Macular Telangiectasia Type 2 (MacTel) Disease State

June 2025

US-EO-SC-25060002

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MacTel: Overview and Epidemiology

Three Types of Macular Telangiectasia (MacTel)

MacTel 1: Aneurysmal Telangiectasia

- Unilateral, progressive ocular disease that leads to vision loss[1,2]
- Defined by aneurysmatic dilation of blood vessels in the temporal region of the macula[2]
- Characterized by decreased deep capillary plexus density, macular edema, and ellipsoid-zone layer disruption[3]
- **Neovascularization is not present[1]**

MacTel 2: Perifoveal Telangiectasia

- **Bilateral, progressive, retinal neurodegenerative disease[2,4]**
- Characterized as nonproliferative or proliferative[1,4]
  - Nonproliferative stages: inner retinal thickening and cysts, loss of retinal transparency, and foveal involvement[4]
  - **Proliferative stages: presence of telangiectatic vessels and subretinal vascular complex[4]**

MacTel 3: Occlusive Telangiectasia

- Rare ocular disease[1]
- Characterized by the presence of perifoveal capillary nonperfusion[1]
- **Appears to be driven by systemic or cerebral diseases[1]**
- Shares clinical features with cerebroretinal vasculopathy[5]

1. Yannuzzi LA, et al. *Arch Ophthalmol*. 2006;124(4):450-460. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Guo J, et al. *BMC Ophthalmol*. 2018;18(1):69. **4.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **5.** Seraly MP, et al. *Am J Ophthalmol Case Rep*. 2020;20:100985.

MacTel 2: Neurodegenerative Retinal Disease Associated With Central Vision Impairment[1]

MacTel 2 is a **neurodegenerative retinal disease** that leads to **vision loss**; it may start in one eye, but it almost always affects **both eyes**[1]

Photoreceptor loss occurs in MacTel 2 and leads to central vision loss and functional impairment[1,2]

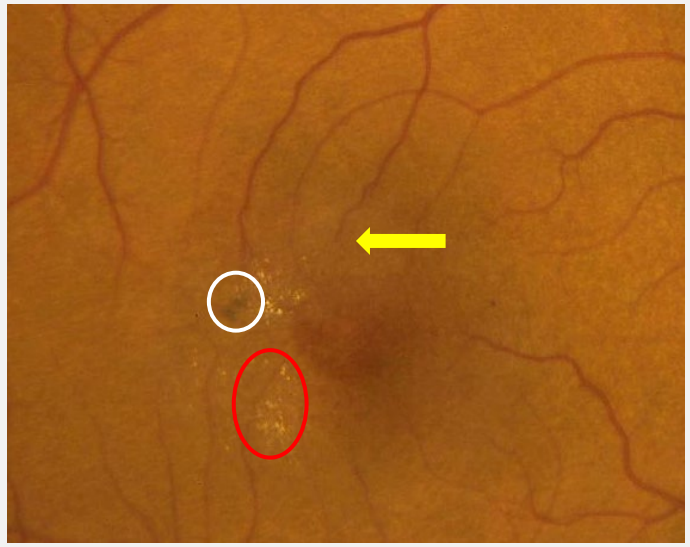
Patients experience substantial burden of illness due to loss of visual acuity, including visual field defects and **impaired reading and driving ability**[2-4]

No curative or disease-altering treatments currently exist[1,2]

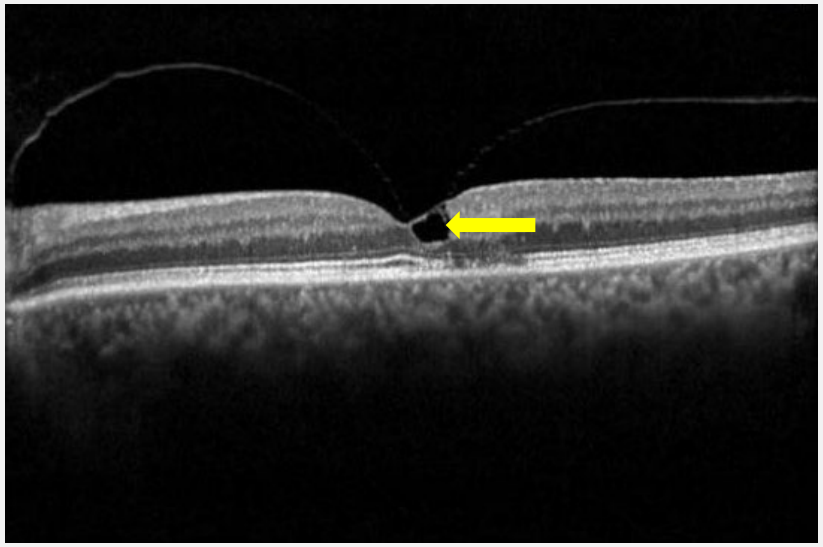
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Heeren TFC, et al. *Retina*. 2014;34(5):916. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309.

MacTel 2 Results in Changes to the Retina[1,2]

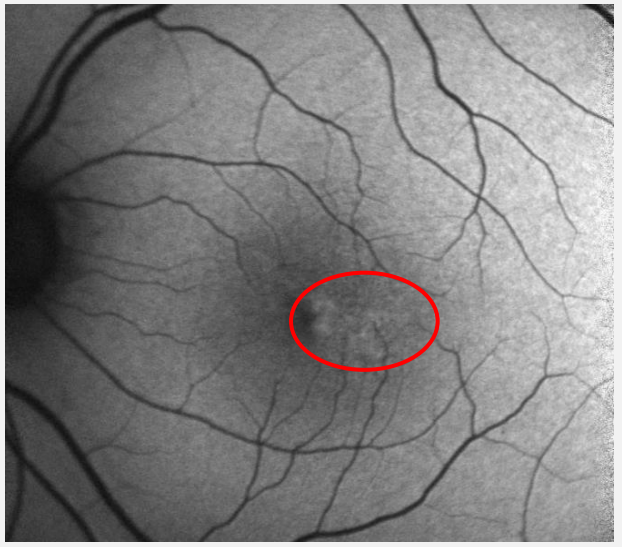
Microvascular Abnormalities (arrow), Crystals (red circle), Pigment Hyperplasia (white circle)



Cavitary Lesion on OCT (arrow)



Luteal Pigment Loss on AF (red circle)



These early changes seen in OCT and AF are often misdiagnosed as lamellar holes, vitreomacular traction, or cysts, contributing to the underdiagnosis of MacTel 2

AF, autofluorescence; OCT, optical coherence tomography. Images provided by Dr. Thomas Aaberg.

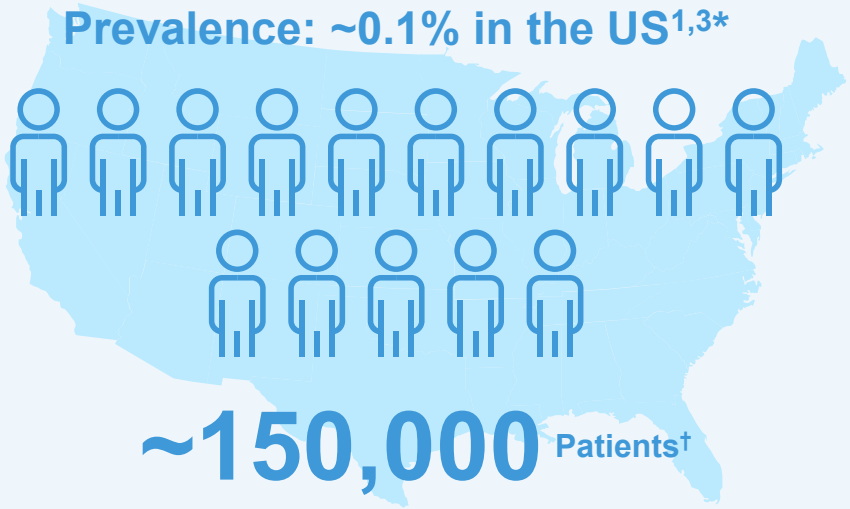
1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77.

