



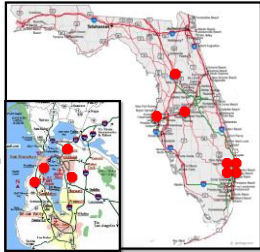
Role of Nutrition in Management of Retinal Disease



by
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The Macula Center A
Vision Integrated Partners
Company

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University of Central Florida
Dept of Ophthalmology
7 19 2018



Objective

How to create a Macular Degeneration Center in an optometric practice:

- Understand Macular Degeneration (Wet/Dry) the role of Blue light damage, oxidation and inflammation in the pathogenesis
- Learn to detect macular degeneration early with dark adaptometry.
- Comprehend lens technology and why optimized biologic pigment impregnated lenses are the best for the AMD patient.
- Learn about macular pigment and how to effectively restore with triple carotenoid therapy.
- Learn to use high dose triple carotenoid therapy to prevent, enhance and eliminate the need for anti-VEGF therapy



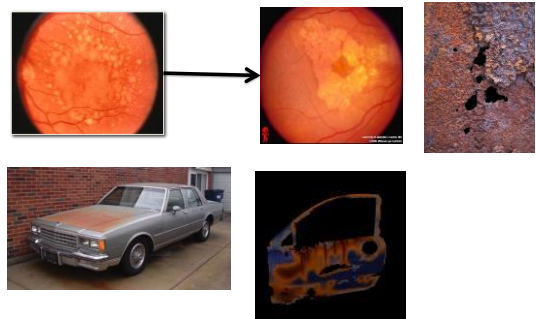
Financial Disclosure

- **Consultant/ Speakers Bureau**
 - Regeneron, Allergan, Novartis/Alcon, Promedior, Notal Vision, Ophthotech, Bausch and Lomb/Valeant, Bayer, Genentech/Roche, Autogenomics, Alimera, Thrombogenics, Allegro, Panoptica, Personal Dx, True Blue Vision, Essilor-Luxottica, Macuhealth.
- **Research Grants**
 - Bayer, Ophthotech, Allergan, GlaxoSmithKline, Novartis/Alcon, Allegro, Tyrogenix, Genentech/Roche, Lpath, Pfizer, Regeneron, Thrombogenics, NEI, Notal Vision, Santen, Xoma, I-Cos, Alimera, Astellas, Opthea.
- **Stocks/Patents/Founder/Executive**
 - OPKO Health, Panther Pharmaceuticals, Aviceda Therapeutics, Vision Integrated Partners, Blue Ocean Clinical Research

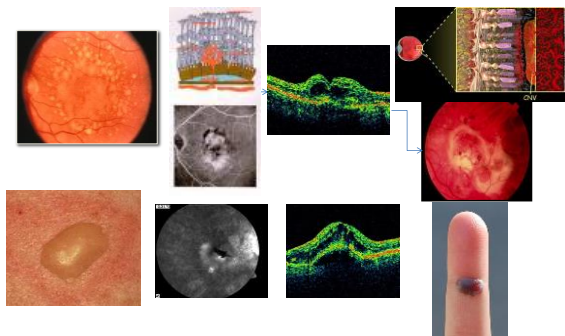
2



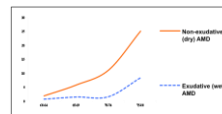
Dry Macular Degeneration = Rust



Wet Mac Degeneration= Inflammatory or Blood Blister



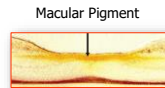
AMD Risk Factors



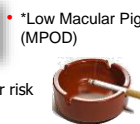
NON-MODIFIABLE

- AGE
- Caucasian
- Family History, Genetics
 - Inflammatory genes
 - Oxidation genes

MODIFIABLE



- *Low Macular Pigment Density (MPOD)
- Smoking – 3x greater risk



- Light Exposure Blue Light





Blue Light in AMD

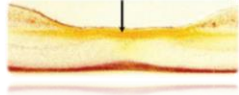
Modifiable risk factors for Age Related Macular Degeneration

