *Neurology* 2017;88:809–810.

The authors describe the case of a 58-year-old female with two episodes of transient right monocular visual loss that occurred after awakening in the morning and reading her smartphone in bed with one eye. After setting the phone down and getting up, she noted painless dimming of right eye vision, resolving after a minute. She had no other neurologic or orthostatic symptoms. She had extensive ophthalmic, neurologic, and cardiovascular examinations that included magnetic resonance imaging (MRI), spinal tap, and metabolic and inflammatory laboratory tests. Her MRI revealed bilateral cerebral white matter lesions that were initially attributed to multiple sclerosis, and her vision loss to optic neuritis. Disease-modifying therapy was recommended. A second evaluation correctly led to the diagnosis of transient smartphone blindness (TSB), with MRI lesions more likely representing small vessel ischaemic disease. TSB is a physiologic phenomenon related to differential retinal light sensitivity in one eye compared with the other, as may happen when viewing a smartphone in bed while lying on one's side and occluding an eye, causing it to become dark adapted while the viewing eye becomes light adapted. When viewing with both eyes in low light after putting the phone down, the light-adapted eye experiences transient dim vision that recover in several minutes. The correct diagnosis may be elicited by careful history and can prevent unnecessary investigations or interventions.

Peter MacIntosh

Opicinumab

Cadavid D, Balcer L, Galetta S, Aktas O, Ziemssen T, Vanopdenbosch L, Frederiksen J, Skeen M, Jaffe GJ, Butzkueven H, Ziemssen F, Massacesi L, Chai Y, Xu L, Freeman S, for the RENEW study principal investigators. Safety and efficacy of opicinumab in acute optic neuritis (RENEW): a randomised, placebo-controlled, phase 2 trial. *Lancet Neurol* 2017;16:189–199.

The holy grail for treatment of demyelination remains remyelination. That remyelination is possible has long been recognised histologically. However, it was not until 40 years ago that British scientist Bill Blakemore demonstrated this experimentally. The RENEW trial provides indirect evidence for remyelination following optic neuritis using a human monoclonal antibody (opicinumab, BIIB033) which antagonises leucine-rich repeat and immunoglobulin domain-containing protein (Lingo-1). To remember, Lingo-1 is a potent negative regulator of myelination and neurite outgrowth and is expressed in the optic nerve. Therefore antagonising this inhibitor can help remyelination.

When first presented at ECTRIMS 2016, the phase 2 trial with opicinumab (NCT01721161) was just completed. At the time, treatment with opicinumab was associated with an increased visual evoked potential (VEP) latency recovery (22.24 ms) compared with placebo (14.69, $p = 0.0504$). There was no effect on retinal nerve fibre layer thickness. Because of the encouraging results on VEP latency, the trial was extended (NCT02657915). The present publication by Cadavid and colleagues presents the data of this extended trial. It is straightforward in stating that intention-to-treat analysis did not show significant difference in primary and secondary outcome measures.

This negative outcome aside, the main positive finding regards full-field VEP (FF-VEP) difference between the affected eye and the fellow eye. After 24 weeks, the FF-VEP difference between eyes was -3.5 ms (95% confidence interval [CI]: -10.6 to 3.7) in patients who were treated with opicinumab ($p = 0.33$). After 32 weeks, the difference was -6.1 ms (-12.7 to 0.5 , $p = 0.071$). In contrast, in the

non-opicinumab group, the inter-eye FF-VEP differences were -7.6 ms (95% CI: -15.1 to 0.0 , $p = 0.05$) at week 24 and -9.1 (95% CI: -16.1 to -2.1 , $p = 0.011$) at week 32. Because of this difference, the data suggest that opicinumab may indeed enhance remyelination. Conceptually, the trial demonstrates relative safety of a drug which may promote remyelination. Whether or not the observed improvement of FF-VEP latency will be clinically relevant remains to be seen.

Axel Petzold

Ocular myositis and Whipple's disease

Parkash V, Mudhar HS, Wagner BE, Raoult D, Batty R, Lepidi H, Burke J, Collini P, de Silva T. Bilateral ocular myositis associated with Whipple's disease. *Ocul Oncol Pathol* 2017;3:17–21.