MacTel 2 is Underdiagnosed, With an Estimated Prevalence of 0.1% in the US[1*]

Incidence: ~0.8/100,000 persons/year[2,3]

~2,700 new cases/year†

Prevalence: ~0.1% in the US[1,3*]



~150,000 Patients†

Patients are diagnosed in mid-late decades

Symptoms appear around age **40–50 years**[4]

Mean age of diagnosis is **57 years**[5]

Approximately **2% of MacTel patients are under age 40 years**[6]

Patient population may be underestimated

Underdiagnosis and misdiagnosis of MacTel contributes to the potentially **underestimated patient numbers**[4]

*Among patients aged 43–86 years; based on Beaver Dam, Wisconsin. †Calculation performed using the US 2020 population (331,449,281).[3]

1. Klein R, et al. *Am J Ophthalmol*. 2010;150(1):55-62.e2. **2.** Starr MR, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2020;51(5):S35-S42. **3.** United States Census Bureau. "Populations and People." Accessed Jan 2024. **4.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **5.** Clemons TE, et al. *Ophthalmic Epidemiol*. 2010;17(1):66-73. **6.** Reddy NG, et al., *Int J Retina Vitreous*. 2023;9(1):47.

Risk Factors Associated With MacTel 2

MacTel 2 has a slightly **increased prevalence in women**[1,2]

MacTel 2 has a **possible genetic component**[2]

Although no inheritance pattern has been found for MacTel, it has been observed in **familial clusters** and among **monozygotic twins**

Risk loci for MacTel 2 have been identified across the genome

Certain systemic conditions are commonly seen in patients with MacTel 2[1-3]

Hypertension or prehypertension

Diabetes mellitus or **impaired fasting glucose**

Being a **current or former smoker** may increase the risk of MacTel 2[1,2]

1. Clemons TE, et al. *Ophthalmic Epidemiol*. 2010;17(1):66-73. **2.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **3.** Reddy NG, et al., *Int J Retina Vitreous*. 2023;9(1):47.

MacTel 2 Disease Diagnosis

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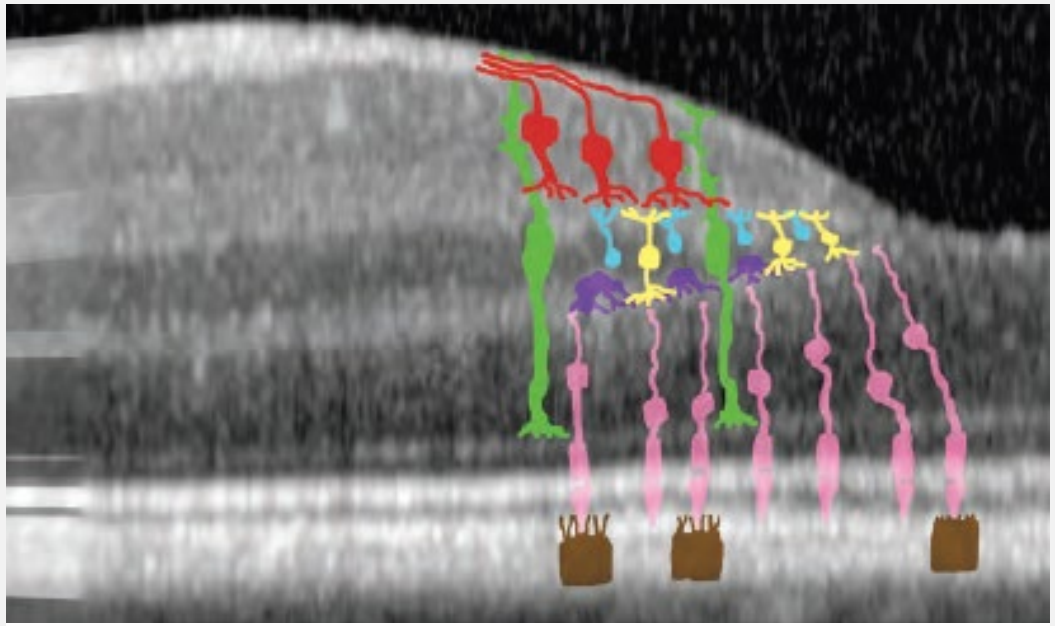
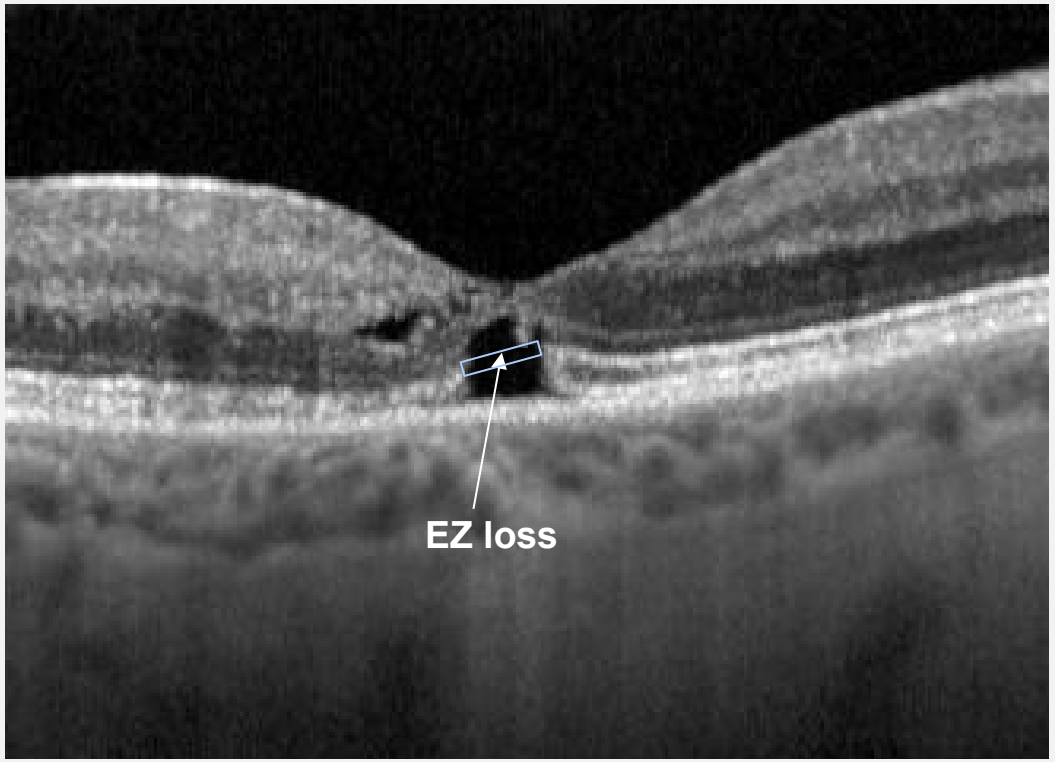
Photoreceptor Loss in MacTel 2 Leads to Functional Vision Loss[1]

Healthy retina OCT

(Cross-section through the fovea[2])



MacTel OCT



EZ, ellipsoid zone; OCT, optical coherence tomography. Image on left reprinted with permission from Neal Adams, M.D., under a license agreement. Image on right provided by Dr. Thomas Aaberg.

1. Heeren TFC, et al, *Ophthalmology*. 2020;127(11):1539-1548. **2.** Adams NA. *Atlas of OCT*. Franklin, MA, USA: Heidelberg Engineering; 2024.