Outdoor light exposure

6.5 RR >8 hrs
5.5 RR < 8 Hrs



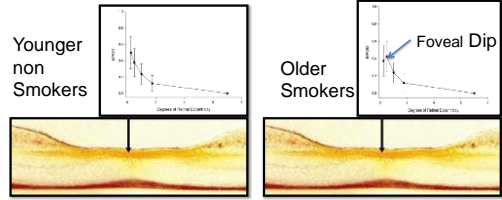
Low Macular Pigment



Smoking -2.4 RR



Decline in Macular Pigment near the fovea associated with increasing age and smoking history



Mark L. Kirby, Stephen Beatty, Edward Loane, Mukunda C. Akkali, Eithne E. Connolly, Jim Stack, and John M. Nolan, Invest Ophthalmol Vis Sci. 2010;51: 6722-6728



Molecular Description of AMD

Photooxidation + Oxidation + Genetic Dysfunction+
Blue Light Optogenetic Induced Cell Death + AGE=
ANTIOXIDATION/INNATE IMMUNITY DYSFUNCTION

CHRONIC INFLAMMATION

DRUSEN
CELL DEATH
PHAGOCYTOSIS
GEOGRAPHIC ATROPHY

VEGF
RETINAL EDEMA
CNV



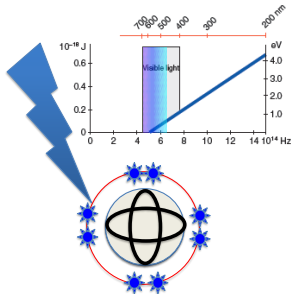
The Path to Blindness

- Chronic Blue Light Over Exposure.
 - Blue Light Phototoxicity /Photo Oxidation
 - Production of Oxidative byproducts malondialdehyde or carboxyethylpyrrole.
 - Blue Light/ All Trans Retinal Optogenetic PIP2 mediated RPE and photoreceptor cell death
- Chronic Activation of the complement and Innate Immune System
- Activation of Macrophages
 - M1 to M2d(VEGF producing macrophages)
 - M2 a,b (Phagocytic macrophages)

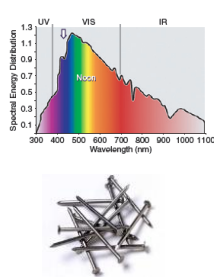


Blue light causes photooxidation

Blue light can produce electricity



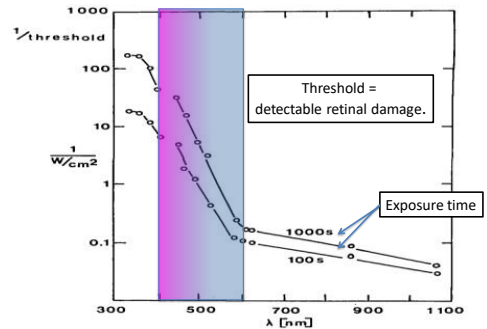
Sun light has lots of blue



Algevere P, et al. Acta Ophthalmol. Scand. 2006; 84: 4-15

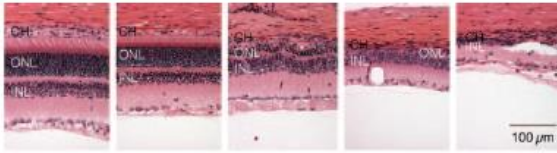


Blue /Violet is Most Retinal Toxic Wavelength of Light





Blue Light Can Produce Geographic Atrophy in a Mouse

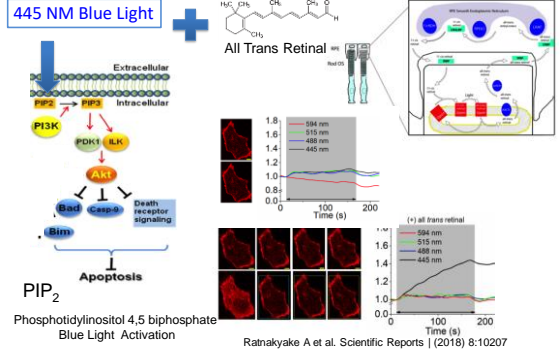


Tanito et al. IOVS, April 2007, Vol. 48, No. 4

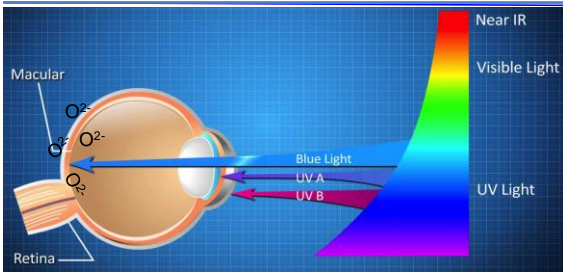


445 nm Blue Light activates PIP₂ mediated cell death.

