

Department of Ophthalmology

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General Summary

The main research interest of our department is the pathophysiology of the visual processing system. The following topics are the subjects of basic and clinical studies: cataract, neuro-ophthalmology, ocular oncology and histopathology, biochemistry, functional magnetic resonance imaging (MRI), glaucoma, electrophysiology, diabetes, vitreoretinal diseases, age-related macular degeneration, uveitis, color vision, cornea, and the oculoplastic.

Research Activities

Cataract

We are able to choose various premium intraocular lenses (IOLs), for example, multifocal IOLs, toric IOLs, and yellow IOLs. We implant these new IOLs through microincisions and evaluate subsequent visual function.

Neuro-ophthalmology

1. We performed a large-scale cohort study of the clinical and epidemiologic characteristics of optic neuritis in Japan. Serum samples from patients with optic neuritis were tested for aquaporin-4 antibodies (AQP4-Abs) and anti-myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) and were correlated with the clinical findings. Among 531 serum samples from patients with optic neuritis, 12% were AQP4-Ab-positive and 10% were MOG-Ab-positive. Pretreatment visual acuity worsened to more than a median 1.0 log minimum angle of resolution in patients. Patients who were AQP4-Ab-positive were more likely to be a woman and exhibit diverse visual field abnormalities and 22% of patients demonstrated concurrent spinal cord lesions on MRI. Patients who had optic neuritis and were positive for AQP4-Ab had poor visual outcomes. Patients who were positive for MOG-Ab had rates of optic disc swelling and pain with eye movement which were significantly higher than those in the AQP4-Ab-positive patients. Patient who were MOG-Ab-positive manifested severe clinical findings of optic neuritis before treatment but generally showed good treatment responses with favorable visual outcomes. Most patients showed isolated optic neuritis lesions on MRI. Multivariate logistic regression analysis of all patients identified age and presence of antibodies as significant factors

affecting visual outcome. These findings indicate that autoantibody measurement is useful for the prompt diagnosis and proper management of cases of optic neuritis that tend to become refractory.

2. We reported the usefulness of a head-mounted perimeter in unilaterally nonorganic visual loss, spontaneous recovery in cases of Leber's hereditary optic neuropathy with the 11778 mutation, demyelinating optic neuritis associated with golimumab, and intravenous immunoglobulin treatment for steroid-resistant optic neuritis.

Ocular oncology and histopathology

1. Optic nerve sheath meningioma (ONSM) is a rare tumor. We examined the efficacy and complications associated with intensity-modulated radiation therapy (IMRT) for ONSM in 15 patients and compared visual function before and after treatment. After IMRT, tumor enlargement was not detected in any eyes. At the final posttreatment follow-up visit, eyes with fusiform and globular growth were found to have maintained better visual acuity. Final posttreatment visual field abnormalities improved in 11 eyes. All adverse events identified during IMRT improved rapidly during the treatment period. The use of IMRT for patients with ONSM improved and preserved visual function. In particular, early IMRT before the appearance of optic disc edema and atrophy can be more effective for improving visual function.

2. We reported a case of sebaceous gland carcinoma with perineural spread in the orbital apex and recurrent and giant pilomatricoma.

Glaucoma

1. Improve efficiency and precision of glaucoma checkup examination

Glaucoma is a progressive and irreversible disease that causes blindness. Early detection with checkup examinations and early treatment is essential for preventing severe visual impairment because early symptoms are rarely reported by patients. We evaluated the efficiency of a plurality of examination items using big data and the Markov model.

2. Quality of vision after glaucoma surgery

Although the purpose of glaucoma treatment is to protect visual function, glaucoma surgery decreases quality of vision and increases both regular and irregular astigmatism. We are investigating causes of the development of astigmatism by using corneal topographies and anterior optical coherence tomography.

3. Personality traits of glaucoma patient

Glaucoma is an incurable and irreversible disease requiring endless eye drop therapy. To prevent disease progression, patients must adhere to constant therapy. To study five-factor model of personality traits of patients with glaucoma, we have used TIPI-J, a Japanese version of the Ten Item Personality Inventory. To improve patient adherence, we evaluated the relationship between patients' adherence and five-factor model.

4. Basic research on neuroprotection and regeneration

Of patients with glaucoma in Japan, approximately 70% have normal-tension glaucoma. Glaucoma can progress even if intraocular pressure is sufficiently decreased. Studies are urgently needed to develop a radical cure for direct nerve protective or reproduction treatment.

5. Improve diagnosis and detection of progression methods

Because many patients with glaucoma report no symptoms until the late stage, both undiagnosed cases at an early stage and progressive glaucomatous changes after diagnosis are important to detect. We have attempted to improve clinical examinations, such as the visual field test and optical coherence tomography.

Functional neuroimaging

Many researchers have recently applied graph theory to estimate the efficiency of complex brain networks. Graph theory is a mathematical theory which uses a graph consisting of a pairwise nodes and edges. Our team has succeeded in constricting cerebral functional and morphological connectivity matrices by using a MR scanner. We are now ready to examine brain networks by means of graph theory analysis.

