BLUE LIGHT

A review of the evidence on the potential benefits and harms of blue-filtering lenses

• Thierry Villette  PhD, Essilor International
• Prof. John Lawrenson  FCOptom, City U. London

LECTURE. Monday 13 March. 11:30 am
Blue-light – Part II

AGENDA

01 BLUE-CUT TRADE-OFF

02 PHOTOBIOLOGY

03 LENS TECHNOLOGY & CRITERIA
Blue-cut lenses: their promise

Short-term benefits claimed:
- reduces **visual fatigue, digital eyestrain**, glare
- better contrast, depth perception
- visual comfort, relaxed vision,
- ideally suited for digital world, for indoor activities
  ...

Long-term benefits claimed:
- protects against harmful blue light, prevents retinal ageing, AMD, neurodegenerative process
- visual health, protects visual capital
  ...

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Blue-light – Part II
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PHOTORECEPTION

VISUAL
VA, CS
scotopic, color
...

NON VISUAL
sleep, mood, alertness,
cognition,
pupil reflex
...

PHOTOTOXICITY
photochemical damage
oxidative stress
inflammation
→ tissue dysfunction
→ eye diseases
Photoreception
Photoreception – Light is essential for vision...
Photoreception – … but also for non visual functions

Light is the main synchronizer of our biological clock.
New photoreceptor identified in 2002: ip–RGC (1 – 3% of RGCs)

Blue–Turquoise
480 nm

ipRGC

Melanopsin
Without light, the biological clock drifts in phase

Sleep hours

Michel Siffre, 24 yo
Summer 1962
62 days in French alps

Jours consécutifs dans le gouffre

33h shift
Consequences of a poor light synchronization

- Fatigue
- Alertness disorders
- Difficulties of concentrating
- Memory disorders
- Sleepiness
- Fragmented sleep
- Poor sleep efficiency
- Metabolic troubles
- Muscular troubles
- Digestive troubles
- Cardiovascular troubles

Nature reviews, Neurosciences
Phototoxicity
State of the art
Light & the eye, multiple risk parameters

Light environment
- Orientation
- Distance
- Time
- Season
- Altitude
- Latitude
- Luminance ratios
- Surface reflectances

Radiance
Spectrum
Individual risk profiling
Surface reflectances
Eye absorption
Genetics

Patient
- Age
- Ethnics
- Gender
- Lifestyle (food, smoking...)

Lifestyle
- Protections

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Acute phototoxicity

Rapid, bright light & short duration exposure
Chronic / cumulative phototoxicity

Long-term, moderate light & long duration exposure / repetitions / wavelength–dependent (photochemical reactions)
Our light exposure behaviours are rapidly evolving
Artificial light sources vs Sunlight

Over 90% of light sources worldwide based on LEDs by 2020.
Photoreception VS Phototoxicity
a threatened equilibrium

PHOTORECEPTION
Vision / Well-being

PHOTOTOXICITY
Pathology
Blue light, an identified risk factor for AMD

• The Chesapeake Bay study, 1992 (Taylor et al., Arch Ophthalmol, 1992)
  • 838 watermen
  • Significant correlation (p=0.05) between blue light exposure during the previous 20 years and severe AMD.
  • Compared with age-matched controls, AMD patients were significantly higher exposed to blue light but equally exposed to UV.

• The Beaver Dam Eye Study, 2004
  • 5000 individuals, 43 – 84 yo
  • The amount of time spent outdoors between 13 and 19 and between 30 and 39 yo was significantly associated with development of both early and late AMD.

• The EUREYE study, 2008
  • Correlation between blue exposure and wet AMD for patients with lower antioxidant level

• Sui et al., Br J Ophthalmol, 2012, Meta-analysis, 14 pooled studies. 12 studies concluded to an increased risk of AMD with greater sunlight exposure (OD 1.379). 6 studies reported significant risks.