445 NM Blue Light



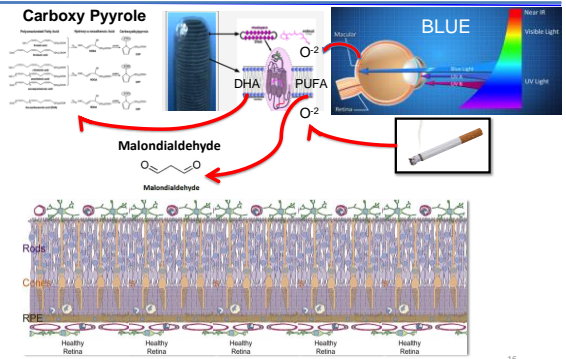
Oxidative Stress+ Blue Light Cell Death



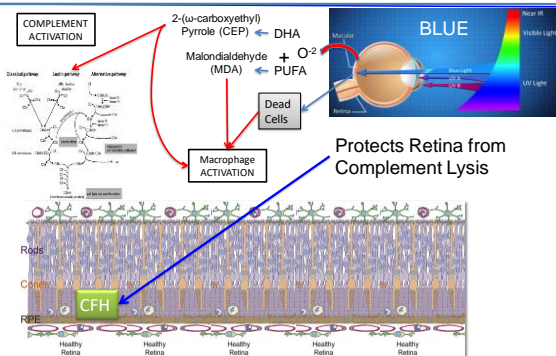
NADPH Oxidase
Mitochondria Cytochrome
Xanthine Oxidase
Cyclooxygenase



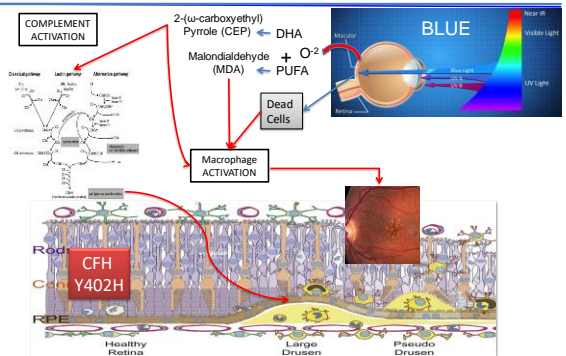
OXIDATIVE BYPRODUCTS



ACTIVATE INNATE IMMUNITY



DRUSEN FORMATION



Innate Immunity

Classical pathway **Lectin pathway** **Alternative pathway**

Complement

CFH

Macrophage ACTIVATION

Membrane Attack Complex

Diagram illustrating the three pathways of complement activation (Classical, Lectin, and Alternative) leading to the formation of the Membrane Attack Complex (MAC). It also shows the role of Complement Factor H (CFH) in regulating the alternative pathway. A diagram of a macrophage shows its activation and the formation of the Membrane Attack Complex (MAC) on its surface.

Chronic Inflammation

COMPLEMENT ACTIVATION

2-(ω-carboxyethyl) Pyruvate (CEP) → DHA
 Malondialdehyde (MDA) + O₂ → PUFA

Dead Cells

Macrophage ACTIVATION

M1 **M1+ M2** **VEGF**

Geographic Atrophy **Wet AMD**

CFH Y402H

Diagram illustrating the biochemical pathways of chronic inflammation, showing the conversion of CEP to DHA and MDA to PUFA, leading to dead cells and macrophage activation. It also shows the role of VEGF in the progression of AMD, specifically Geographic Atrophy and Wet AMD. A diagram of the retina shows the impact of these factors on the RPE, rods, and cones, leading to the formation of drusen and neovascularization.

Blue Light Pollution a new threat to the modern world

SU **UV** **VIS** **IR**

Spectral Energy Distribution

Wavelength (nm)

INDOOR LIGHTING

Light sources **Spectrum**

1.5kW **LED bulb**

1.5kW **Compact Fluorescent Lamp**

1.5kW **Incandescent bulb**

1.5kW **Candle**

1.5kW **Candle-light-candle**

SMART DEVICES

iPhone 6 Plus **iPhone 6**

Man has not evolved enough to adapt to this problem.