Size and Rate of Enlargement of EZ Loss in MacTel 2

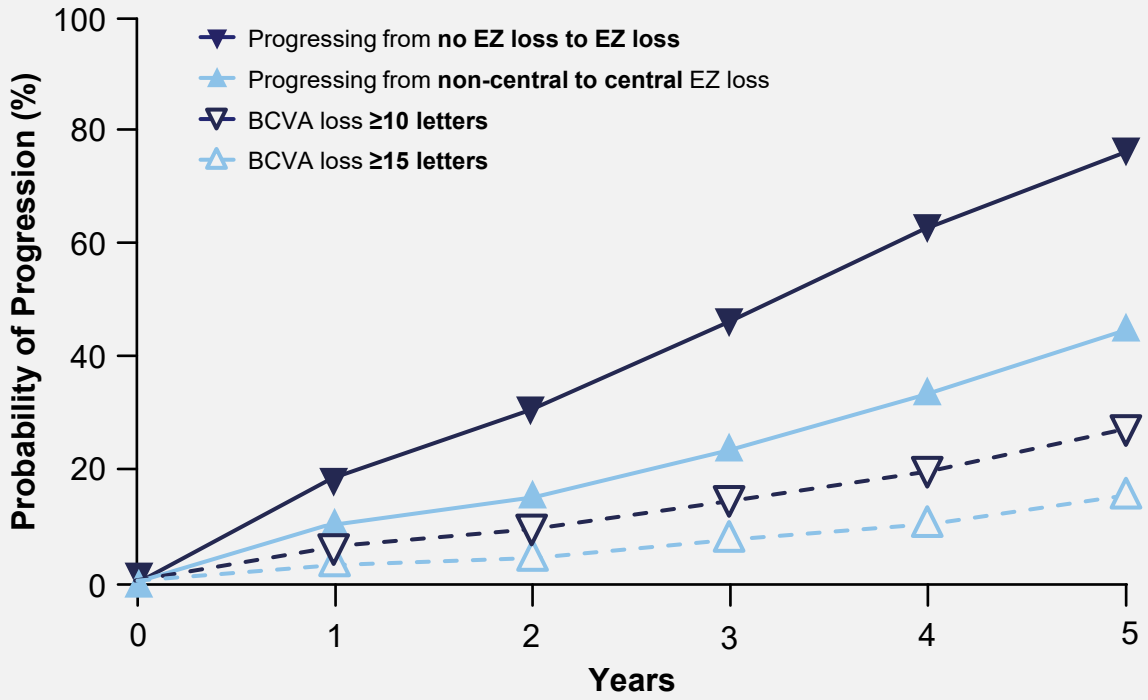
In healthy eyes, the **mean area ± SD of superficial foveal avascular zone was 0.27 ± 0.101 mm²** based on OCT-A[1]

In studies of MacTel 2, baseline **EZ loss area has been ~0.5–0.6 mm²**, with a **rate of change of ~0.08 mm² per year**[2,3]

EZ, ellipsoid zone; OCT-A, optical coherence tomography angiography; SD, standard deviation.
1. Shahlaee A, et al. *Am J Ophthalmol*. 2016;161:50-55.e1. **2.** Heeren TFC, et al. *Retina*. 2018;38(Suppl 1):S20-S26. **3.** Neurotech data on file.

Most MacTel 2 Patients Develop EZ Loss With a Subsequent Impact on Vision[1]

Based on findings from the MacTel Natural History Study (N=507)[1]



5

76% develop an EZ loss 5 years after diagnosis[1]

45% progress from non-central to central EZ loss 5 years after diagnosis[1]

Total EZ area loss results in significant BCVA loss[1,2]

BCVA, best corrected visual acuity; EZ, ellipsoid zone.

1. Peto T, et al. *Retina*. 2018;38(Suppl 1):S8-S13. **2.** Chew EY, et al. *Ophthalmol Sci*. 2023;3(2):100261.

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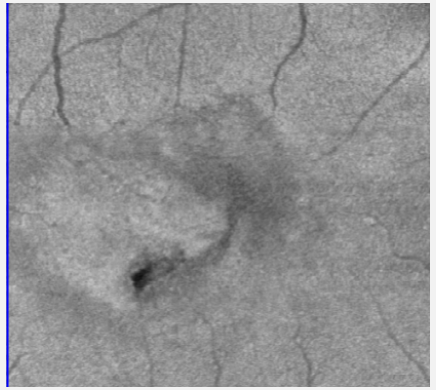
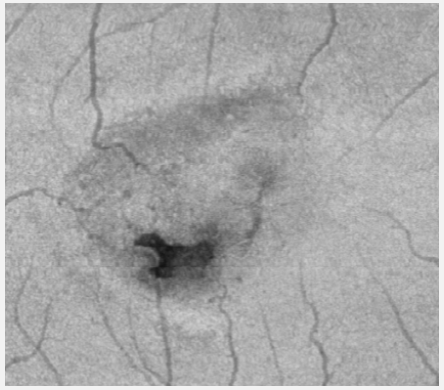
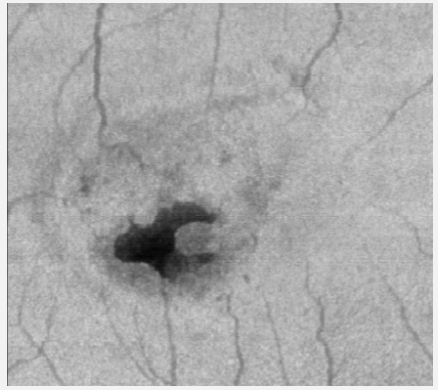
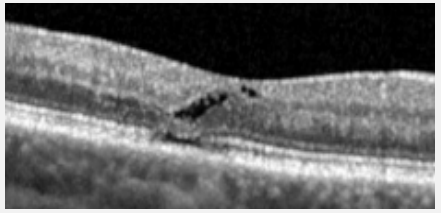
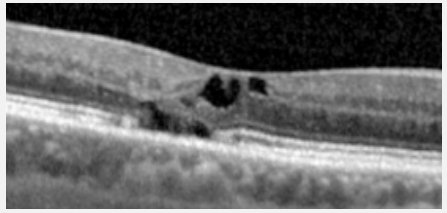
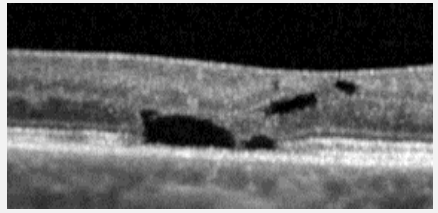
BCVA Over Time May Not Adequately Capture MacTel 2 Progression or Visual Function[1]