• Higher prevalence of AMD after cataract surgery (loss of natural blue filtering)
YELLOW IOL’s & RETINAL PROTECTION

Wang JJ, Klein R, Klein BE, Mitchell P et al. Increased risk (OR 5.7) for developing late-stage ARM, particularly wet AMD, after 5-year of cataract surgery >6000 subjects; Pooled data from Beaver Dam Eye & Blue Mountains studies. Ophthalmology 2003 110(10):1960-7

Prevention of increased abnormal fundus autofluorescence with blue light-filtering intraocular lenses. Fifty-two eyes with a yellow-tinted IOL and 79 eyes with a colorless IOL.

CONCLUSIONS: Two years after cataract surgery, significant differences were seen in the progression of abnormal fundus autofluorescence between the 2 groups. The incidence of AMD was lower in eyes with a yellow-tinted IOL.


- Photoreception
  - Transmission
  - Scotopic vision
  - VA
  - VA low contrast
  - contrast sensitivity
  - color vision
  - Sleep/circadian
  - good ++
    - superior
    - good
  - good
  - good (save in low light)
  - good (except blue nuances)
  - good (Mind the spectrum!)

- Photoprotection
  - Low
  - High

25% blue-filtering IOLs (54% in the USA)

TREND:
- typically similar to 53 y.o.
- may be altered in some subjects
- good
- good (save in low light)
- good (> in mesopic)
- good (except blue nuances)
- good (Mind the spectrum!)
Blue-light – Part II

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Phototoxicity mechanism in outer retina – AMD

Retinal Pigment Epithelium (RPE) cells ensure SURVIVAL, FUNCTIONING and RENEWAL of photoreceptor degenerate in maculopathies such as AMD.
Phototoxicity mechanism in outer retina – AMD (2/2)

- RPE
- Reactive oxygen species
- Lipofuscin
- ATR
- hv

AND / OR
O2

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Lipofuscin: pathological photosensitizer in aging and AMD

Delori et al., IOVS, 2012  Wing et al., IOVS; 1978

Fast lipofuscin accumulation in early age and after 45 yo
Mains *in vivo* studies

Blue light: lower thresholds for photochemical damages – Photoreceptor action spectra

![Graph showing dose vs. wavelength for retinal damage](image)

**Figure 1.** Dose for retinal damage as a function of wavelength. The literature source is indicated by first author and year of publication. An inverted dose scale is used as a compromise between easy reading of absolute dose, and comparison with most literature data where sensitivity or susceptibility (1/dose) is provided. (a). Data for rats, except when stated otherwise. (b). Data for macaque, except when stated otherwise.

*van Norren & Gorgels, PP, 2011*
## Putting et al., IOVS, 1994

<table>
<thead>
<tr>
<th>Model</th>
<th>in vivo, rabbits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral band</td>
<td>12 nm-wide blue bands 408, 418, 439, 455 and 485 nm</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>1 to 6 h</td>
</tr>
<tr>
<td>Light level</td>
<td>35 - 208 mW/cm² - high level</td>
</tr>
</tbody>
</table>

### Analysis

![Fluorescein (permeability damage)](image)

**Conclusion**

439 nm is the most toxic wavelength for permeability damage in rabbits.
**Sparrow et al., IOVS, 2000**

<table>
<thead>
<tr>
<th>Model</th>
<th>in vitro, ARPE-19 cell line treated with A2E (100 µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral band</td>
<td>1/ Blue light ; 2/ Green light</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>60 s</td>
</tr>
<tr>
<td>Light level</td>
<td>1/ 75 mW/mm² ; 2/ 200 mW/mm² - high level (acute)</td>
</tr>
</tbody>
</table>

**Analysis**

[Sparrow et al., IOVS, 2000](https://dx.doi.org/10.1167/iovs.00-4701)

**Conclusion**

No phototoxicity without photosensitizer. The higher the concentration in photosensitizers, the higher the phototoxicity. Blue light is 6.5 to 7.5 x more toxic than green light for RPE cells.
Godley et al., JBC, 2005

<table>
<thead>
<tr>
<th>Model</th>
<th>in vitro, RPE cells treated with lipofuscin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectral band</td>
<td>Blue-green light [390 nm – 550 nm]</td>
</tr>
<tr>
<td>Exposure duration</td>
<td>1 to 6 h</td>
</tr>
<tr>
<td>Light level</td>
<td>2,8 mW/cm² - low level (chronic)</td>
</tr>
</tbody>
</table>

**Analysis**

![Graph A](image1.png)  
**Graph A**: mtDNA lesions per 10 kb over time. 
- **Graph B**: nDNA lesions per 10 kb over time. 