We Have Brought Day Light Into Our Night

Graphs showing the Spectral Energy Distribution (SED) of sunlight and indoor lighting sources. The indoor lighting spectra show a significant increase in blue light energy compared to natural light. A graph shows the spectral energy distribution of smart devices like iPhones. An illustration shows the evolution of man, highlighting the mismatch between modern light exposure and evolutionary adaptation.

Lumens and Lux

Lumens

Lux

Light Source	Lux cd/m ²
Iphone 7	705
Iphone 6	558
Samsung Galaxy 8	1020
Surface Pro	371
Very Overcast Day	100
Sunset/Sunrise	400
Overcast Day	1000
Indirect Sun	10000-25000
Direct Sun	32000-100000

Diagram illustrating the difference between Lumens (total light output) and Lux (illumination intensity in a specific area). A table lists various light sources and their corresponding Lux values. An illustration shows a smartphone emitting light, with arrows indicating the direction of light rays.

Refraction = Blue Light Magnification on The Fovea

Lenses Focus Oxidative Blue Light on the Fovea.

Magnify Energy

$I = (r/0.1mm)^2 \text{ kW/M}^2$

250,000 x increase in energy of the blue light

Diagram illustrating the refraction of light through the eye's lens, showing how blue light is focused on the fovea. It compares the energy of blue light before and after refraction, showing a significant increase. A diagram shows the eye's lens focusing light on the retina, with a magnified view of the fovea. A diagram shows the eye's lens focusing light on the retina, with a magnified view of the fovea. A diagram shows the eye's lens focusing light on the retina, with a magnified view of the fovea.

What is the best way to protect against Blue Light.

- 1) Glasses Impregnated with Melanin and or Ocular Lens Pigment (External Protection)
- 2) Enhancing Macular Pigment (Internal Protection)

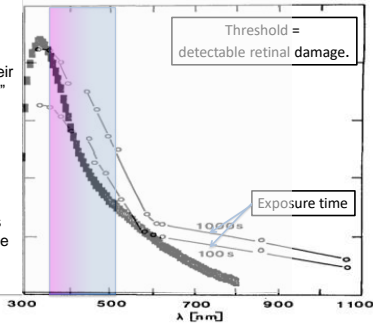
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Melanin Protects Proportionally

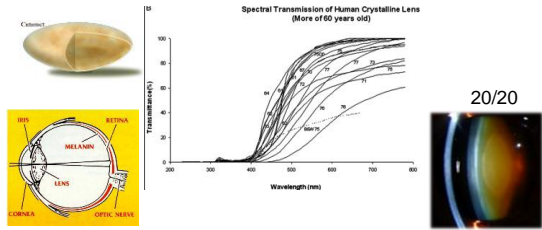
"the wavelengths of the visible light should be filtered in proportion to their ability to cause damage."
Dr. Jim Gallas

Nature/Evolution has developed the pigments OLP and Melanin to serve this purpose

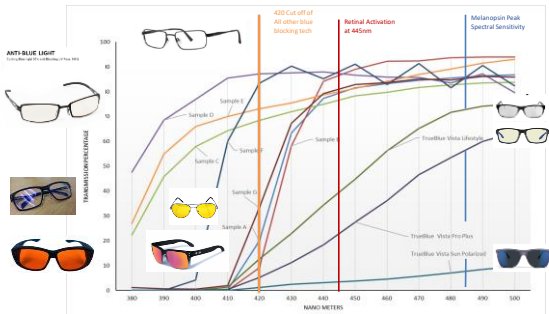


Melanin OLP= Natures Anti-Blue Light

Dr. Gallas Invented the method to Impregnate natures native protection into plastic.



True Blue Protection Technology



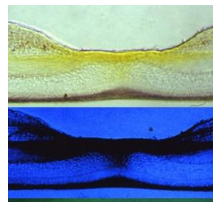
As Eye Doctors it is our duty to educate our patients on the potential harmful effects of blue light overexposure and recommend EXTERNAL PROTECTION in the form of melanin ocular lens pigment impregnated lenses the most effective way to protect against this threat

We also need to recommend Macular Pigment enhancement which represents INTERNAL PROTECTION against blue light and as we will see an effective way of preventing and enhancing therapies against exudative macular degeneration.