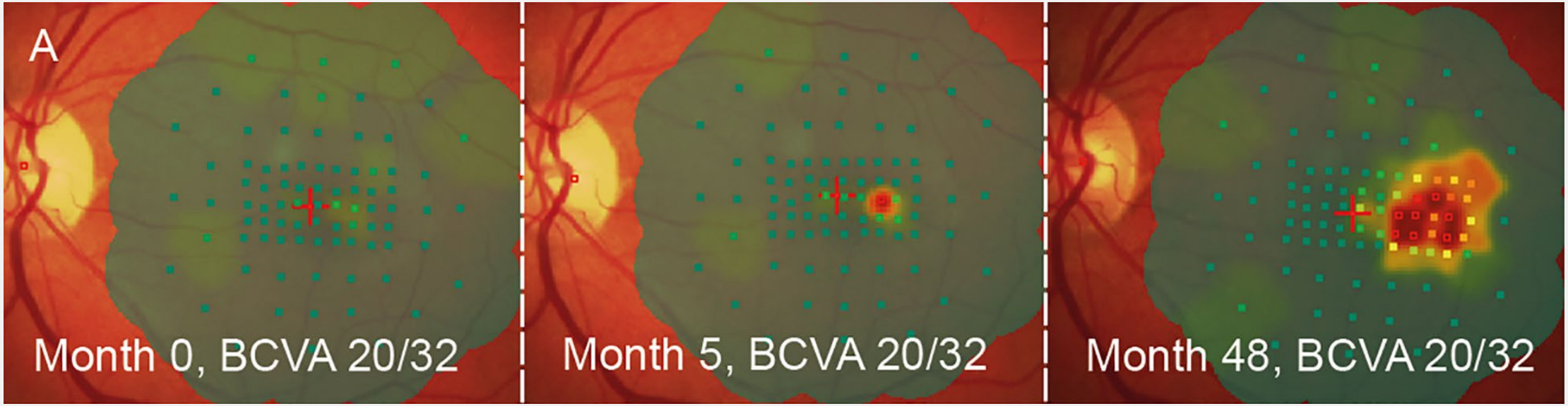
	2020	2022	2024
En Face Area of EZ loss			
Corresponding SD-OCT			
	Small area of EZ loss; fovea spared	Expanding EZ loss; fovea spared	Expanding EZ loss; fovea surrounded
	20/30 BCVA with minimal symptoms	**20/30 BCVA, complains of difficult reading**	**20/40 BCVA, complains of missing vision**

BCVA, best corrected visual acuity; EZ, ellipsoid zone; SD-OCT, spectral domain optical coherence tomography. Images provided by Dr. Thomas Aaberg.

1. Pauleikhoff D, et al. *Acta Ophthalmol*. 2019;97(7):e998-e1005.

BCVA Often Does Not Reflect Disease Burden[1,2]

Progression of disease over 4 years[1]



These microperimetry images mapping areas of photoreceptor loss demonstrate the development and subsequent expansion of a scotoma in a MacTel patient, yet visual acuity remains stable[1-3]

BCVA, best correlated visual acuity. Images reprinted with permission under a license agreement with Copyright Clearance Center on behalf of Association for Research in Vision & Ophthalmology.

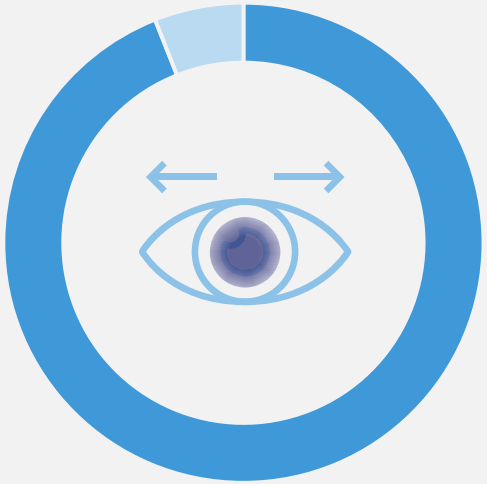
1. Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912. **2.** Charbel Issa P, et al. *Invest Ophthalmol Vis Sci*. 2007;48:3788-3795. **3.** Heeren TFC, et al. *Ophthalmology*. 2020;127:1539-1548.

Irreversible Vision Loss and Compromised Visual Function[1,2]

Patients with a scotoma have a mean BCVA of 20/63[3]

Scotomas, or visual field defects, force patients to compensate with small eye movements, resulting in delayed reactions and other impairments not reflected in visual acuity[4]

47%
Patients with absolute scotomas[1]



94%
Patients with scotomas that expanded within 5 years[5]*

*Those with an initial scotoma had an average growth rate of 1.3 new test points with an absolute scotoma per year.[4]
BCVA, best correlated visual acuity.

1. Vujosevic S, et al. *Retina*. 2018;38(Suppl 1):S14-S19. **2.** Dalkara D, et al. *Hum Gene Ther*. 2016;27(2):134-147. **3.** Finger RP, et al. *Invest Ophthalmol Vis Sci*. 2009;50(3):1366-1370. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309. **5.** Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912.

Misdiagnoses or Diagnostic Delays Due to the Similarity of MacTel 2 to Other Ocular Conditions[1,2]

MacTel may be misdiagnosed as the following retinal diseases[1,2]:

- **Diabetic retinopathy/ macular edema**
- **Retinal vein occlusion**
- **Retinal dystrophies**
- **Age-related macular degeneration**

MacTel is difficult to diagnose due to[3,4]:

Asymptomatic onset initially

Subtle early clinical findings

1. Clemons TE, et al., *Ophthalmic Epidemiol*. 2010;17(1):66-73. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Nicolai H, et al., *BMJ Case Rep*. 2014;2014:bcr2014204802. **4.** Reddy NG, et al. *Int J Retina Vitreous*. 2023;9(1):47.

Fundus Changes Can Be Subtle in Early MacTel 2[1]

Crystalline Deposits

Retinal Graying

Advanced Hyperpigmentation

Images provided by Dr. Thomas Aaberg.

1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77.

OCT and OCT-A Can Aid in Making a MacTel 2 Diagnosis and Monitoring for Neovascularization[1,2]

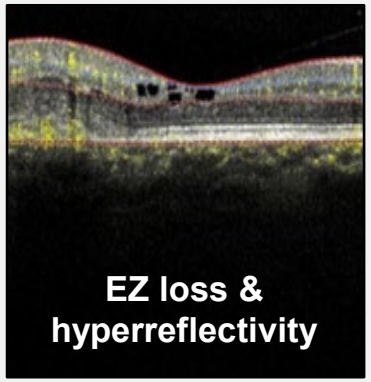
Common OCT findings[1,2]:

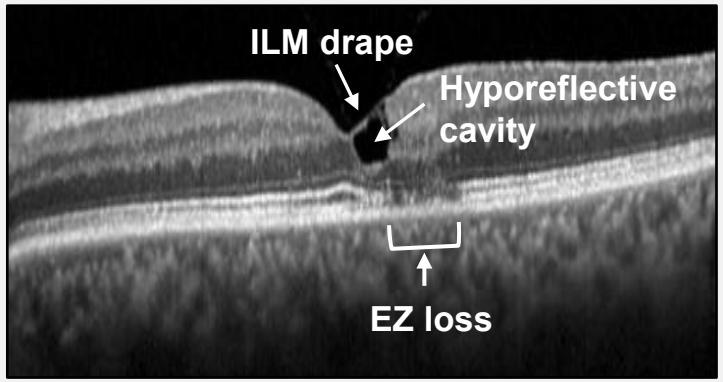
Disruption/loss of EZ

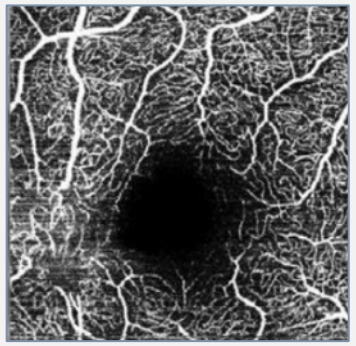
Hyporeflective cavities in the inner and outer neurosensory retina

ILM drape

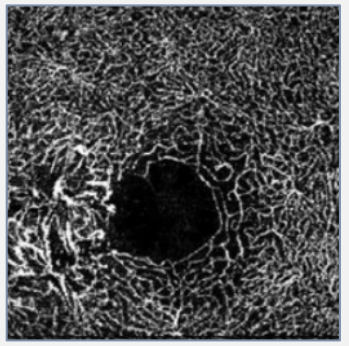
OCT-A shows retinal and choroidal vasculature in high resolution without the need for intravenous dye[1,3]