The authors describe a case of a 38-year-old woman with Whipple's disease. She had been treated with immunosuppressants prior to the correct diagnosis of Whipple's disease being made. Once the correct diagnosis was made, antibiotic therapy was initiated and she was taken off immunosuppressants. She developed diplopia, and orbit magnetic resonance imaging (MRI) showed stranding and enhancement of orbital fat and enlargement of the extraocular muscles. A biopsy showed macrophages that had an antibody to *T. whipplei*. The diplopia resolved quickly with a course of steroids. The authors reasoned that the ocular myositis could have been a direct result of infection and initial treatment failure. However, since polymerase chain reaction (PCR) study of the muscle was negative for *T. whipplei*, the other possible mechanism could have been immune reconstitution inflammatory syndrome (IRIS), which is a dysregulated immune response due to the rapid withdrawal of immunosuppressants. The patient was doing well after 8 months of proper treatment. Keep Whipple's disease in mind when encountered with a patient having diplopia and myositis, especially if there is a history of undiagnosed arthralgias, fever, and gastrointestinal problems.

John Pula

Venous thrombosis after therapeutic hypothermia in infants

Radicioni M, Bini V, Chiarini P, Fantauzzi A, Leone F, Scattoni R, Camerini PG. Cerebral sino-venous thrombosis in the asphyxiated cooled infants: a prospective observational study. *Pediatr Neurol* 2017;66:63–68.

The use of therapeutic hypothermia for hypoxic-ischaemic encephalopathy is still controversial in infants, due to concerns about its efficiency and a higher risk of infectious complications. The authors studied the incidence of cerebral venous sinus (CVS) thrombosis in asphyxiated infants treated with hypothermia. They systematically performed brain magnetic resonance venography (MRV) after rewarming in 37 such infants and found CVS thrombosis in 10 of them (27%). This study raises practical issues such as the need for routine brain MRV in this population and the meaning of CVS in terms of specific treatments and prognosis. It also raises theoretical questions about the pathophysiology of this complication.

Matthieu Robert

Grey matter in NMO is different from MS

Eshaghi A, Wottschel V, Cortese R, Calabrese M, Sahraian MA, Thompson AJ, Alexander DC, Ciccarelli O. Gray matter MRI differentiates neuromyelitis optica from multiple sclerosis using random forest. *Neurology* 2016;87:2463–2470.

The authors tested whether brain MR imaging measures can differentiate between multiple sclerosis (MS) and neuromyelitis optica (NMO) using random-forest classification in 90 patients. The patients with MS showed greater atrophy compared with those with NMO with an accuracy of 80%. This study provides Class II evidence that grey matter imaging biomarkers can distinguish patients with NMO from those with MS.

Michael Vaphiades

Treatment and retinal atrophy in multiple sclerosis

Button J, Al-Louzi O, Lang A, Bhargava P, Newsome SD, Frohman T, Balcer LJ, Frohman

EM, Prince J, Calabresi PA, Saidha S. Disease-modifying therapies modulate retinal atrophy in multiple sclerosis: a retrospective study. *Neurology* 2017;88:525–532.

The authors retrospectively investigated 402 patients with relapsing-remitting multiple sclerosis (RRMS) to determine if disease-modifying therapies (DMTs) including glatiramer acetate, natalizumab, and interferon- β -1a exert differential effects on rates of retinal atrophy as assessed by using optical coherence tomography (OCT). The authors determined that rates of combined thickness of the ganglion cell + inner plexiform atrophy in patients with RRMS vary according to DMT utilisation. They also found that natalizumab, which slows the rate of brain atrophy, also slows the rate of retinal thinning relative to glatiramer acetate and interferon- β -1a. The study limitations include its retrospective design, that only four DMT classes were included in the analysis and non-inclusion of MRI brain atrophy data. This study supports using OCT for monitoring neurodegenerative treatment effects in the retina as a practical outcome measure in RRMS clinical trials.