Developmental functional abnormality

We compared patients with strabismus and control groups by using graph theory and by constructing brain morphological connectivity matrices from diffusion MRI. Some graph theory indices show predominance for control group, whereas patients with strabismus also exceed than normal control with several graph theory indices. These results are suggested to reflect a functionally compensated mechanism for patients with strabismus despite fragile binocular function.

Visual neuropsychology

With the use of functional MRI or diffusion MRI or both, many eye diseases have been shown to change the visual cortex and the visual tract. We are now attempting to stabilize a scanning procedure for quantitative MRI and to apply it to a volunteer who has an eye disease. Quantitative MRI allows us to directly measure T1 values. By using T1 values, we can estimate cell compositions at a voxel, each of which is an array of elements in a brain image.

Low vision

We assessed the effect of rehabilitation for patients with visual field loss by using an active field analyzer, which that can be used to clarify a visual search function that is a factor in the specificity of the visual field but not in visual acuity.

Vitreoretinal surgery

We have used 23-, 25-, and 27-gauge transconjunctival vitrectomy systems to treat cases of macular hole, epiretinal membrane, macular edema, and rhegmatogenous retinal detachment. The 25- and 23-gauge sutureless vitrectomy techniques decrease the surgical trauma and improve patients' postoperative comfort. The 25- and 23-gauge instrumentation is effective for a variety of vitreoretinal surgical indications. Although the infusion and aspiration rates of the 25- and 23-gauge instruments are lower than those for the 20-gauge high-speed vitrectomy system, the use of 25- and 23-gauge transconjunctival vitrectomy systems might effectively reduce operative times of select cases that do not require the full capability of conventional vitrectomy.

To evaluate clinical efficacy of a 7-mm IOL (ETERNITY[®], Santen Pharmaceutical Co. Ltd.) for combined pars plana vitrectomy, phacoemulsification, and IOL implantation, we observed the visibility of the retina during vitrectomy and measured the depth of anterior chamber preoperatively and postoperatively with the PENTACAM[®] corneal tomographic scanner (Oculus Optikgeräte GmbH).

We are planning to evaluate the changes in regular and irregular corneal astigmatism after 25- and 23-gauge transconjunctival sutureless vitrectomy.

We investigated changes in corneal thickness following vitreous surgery and determined whether such changes can be used as a criterion for evaluating the invasiveness of vitrectomy.

As a method of treating a dropped lens nucleus that occurred during cataract surgery, we removed the dropped lens nucleus through the corneal wound without performing pars plana vitrectomy.

Electrophysiology

We are recording electroretinograms to evaluate whether there are functional disorders at the retinal-cell level in hereditary retinopathy, retinal dystrophy, and macular disease. The electroretinographic waveforms are compounded from the responses of various retinal cells, such as ganglion, amacrine, bipolar, and photoreceptor cells, which are recorded as a single wave pattern.

Diabetic Retinopathy section

A group of vulnerable retina ganglion cells has been reported in patients with diabetes mellitus and in animal models of diabetes. We are recording electroretinograms to evaluate retinal function in patients with diabetes but without retinopathy, as shown with ophthalmoscopy.

Uveitis

We reported on a patient with an atypical presentation of a phakic IOL who initially had vitelliform submaculopathy, a vitreous haze, and a peripheral retinal focus. We described detailed enface imaging of swept-source optical coherence tomographic findings for 3 patients with acute zonal occult outer retinopathy.

Macular degeneration

We reported the effects of photodynamic therapy plus intravitreal aflibercept with subtenon triamcinolone acetate injections for treating aflibercept-resistant polypoidal choroidal vasculopathy. Triple therapy improved visual and anatomical outcomes in patients who had polypoidal choroidal vasculopathy with recurrent or resistant retinal fluid and pigment epithelial detachment after multiple injections of intravitreal aflibercept.

Biochemistry

We examined the role of chemokines in a *Abca4(-/-)Rdh8(-/-)* mouse model of Stargardt disease and a *Mertk(-/-)* mouse model of retinitis pigmentosa. Our results indicated that the chemokine (C-C motif) ligand 3 gene (*Ccl3*) plays an essential role in

regulating the severity of retinal inflammation and degeneration in these mouse models.

Color vision defects and genetic analysis of retinal diseases

1. Retinitis pigmentosa and its allied disorders have genetic heterogeneity. To identify pathogenic variants, we performed direct sequencing of target genes and whole-exome sequencing for these disorders and successfully identified several novel pathogenic variants. In addition, among patients with congenital color blindness, we analyzed genetic variations for congenital achromatopsia and blue cone monochromacy.

Cornea

We will assess the age and disease condition of patients with keratoconus and determine the most appropriate approach for improving vision and quality of life.

Oculoplastic

1. We reported the effect of epinephrine contained in local anesthetics on upper eyelid height in transconjunctival blepharoptosis surgery.
2. We examined the relationship between the postlevator aponeurosis fat-pad and the results of phenylephrine testing.

Publications

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