840 Histologic Correlation of OCT with Diseased Retina in Humans

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Purpose

Direct correlation of ocular coherence tomography (OCT) data with histology of the retina has been lacking, particularly in human retinal disease. This study is designed to refine understanding of both normal and pathological OCT data with high performance histological methods.

Methods

A Heidelberg Spectralis OCT system was used to obtain retinal scans from collected normal human globes as well as globes from patients who suffered from retinitis pigmentosa (RP), wet and dry age-macular degeneration (AMD) and geographic atrophy (GA). The globes were resected post-mortem, fixed in 1% paraformaldehyde, 2.5% glutaraldehyde, anterior segment removed and mounted in normal saline in a spectrophotometer chamber. OCT imaging was then performed on regions of interest and data saved with landmarks. The globes were then removed, portions corresponding to regions imaged by OCT were punched out, dehydrated, embedded in eponates and histologically analyzed with computational molecular phenotyping and ultrastructural analysis.

Results

While some data exists in the literature, a high performance correlation of OCT data with human histology has not to our knowledge been previously performed. Normal retinal tissues reflect the precise understanding of landmarks associated with OCT data and correspond with previously published results. However, pathological retinas presented a number of refinements of our understanding of OCT data including detailed evaluation of Müller cell structure and representation in pigmented bone spicules complete with pigment granules derived from the RPE in mid stage and advanced RP. Additionally, AMD findings of localized atrophy, sub-RPE drusen in AMD and pigment epithelial detachments along with interface alterations between the RPE and retina and sub-retinal deposits are described.

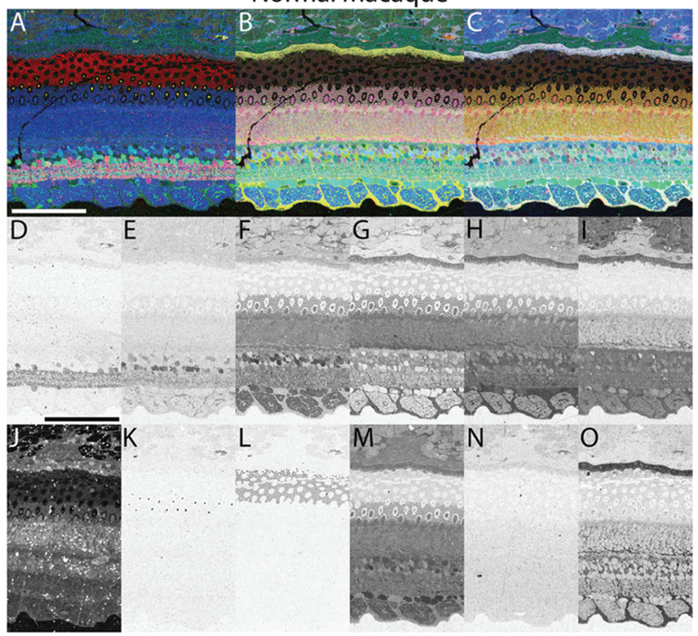
Conclusions

OCT has proven invaluable in the clinic to diagnose and track disease progression. Defining precise understanding of OCT correlates with the histology of retinal structure and function in retinal degenerative diseases will assist the definition of windows of opportunity for various vision rescue strategies.

Abbreviations

Cr: Choroid
CRALBP: anti-Cellular Retinaldehyde-Binding Protein
D: anti-Aspartate
E: anti-Glutamate
G: anti-Glycine
GCL: Ganglion Cell Layer
GFAP: anti-Glial Fibrillary Acidic Protein
INL: Inner Nuclear Layer
IPL: Inner Plexiform Layer
IS: Inner Segments
J: anti-Glutathione
NR: Neural Retina
OCT: Optical Coherence Tomography
ONL: Outer Nuclear Layer
OPL: Outer Plexiform Layer
OS: Outer Segments
Q : anti-Glutamine
R: anti-Arginine
RPE: Retinal Pigment Epithelium
τ: anti-Taurine
γ: anti-GABA