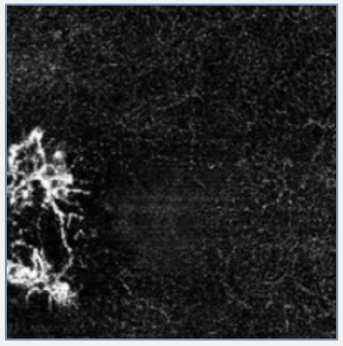




Telangiectasia in SVP



Telangiectasia in DVP

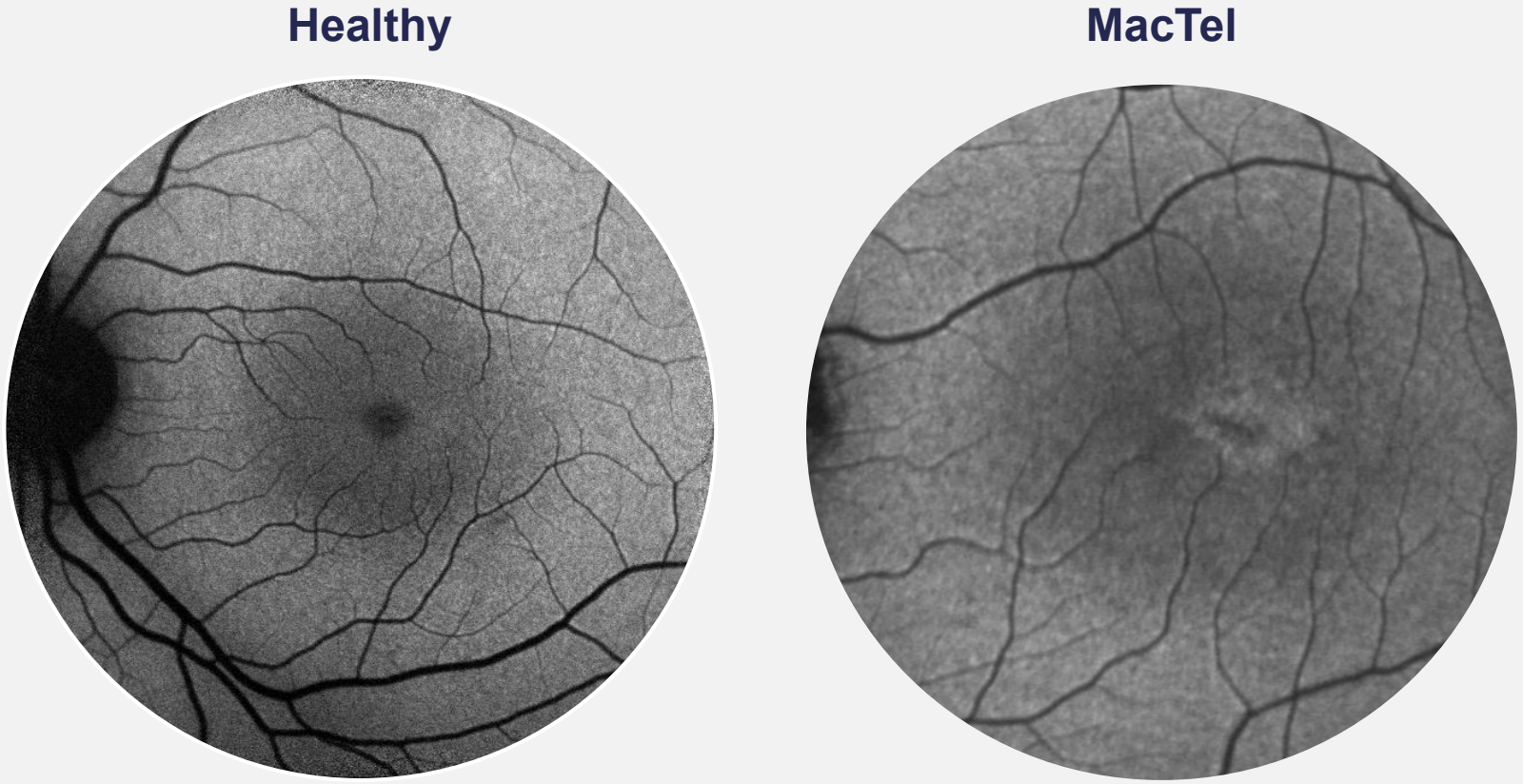


Neovascularization in AVZ

AVZ, avascular zone; DVP, deep vascular plexus; EZ, ellipsoid zone; ILM, internal limiting membrane; OCT, optical coherence tomography; OCT-A, optical coherence tomography angiography; SVP, superficial vascular plexus. Images provided by Dr. Thomas Aaberg.

1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** AAO What is Macular Telangiectasia? 2023 Available: https://www.aao.org/eye-health/diseases/macular-telangiectasia#:~:text=Published%20Sep.,vision%20for%20activities%20like%20reading. Accessed Nov 2024.

FAF Can Detect the Earliest Stages of MacTel 2[1-3]



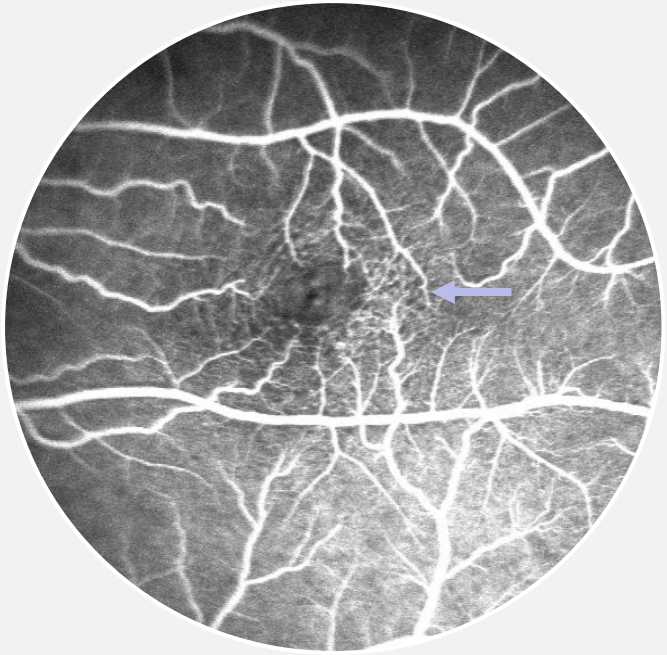
Macular pigment loss in eyes with MacTel is associated with increased auto-fluorescence[2]

FAF, fundus autofluorescence. Images provided by Dr. Thomas Aaberg.