Michael Vaphiades

Imaging the paediatric posterior fossa

Rossi A, Martinetti C, Morana G, Severino M, Tortora D. Neuroimaging of infectious and inflammatory diseases of the pediatric cerebellum and brainstem. *Neuroimag Clin N Am* 2016;26:471–487.

The authors review the neuroimaging characteristics of a variety of cerebellar ataxias and stress that magnetic resonance (MR) imaging is crucial in evaluating patients suspected of harboring inflammatory-infectious involvement of the cerebellum and brainstem. They conclude that knowledge of the imaging features of these disorders and technical competence on paediatric MR imaging are necessary for a correct interpretation of findings, which in turn prompts further management.

Michael Vaphiades

Acute macular neuroretinopathy

Bhavsar KV, Lin S, Rahimy E, Joseph A, Freund KB, Sarraf D, Cunningham ET. Acute macular

neuroretinopathy: a comprehensive review of the literature. *Surv Ophthalmol* 2016;61:538–565.

The authors reported 101 patients with acute macular neuroretinopathy (AMN) from 1975 to December 2014. They concluded that AMN preferentially affects young white women and over half in the third decade of life. It was most commonly associated with nonspecific flu-like illness, fever, or oral contraceptive use. With the advent of spectral-domain optical coherence tomography (SD-OCT), it was determined that AMN lesions typically show hyper-reflectivity at the junction between the outer plexiform layer (OPL) and outer nuclear layer (ONL) and frequently associated with disruption of both the ellipsoid zone (EZ) and interdigitation zone (IZ). Furthermore, anatomical data have been able to support the critical role of deep capillary plexus (DCP) compromise in AMN.

Michael Vaphiades

Diplopia and glaucoma

Sun PY, Leske DA, Holmes JM, Khanna CL. Diplopia in medically and surgically treated patients with glaucoma. *Ophthalmology* 2017;124:257–262.

In this prospective cohort study, 195 adult patients with glaucoma who had undergone surgical or medical management completed a diplopia questionnaire. A chart review was performed jointly by a strabismus specialist and a glaucoma subspecialist to characterise the type and cause of diplopia. Diplopia was reported in 41 of 195 medically and surgically treated patients (21%) with glaucoma. The authors concluded that diplopia may be under-recognised in medically and surgically treated patients with glaucoma. The prevalence of monocular diplopia and binocular diplopia unrelated to glaucoma surgery was similar among medical and surgical groups.

Michael Vaphiades

Cerebellar control of eye movements

Beh SC, Frohman TC, Frohman EM. Cerebellar control of eye movements. *J Neuroophthalmol* 2017;37:87–98.

The authors searched and reviewed a variety of sources regarding the cerebellum and ocular motility. They concluded that the cerebellum guarantees the precision of ocular movements to optimise visual performance and occupies a central role in all classes of eye movements both in real-time control and in long-term calibration and learning. The most important role of the cerebellum in eye movement control is its ability to constantly monitor the brain's performance, detect errors, readjust, and recalibrate its responses to guarantee optimal visual acuity.

Michael Vaphiades

Decreased peripapillary thickness in NAION

García-Basterra I, Lahrach I, Morillo Sánchez MJ, Kamal-Salah R, Rius-Díaz F, Dawid Milner MS, García-Campos JM. Analysis of peripapillary choroidal thickness in non-arteritic anterior ischaemic optic neuropathy. *Br J Ophthalmol* 2016;100:891–896.

The authors conducted a retrospective study to assess peripapillary choroidal thickness (PCT) in patients with non-arteritic anterior ischaemic optic neuropathy (NAION). PCT was measured with optical coherence tomography (OCT) after optic disc swelling resolved completely (3.1 ± 0.7 months). They found that eyes affected by NAION showed a significantly thinner PCT compared with eyes of normal control individuals, even after adjusting for refractive error. Interestingly, the unaffected contralateral eyes of NAION patients also showed a significantly thinner PCT compared with eyes of normal control individuals. The authors concluded that a thin PCT may be a predisposing factor for NAION.

An-Guor Wang