

## 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, and the cornea.

### Research Activities

#### *Cataract*

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

#### *Neuro-ophthalmology*

We reported on a patient with recurrent refractory bilateral optic neuritis who twice tested negative for antibodies against aquaporin 4 before testing positive. Because seroconversion of these antibodies may occur at any time in patients with neuromyelitis optica spectrum disorders, this antibody should be measured several times if a patient has refractory optic neuritis with repeated episodes of recurrence.

#### *Ocular oncology and histopathology*

Optic nerve sheath meningiomas (ONSMs) are rare tumors that most often affect middle-aged women. Recently, stereotactic radiotherapy has been recommended to treat patients with ONSM. We reviewed demographic data, frequency, clinical features, radiological imaging aspects, and the therapeutic strategy for ONSM.

#### *Glaucoma*

Analysis with the Markov model of the effects of an examination program showed that glaucoma produces an irreversible visual field loss and the most common type of visual impairment in Japan. Early detection and treatment are important until the advanced stage because symptoms are poor. We used the Markov model to analyze the effects of screen-

ing for glaucoma in adults. The early detection and early treatment of glaucoma are economically beneficial.

#### *Functional neuroimaging*

Cortical myelination was calculated with T1-weighted images divided by T2-weighted images as cortical myelin mapping with clinical MRI. In patients with hemianopsia and altered optic radiation, myelin content was reduced, particularly in the posterior portion of the primary visual cortex, but was better conserved in the anterior portion, respecting their visual field defects.

#### *Developmental functional abnormality*

Diffusion tensor imaging was performed to evaluate axonal-axonal density by means of fractional anisotropy on major white-matter tracts to compare subjects with and without strabismus. The fractional anisotropy value of the subjects with strabismus was reduced at the forceps major, which connects the occipital lobes via the splenium of corpus callosum.

#### *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 the "Active Field Analyzer," which 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 diseases*

We have used 23-, 25- and 27-gauge transconjunctival vitrectomy system for macular hole, epiretinal membrane, macular edema, and rhegmatogenous retinal detachment. To evaluate the clinical efficacy of the single-piece intraocular lens (W-60<sup>®</sup>, Santen Pharmaceutical Co., Ltd., Osaka, Japan) for combined pars plana vitrectomy, phacoemulsification, and intraocular lens implantation, we observed the visibility of the retina during vitrectomy and measured the depth of the anterior chamber preoperatively and postoperatively with an anterior eye segment tomogram (Pentacam<sup>®</sup>, Oculus Optikgeräte GmbH, Wetzlar, Germany).

#### *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 tomography 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 acetonide injections for treating aflibercept-resistant polypoidal choroidal vasculopathy. Triple therapy improved visual and anatomical outcomes in patients who had PCV (Polypoidal choroidal vasculopathy) with recurrent or resistant retinal fluid and PED (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 the *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*

Retinitis pigmentosa and related disorders have genetic heterogeneity. To identify pathogenic variants, we performed direct sequencing and whole-exome sequencing analysis of these disorders and successfully identified several novel pathogenic variants.

#### *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.

### **Publications**

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