1. Gillies MC, et al. *Ophthalmology*. 2009;116(12):2422-2429. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

FA Has Been Considered the Gold Standard for MacTel 2 Diagnosis[1]

Early phase showing telangiectatic vessels



Late phase showing leakage from telangiectatic vessels

Leakage of dye is one of the earliest signs of MacTel[2]

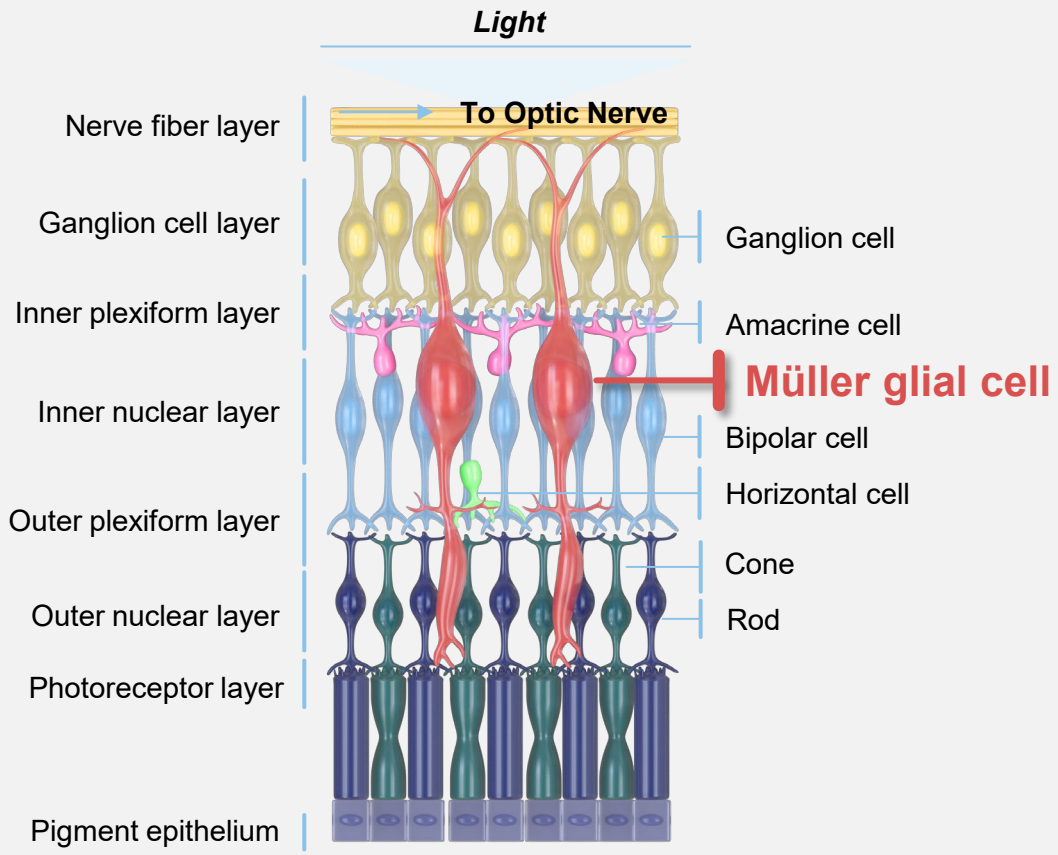
FA, fluorescein angiography. Images provided by Dr. Thomas Aaberg.

1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

Pathogenesis

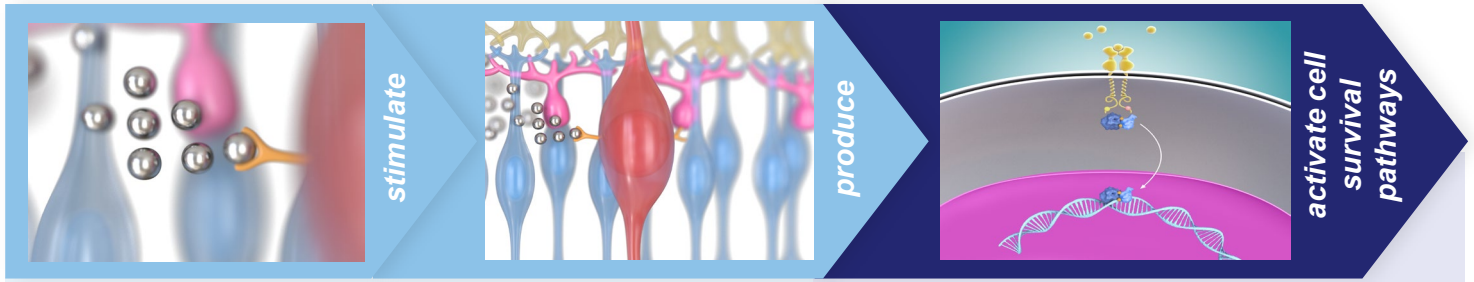
Irreversible Vision Impairment With Müller Glial Cell Dysfunction[1]

- Müller glial cells are the most common glial cell type in the human retina, providing structural and neurotrophic support[2]
- In MacTel, Müller glial cells experience apoptosis, which results in **retinal neurodegenerative effects**[1,3]
- Müller glial cell dysfunction and apoptosis lead to **macular photoreceptor and ganglion cell loss**, causing **impaired central and sharp vision** in affected patients[1,4,5]



1. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309 **2.** Kobat SG, Turgut B. *Beyoglu Eye J*. 2020;5(2):59-63. **3.** Powner MB, et al. *Ophthalmology*. 2013;120(11):2344-2352. **4.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **5.** Muller S, et al. *Ophthalmologica* 2019;241(3):121-129.

CNTF Is Key to Protecting Retinal Neurons[1,2]



CNTF
(ciliary neurotrophic factor)

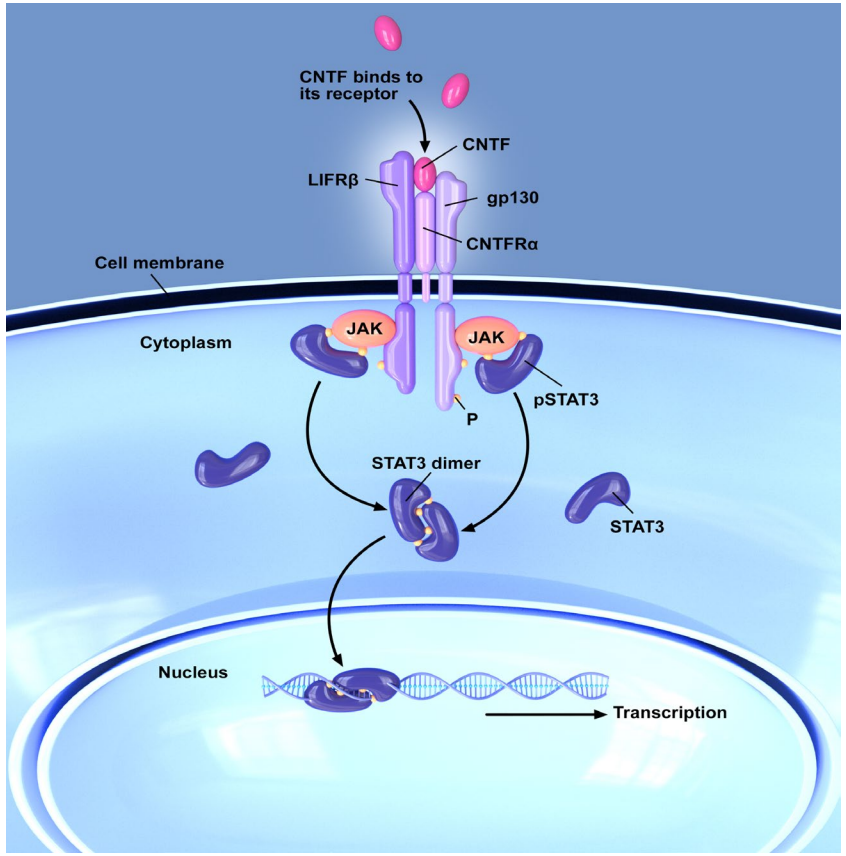
Müller glial cell

- CNTF binds to CNTF receptors on Müller glial cells, activating the JAK-STAT pathway[1,3]
  - Prompts production of growth factors and neuroprotective factors, including CNTF[1]

Neuroprotective factors, including CNTF

- Neuroprotective factors provide structural/ neuroprotective support by activating cell survival pathways[3,4]
- Müller glial cell dysfunction and apoptosis impede production and effectiveness of neuroprotective factors[3]

Enabling macular photoreceptor protection[1,2]



CNTF, ciliary neurotrophic factor; JAK-STAT, Janus kinase/signal transducers and activators of transcription.