WHAT PROTECTS THE MACULA?

- LOCALIZED IN THE MACULA/FOVEA
- LOCALIZED BETWEEN FATTY ACID MOLECULES
- ANTI-OXIDANT
- ANTI-INFLAMMATORY
- BLUE LIGHT FILTER
- NON TOXIC

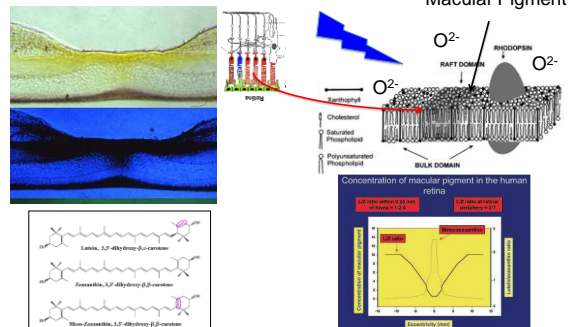


MACULAR PIGMENT

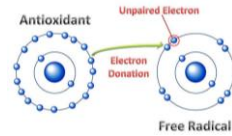
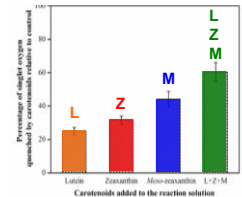


Macular Pigment Main Macular Protectant

- Localized Correctly



Meso/Lutein/Zeaxanthin
Most Potent Anti-Oxidant in The Macula.

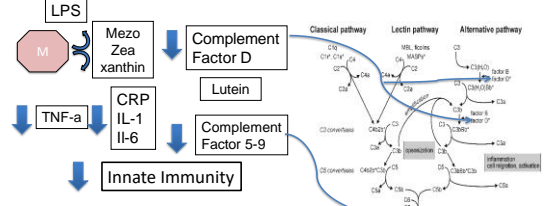


M > Z > L



Li, Ahmed, and Bernstein: 2010
 Department of Ophthalmology and Visual Sciences
 Moran Eye Center, University of Utah School of Medicine

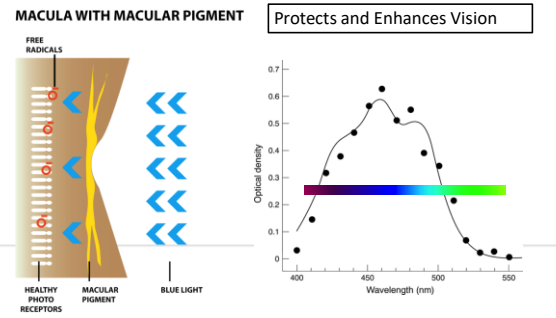
Macula Pigment MZL
Potent Anti-Inflammatory



AP Findous, G Kuttan R Kuttan. **Anti-inflammatory potential of carotenoid meso-zeaxanthin and its mode of action** Pages 961-967 | 05 Mar 2015

Yuan Tian. **The Effect of Lutein on the inflammatory pathway in AMD.** Dissertation Maastricht University

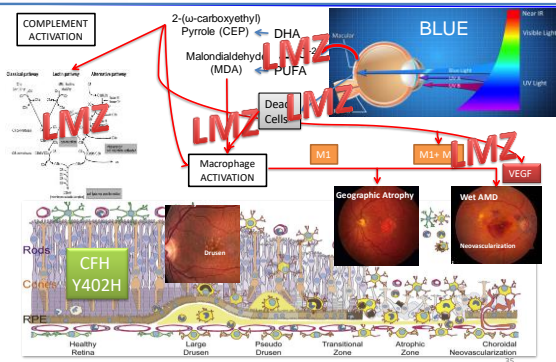
MP is a natural blue light filter



MZ is Safe

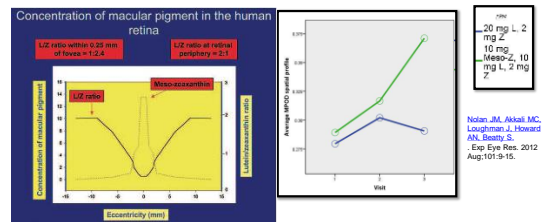
No Observed Adverse Effect Level (NOAEL) = 344 mg/kg/day
 344mg x 70 kg = 24080 mg or 24.08 kg per day
 Dec Mutagenicity and carcinogenic potential of environmental carcinogens in animals. Reduced Liver Damage and Cancer