Normal Macaque



Images from a normal macaque monkey. Computational Molecular Phenotyping (CMP) was done to provide control tissue to compare with human retina. **A**, CMP sections γGE > RGB with a color overlay of 1D4 and red green opsin in red and yellow respectively. **B**, CMP sections τQE > RGB. **C**, CMP sections τQJ > RGB. **D**, anti-GABA. **E**, anti-Glycine. **F**, anti-Glutamate. **G**, anti-Taurine. **H**, anti-Glutamine. **I**, anti-Glutathione. **J**, DAPI. **K**, anti-Red Green Opsin. **L**, anti-1D4. **M**, anti-Aspartate. **N**, anti-Arginine. **O**, anti-CRALBP. Scale bars = 100 µm.

Early Dry AMD

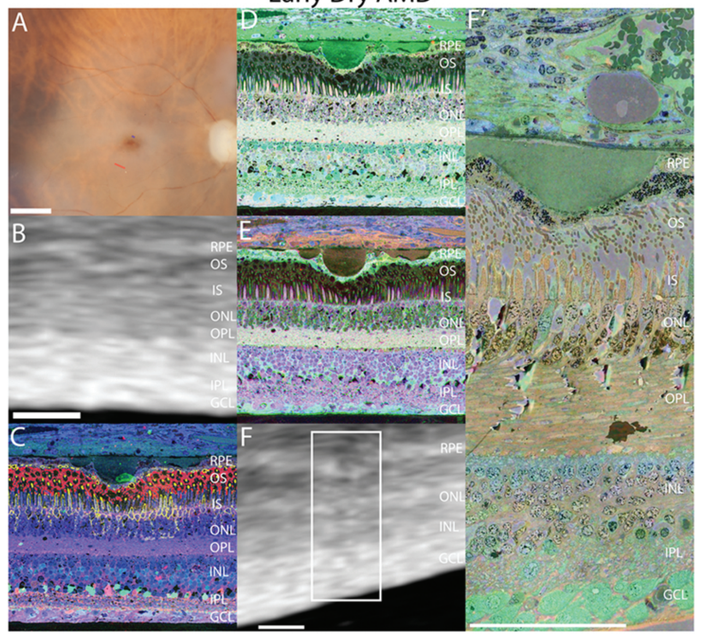


Image panel of early dry age-related macular degeneration. **A**, Fundus image of patient eye postmortem. **B-E** are slices taken from red region in image A. **B**, OCT. **C**, CMP sections γGE > RGB with color overlay of 1D4 and red green opsin in red and yellow respectively. **D**, CMP sections τQE > RGB. **E**, CMP sections RCRALBPJ > RGB. **F**, OCT image of blue region in image A. Inset refers to F'. **F'**, τQJ > RGB color overlayed on TEM. A, Scale bar = 2 mm. B-E, Scale bar = 100 µm.