1. Bringmann A, et al. *Prog Retin Eye Res*. 2009;28(6):423-451. **2.** Wen R, et al. *Prog Retin Eye Res*. 2012;31(2):136-151. **3.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110(47):E4520-E4529. **4.** Cayouette M, et al. *J Neurosci*. 1998;18(22):9282-9293.

Preclinical Data: Ocular Delivery of CNTF Can Significantly Slow Progression of Retinal Degeneration[1-8]

Authors	Publication Date	Study Subjects	Key Findings
Cayouette et al.	1998	Mouse	Demonstrated that intraocular adenovirus-mediated gene transfer of CNTF reduces photoreceptor loss in homozygous *rds* mouse[1]
Peterson et al.	2000	Rat	Showed that, in rat retinas, CNTF-mediated changes in Müller cell function yield a secondary neuroprotective signaling to photoreceptors and suggested that the impact of CNTF on the JAK-STAT pathway influences neuronal survival[2]
Liang et al.	2001	Mouse and Rat	Found that intravitreal administration of CNTF enables broad and long-term histological photoreceptor protection in mice and rats for 8.5–9.0 months and 6.0 months, respectively[3]
Sieving et al.	2006	Human	Showed improved acuities of 10–15 letters for n=3 of 7 patients who received CNTF delivered via encapsulated cells implanted into the vitreous[4]
Kassen et al.	2009	Zebrafish	Demonstrated that CNTF has neuroprotective effects on photoreceptors in retinas of adult zebrafish[5]
Talcott et al.	2011	Human	Showed improved photoreceptor survival vs contralateral eyes which experienced progressive photoreceptor death[6,*]
Zhang et al.	2011	Human	Demonstrated CNTF delivery via intraocular encapsulated cell technology led to improved BCVA loss of <15 letters in the high dose group (96.3%) vs low dose (83.3%) and sham (75%)[7]
Rhee et al.	2013	Mouse	Found that low levels of CNTF intravitreally injected in mouse retinas stimulate Müller glial cells and promote photoreceptor neuroprotection[8]

*Included n=2 patients with retinitis pigmentosa and n=1 with Usher syndrome type 2.[6]
CNTF, ciliary neurotrophic factor; JAK-STAT, Janus kinase/signal transducers and activators of transcription.
1. Cayouette M, et al. *J Neurosci*. 1998;18(22):9282-9293. **2.** Peterson WM, et al. *J Neurosci*. 2000;20(11):4081-4090. **3.** Liang FQ, et al. *Mol Ther*. 2001;4(5):461-472. **4.** Sieving PA, et al. *Proc Natl Acad Sci U S A*. 2006;103(10):3896-3901. **5.** Kassen SC, et al. *Exp Eye Res*. 2009;88(6):1051-1064. **6.** Talcott KE, et al. *Invest Ophthalmol Vis Sci*. 2011;52(5):2219-2226. **7.** Zhang K, et al. *Proc Natl Acad Sci U S A*. 2011;108(15):6241-6245. **8.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110(47):E4520-E4529.

Impact on Patients

US-EO-SC-25060002

Vision Impairments Significantly Impact Daily Life[1-6]

Reduction in reading capability[3,5]

- **Decreases by 50 WPM** on average for MacTel patients from the healthy average of 190 WPM
- **Struggle reading numbers:** paying bills, dialing phone numbers, seeing prices correctly when shopping
- **Difficulties with daily tasks:** reading medication bottles, computer usage, reading and following recipes

I can't read books anymore. I literally pick up a book to read it and I have to move my head around and I go through the first few pages and really bad eye starts burning. I just have to put books down, so I had to give up reading.

– MacTel Patient[5]

Limitations on driving[1,2,4,5]

- **Slower reaction** to road hazards (eg, road hazards suddenly appearing)
- Only able to drive short distances/daylight hours due to **difficulty navigating roads and reading road signs**
- **Difficulty judging distance** and perceiving straight lines

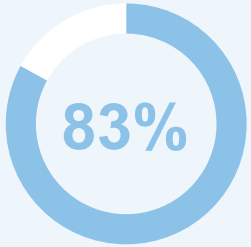
*The first symptoms I was having where I knew something was wrong….was with **driving**. Every linear line is bent in my vision…I constantly see other cars in my lane so I can't pass vehicles anymore because I can't discern where the vehicles are at. And if they are white, silver, or grey I can't see them at all.*

– MacTel Patient[5]

WPM, words per minute.

1. Heeren TFC, et al. *Ophthalmology*. 2020;127(11):1539-1548. **2.** Lee , et al. AAO. "Driving Restrictions per State." 2023; **3.** Finger RP, et al. *Invest Ophthalmol Vis Sci*. 2009;50(3):1366-137033. **4.** Bronstad PM, et al. *JAMA Ophthalmol*. 2013;131(3):303-309. **5.** Neurotech data on file. **6.** Charbel Issa P, et al. *Doc Ophthalmol*. 2009;119(2):133-140.

Distorted Vision With MacTel 2



Patients with **nonproliferative MacTel** often experience **metamorphopsia**[1]

- Present in 83% of MacTel eyes without neovascularization

1. Charbel Issa P, et al. *Doc Ophthalmol*. 2009;119(2):133-140.

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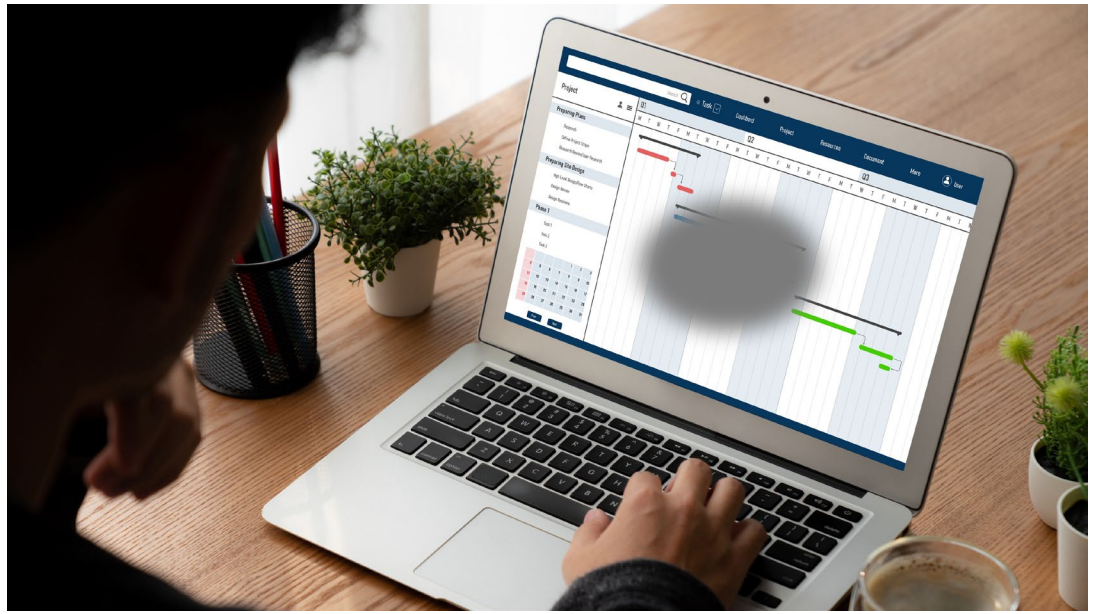
Visual Symptoms Have Significant Impact on Daily Life[1]

1. Neurotech data on file.

MacTel 2 Affects Productivity Leading to Socioeconomic Burdens[1]



MacTel can cause economic burden during prime earning years[2,3]

Employment disruption and reduced wages[1,2]

- Substantial productivity loss for affected patients
- Need to find an accommodating job for their vision symptoms
- Fear of potential job loss
- Feelings of uncertainty about financial stability

Caregiver burden[1]

- Economic cost due to time spent on in-home care and transportation to appointments

1. Rein DB, et al. *Ophthalmology*. 2022;129(4):369-378. **2.** Neurotech data on file. **3.** Heeren TFC, et al. *Retina*. 2014;34(5):916-919.