LMZ Protects The Macula



Need MZL not just M, L or Z

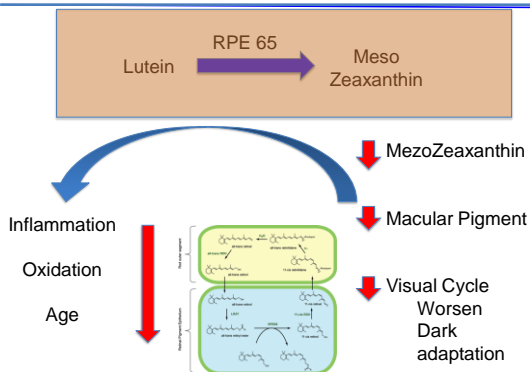
- Macular pigment increases significantly more with MZL versus ZL only. (Best Bioavailability)



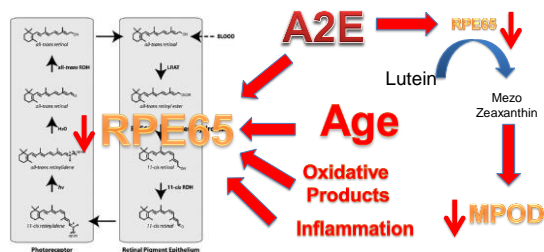
Noton JM, Akkai MC, Loughman J, Howard AN, Scott S. *Exp Eye Res.* 2012 Aug;101:9-15.



WHY WE NEED MZ



RPE65 activity as a measure of AMD



How do we measure RPE65 activity?

↓ Dark Adaptation vs Removing Eyeball

The American Journal of Pathology, Vol. 187, No. 3, March 2017
P1665 | October 12, 2010 | vol. 107 | no. 41 | 17561-17566



Dark Adaptation is the Best Biomarker for Progression of Macular Degeneration

Measures dark adaptation quickly and effectively in a clinical setting.

Diagnostic Sensitivity and Specificity of Dark Adaptometry for Detection of Age-Related Macular Degeneration
Gregory B. Jackson,1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000

- High Sensitivity:**
- Correctly identified 90.6% of confirmed AMD cases
- High Specificity:**
- Correctly identified 90.5% of confirmed normal cases
- High Accuracy:**
- 90.6% overall accuracy



MP Enhancement Therapy

Nutrient	Safety	Anti-Oxidant	Anti-Inflammatory	Localize Macula	Efficacy
Mezozeaxanthin	Excellent	Yes	Yes	Yes	Excellent
Lutein	Excellent	Yes	Yes	Yes	Good
Zeaxanthin	Excellent	Yes	Yes	Yes	Good

With Triple carotenoid therapy (LMZ) is what I recommend. It is the natural and safest way to protect the macula



Oxidative Stress and Macrophage Activation Upregulates VEGF

Reactive Oxygen Intermediates Increase Vascular Endothelial Growth Factor Expression in Vitro and in Vivo

Mauro A. S. et al., "Oxidative Stress Induced by High Energy Visible Light Increases VEGF Expression in Human Endothelial Cells", *Journal of Cellular Biochemistry*, 2007.

VEGF upregulation leads to increased vascular permeability and angiogenesis.