Wet AMD

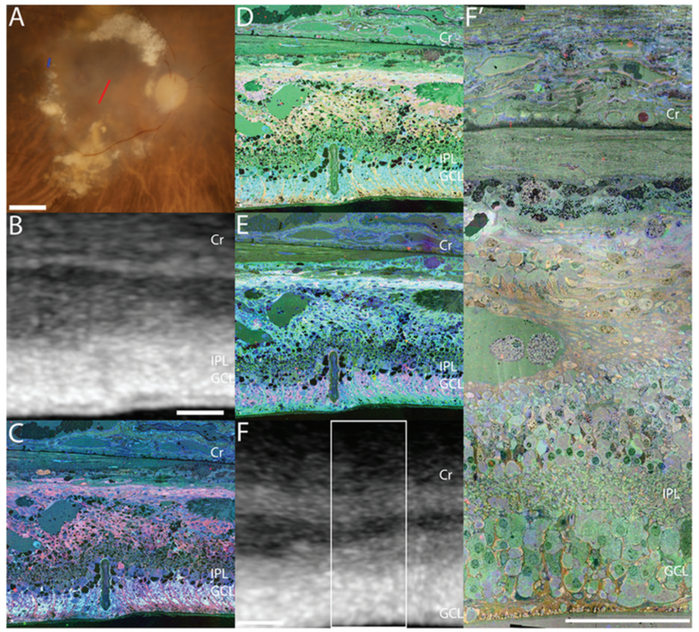


Image panel of wet age-related macular degeneration. **A**, Fundus image of patient eye postmortem. **B-E** are slices taken from red region in image A. **B**, OCT. **C**, CMP sections γGE > RGB. **D**, CMP sections τQE > RGB. **E**, CMP sections GFAPCRALBPJ > RGB. **F**, OCT image of blue region in figure A. Inset refers to F'. **F'** τQJ > RGB color overlaid on TEM. A, scale bar = 2 mm. B,F & F', scale bar = 100 µm.

Geographic Atrophy

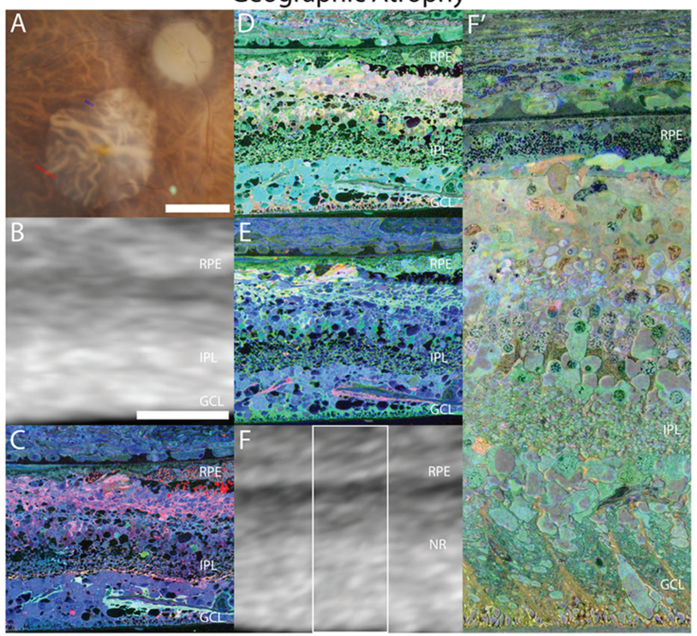


Image panel of geographic atrophy. **A**, Fundus image of patient eye postmortem. **B-E** are slices taken from red region of figure A. **B**, OCT. **C**, CMP sections γGE > RGB. **D**, CMP sections τQE > RGB. **E**, CMP sections GFAPCRALBP > RGB. **F**, OCT image from blue region on figure A. Inset refers to F'. **F'**, CMP sections τQJ > RGB overlaid on TEM. A scale bar = 2 mm. B, F & F' scale bars = 100 µm.