Patients Have Significant Emotional and Psychosocial Burdens

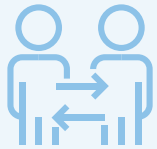
On average, patients with MacTel report

24%

lower mental well-being vs unaffected patients[1,2]

Feelings of vulnerability and isolation[3]

No longer engaging in activities they enjoy



No longer doing certain tasks independently

No longer having good attention to detail at work

Having to give up hobbies

Strains on personal relationships and family life[3]

Feeling as a burden on their family or partner

Unable to read a storybook to grandchildren

"The frustration of not being able to read and do the things I used to do, the hobbies, the projects, the little things… that you always just took for granted."

– MacTel Patient[3]

1. Clemons TE, et al. *Invest Ophthalmol Vis Sci*. 2008;49(10):4340-4346. **2.** Mangione CM, et al. *Arch Ophthalmol*. 2001;119(7):1050-1058. **3.** Neurotech data on file.

MacTel 2 Key Takeaways

Photoreceptor loss in MacTel leads to functional vision loss[1,2]

Most MacTel patients develop **ellipsoid zone loss** with a subsequent impact on vision[3]

BCVA often does not reflect disease burden; patients may develop a scotoma, but visual acuity remains stable[1,4,5]

MacTel may be **misdiagnosed** as other retinal diseases, leading to diagnostic delays[6]

There are currently **no approved disease-modifying treatments** for MacTel, and patients therefore continue to decline[2]

Dysfunction in Müller glial cells and apoptosis leads to vision impairment[1,7,8]

Ocular delivery of CNTF may significantly **slow progression** of retinal degeneration[8,9]

Visual symptoms have a significant **impact on daily life,** including work productivity[10]

Patients with MacTel experience significant **emotional and psychosocial burdens**[11-13]

CNTF, ciliary neurotrophic factor; BCVA, best corrected visual acuity.

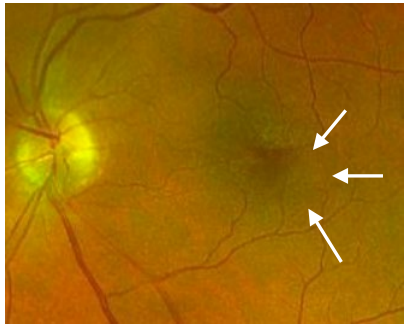
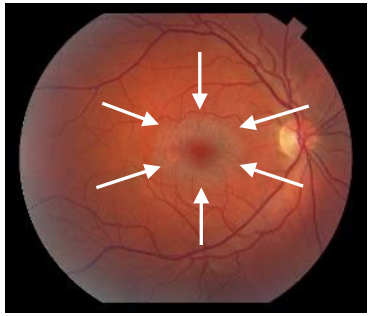
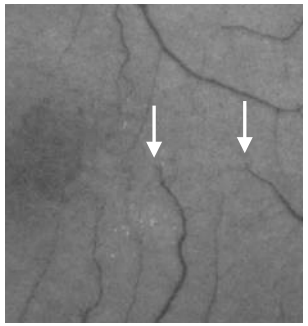
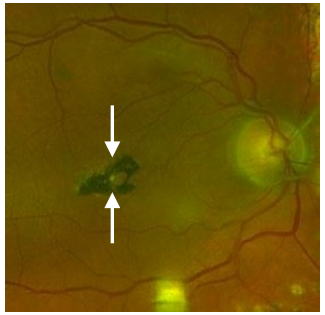
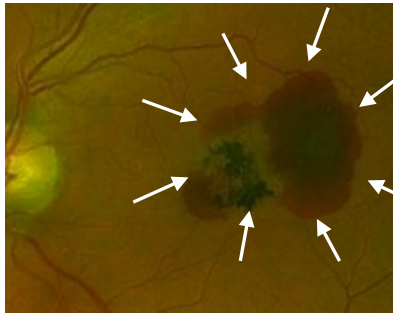
1. Kedarisetti KC, et al. *Clin Ophthalmol.* 2022;16:3297-3309. **2.** Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **3.** Peto T, et al. *Retina*. 2018;38(Suppl 1):S8-S13. **4.** Heeren TFC, et al. *Invest Ophthalmol Vis Sci*. 2015;56(6):3905-3912. **5.** Charbel Issa P, et al. *Invest Ophthalmol Vis Sci*. 2007;48:3788-3795. **6.** Clemons TE, et al. *Ophthalmic Epidemiol*. 2010;17(1):66-73. **7.** Powner MB, et al. *Ophthalmology*. 2013;120(11):2344-2352. **8.** Shen W, et al. *J Neurosci*. 2012;32(45):15715-15727. **9.** Tao W, et al. *Invest Ophthalmol Vis Sci*. 2002;43(10):3292-3298. **10.** Rein DB, et al. *Ophthalmology*. 2022;129(4):369-378. **11.** Clemons TE, et al. *Invest Ophthalmol Vis Sci*. 2008;49(10):4340-4346. **12.** Lamoureux EL, et al. *Invest Ophthalmol Vis Sci*. 2011;52(5):2520-2524. **13.** Neurotech data on file.

Appendix

Different ophthalmologic imaging findings can be observed across the spectrum of MacTel 2 disease severity[1,2*]

Nonproliferative disease
(exudative telangiectasia and foveal atrophy)[2]

Proliferative disease
(subretinal neovascularization)[2]

	Occult telangiectatic vessels	Loss of retinal transparency	Right-angled blood vessels	Retinal pigment clumps	Subretinal neovascularization
					
DFE	**Faint graying and depigmentation; mostly normal**[3]	**Slight graying and loss of transparency of the parafoveolar retina**[3]	**Dilated and blunted right-angle venules; perifoveal telangiectasia**[3]	**Dark pigmented plaque**[3]	**SNV, fibrovascular proliferation in the parafoveal area**[2,4,5]
FA	**Occult vascular abnormalities** are barely detectable[4]	**Mild telangiectatic** and **microaneurysmal changes adjacent to the fovea** with **mild late leakage**[3]		**Ischemia** and marked late **leakage in** the **temporal perifovea**[3]	
OCT	Subtle **hyperreflective middle retinal layer**[3,6]	**Hyporeflective inner retinal cavities**[6]	**Central EZ collapse** and **photoreceptor loss**[3]	Retinal **hyperreflective deposits** and **cysts**[3]	**SNV**, foveal **contour irregularities**[4,6]

*MacTel five-stage classification first defined by Gass and Blodi in 1993[5]; in 2022, Chew et al. introduced a 7-stage classification system using OCT HR, pigment, and EZ loss as an alternative to the Gass-Blodi five-stage system.[7]

DFE, dilated fundus exam ; EZ, ellipsoid zone; FA, fluorescein angiography, OCT, optical coherence tomography; SNV, subretinal neovascularization. Images provided by Dr. Thomas Aaberg.

1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **3.** Chin EK, et al. *Invest Ophthalmol Vis Sci*. 2013;54(7):4459-4470. **4.** Yannuzzi , et al. *Arch Ophthalmol*. 2006;124(4):450-460. **5.** Gass JD, Blodi BA. *Ophthalmology*. 1993;100(10):1536-1546. **6.** Venkatesh R, et al. *Int J Retina Vitreous*. 2022;8(1):26. **7.** Chew EY, et al. *Ophthalmol Sci*. 2023;3(2):100261.