High energy visible light



A2E

Lipid and protein peroxidation



↑ VEGF

Macrophage M2d



Clinical Cases Demonstrating MZL Efficacy in early wet AMD

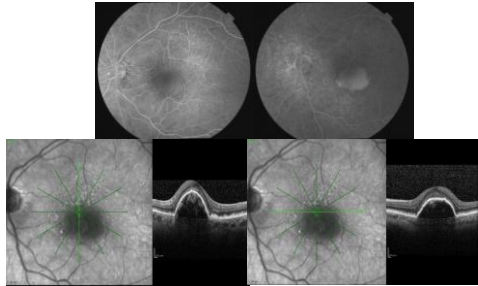
Case 1: Patient with Serous PED

Case 2: Resolve subretinal fluid quickly with high dose MZL



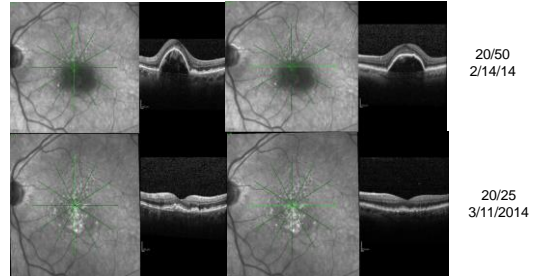
Case 1 AL- Serous PED

65 YO female complains of metamorphopsia. Hx of dry AMD. 20/30 Vision OS. Gave injection of Avastin and started Macuhealth. 2/14/14



Case 1 AL- Serous PED

After 1 month of Macuhealth and 1 injection of avastin complete resolution of PED 20/25. 3/11/14



Case 1 AL- Serous PED

20/40
2/14/14

M2L

20/25
3/11/2014

16 Mo Macuhealth
3 Avastin Injs
Last 6 mo None
20/25
6/30/2015



Case CO- Anti-VEGF rescue

75 YO male presents with metamorphopsia and blurred vision OS. Prior hx of dry AMD and family Hx of Exudative AMD. Started on Avastin.

BaseLine
20/30
7/3/2012



Case CO- Anti-VEGF rescue

Continued on Avastin for 1 year 10 Avastin Injections. Because of subretinal fluid switched to Eyelea.7 Injections of Eyelea Appeared stable.

20/40
7/9/2013

20/50
8/15/2014



Case CO- Anti-VEGF rescue

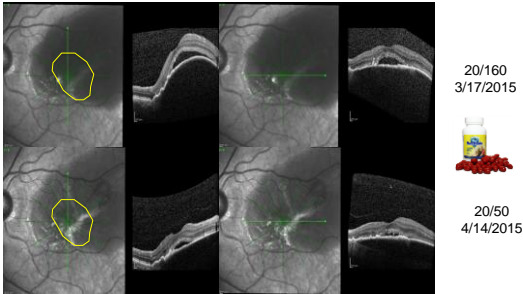
Due to insurance switched back to Avastin.

20/50
9/23/2014

20/100
12/16/2014

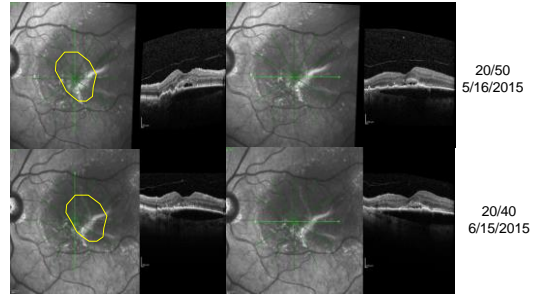
MACULA CENTER Case CO- Anti-VEGF rescue

Continued Avastin but worsened. Started MZL 2 x day on 3/17/15 after an injection of Avastin. Next visit patient felt improved vision.

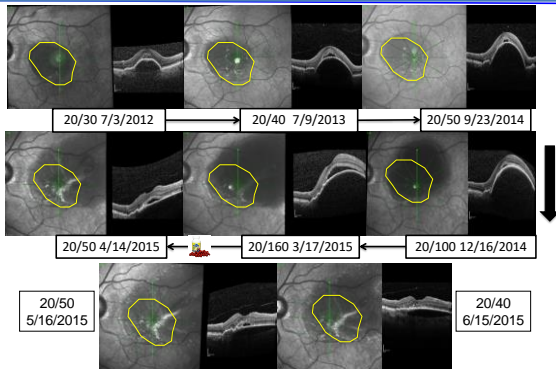


MACULA CENTER Case CO- Anti-VEGF rescue

Continued MZL and Avastin injections.



MACULA CENTER Case CO- Anti-VEGF rescue



MACULA CENTER Conclusion

- Dark Adaptation can detect AMD 3 years before we see it.
- Biological Pigment Impregnated Lenses are the Only Technology that Effectively protects against 445 NM Blue Light.
- LMZ can slow down progression of macular degeneration
- LMZ can serves as enhancer to anti-VEGF injections.
- LMZ is safe as eating spinach and may have anti-cancer properties. (No downside)

I Invite all of you in this room to become and AMD Center of Excellence