Retinitis Pigmentosa

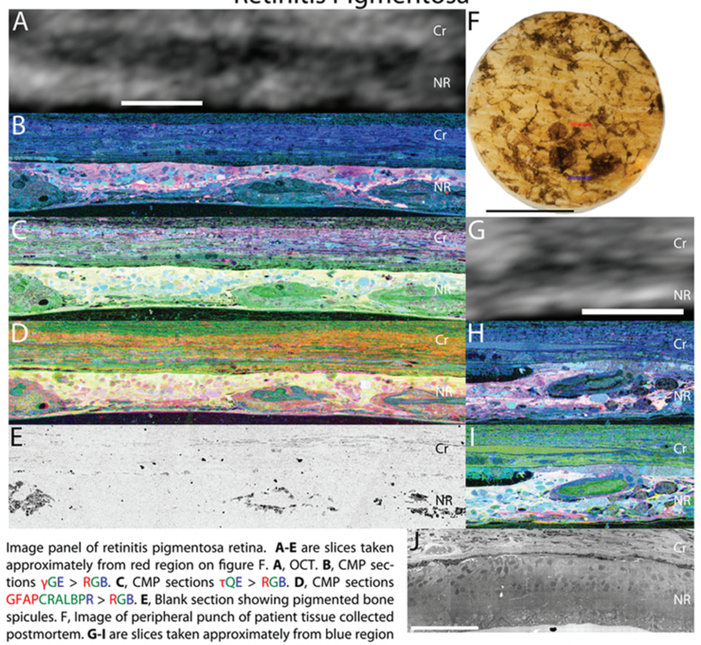


Image panel of retinitis pigmentosa retina. **A-E** are slices taken approximately from red region on figure F. **A**, OCT. **B**, CMP sections γGE > RGB. **C**, CMP sections τQE > RGB. **D**, CMP sections GFAPCRALBPR > RGB. **E**, Blank section showing pigmented bone spicules. F, Image of peripheral punch of patient tissue collected postmortem. **G-I** are slices taken approximately from blue region on figure F. **G**, OCT. **H**, CMP sections γGE > RGB. **I**, CMP sections GFAPCRALBPJ > RGB. **J**, TEM of different patient also diagnosed with retinitis pigmentosa. A, G & J scale bars = 100 µm. F scale bars = 2 mm.

Cobblestone

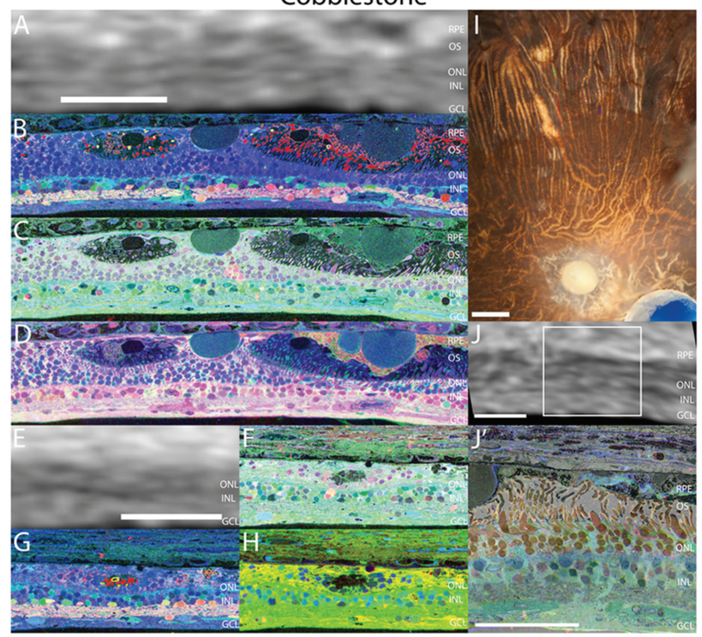


Image panel of cobblestone retina. **A-D** are slices taken from red region in image I. **A**, OCT. **B**, CMP sections γGE > RGB with color overlay of 1D4 and red green opsin in red and yellow respectively. **C**, CMP sections τQE > RGB. **D**, CMP sections JCRALBPD > RGB. **E-H** are slices taken from green region in image I. **E**, OCT. **F**, CMP sections τQE > RGB. **G**, CMP sections γGE > RGB with color overlay of 1D4 and red green opsin in red and yellow respectively. **H**, CMP sections GFAPJDAPI >RGB. **I**, Fundus image of patient eye postmortem. **J**, OCT of blue section shown in image I. Inset represents J'. **J'**, CMP sections τQJ > RGB overlaid on TEM. A,E,J & J' scale bars = 100 µm. I, scale bar = 2 mm.