**Conclusion**

Blue light at chronic light levels induces DNA lesions, especially for RPE cells loaded with the age photosensitizer lipofuscin.
**Model**
in vitro, cell line RPE cells

**Spectral band**
LEDs - blue-468 nm, green-525 nm, red-616 nm and white light

**Exposure duration**
3 light–darkness 12 h/12 h cycles

**Light level**
5 mW/cm²

**Analysis**

**Conclusion**
LED radiations decrease 75–99% cellular viability, and increase 66–89% cellular apoptosis. Higher toxicity for cold-white and blue LEDs.
Phototoxicity refined spectral data
Collaborative research program since 2009

Custom-made cell illumination systems → in vitro models of eye diseases → Biomarker analysis → in vitro photoprotection
Cell model of retinal photoageing and AMD

Primary RPE cell cultures

Major component of lipofuscin

A2E

Nucleus

Tight junctions
LED-based fibered system, 14 narrow illumination bands (10 nm) from 390 to 520 nm + 630 nm, adjustable irradiances

Moderate irradiances normalized to retinal sunlight irradiances
18h light exposure, n≥ 6

\[
E_{e,\text{retina}}(\lambda) = \frac{A_{\text{pupil}}}{u^2} \times L_{e,\text{source}}(\lambda) \times \tau(\lambda)
\]
The phototoxicity action spectrum on RPE cells (outer retina): 415–455 nm

- Toxicity not strictly correlated to irradiances
- Toxicity not strictly correlated to the photon energy
- Very significant increase of cell death 415 – 455 nm
Phototoxic Action Spectrum on a Retinal Pigment Epithelium Model of Age-Related Macular Degeneration Exposed to Sunlight Normalized Conditions

Emilie Arnault\textsuperscript{1,2,3}, Coralie Barrau\textsuperscript{4}, Céline Nanteau\textsuperscript{1,2,3}, Pauline Gondouin\textsuperscript{1,2,3}, Karine Bigot\textsuperscript{1,2,3}, Françoise Viénot\textsuperscript{5}, Emmanuel Gutman\textsuperscript{1,2,3}, Valérie Fontaine\textsuperscript{1,2,3}, Thierry Villette\textsuperscript{4}, Denis Cohen-Tannoudji\textsuperscript{4}, José-Alain Sahel\textsuperscript{1,2,3,6,7,8,9}, Serge Picaud\textsuperscript{1,2,3,8,9}

\textsuperscript{1}Institut de la Vision, UPMC Univ Paris 06, UMR_S 968, Paris, France, \textsuperscript{2}INSERM, U968, Paris, France, \textsuperscript{3}CNRS, UMR_7210, Paris, France, \textsuperscript{4}Essilor International, Charenton-le-Pont, France, \textsuperscript{5}Muséum National d'Histoire Naturelle, Paris, France, \textsuperscript{6}Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, INSERM-DHOS CIC 503, Paris, France, \textsuperscript{7}Institute of Ophthalmology, University College of London, London, United Kingdom, \textsuperscript{8}Fondation Ophtalmologique Adolphe de Rothschild, Paris, France, \textsuperscript{9}Académie des Sciences-Institut de France, Paris, France
Darkness / Red light

↑ peri-nuclear clustering for nucleus protection + globular shape

↑ ROS (reactive oxygen species)

⇊ catalase activity and functioning

↑ SOD activity but ⇊ functioning

⇊ glutathione activity but ⇊ functioning

↑ glutathione activity

↓ cell death

↑ BV light induces…

↓ ROS (reactive oxygen species)

↑ catalase activity and functioning

↓ cell death

Darkness / Red light

BV light at 430 nm
Conclusion – Blue–light induced retinal damage

• Blue–violet toxicity action spectrum on RPE cells confirmed with oxidative stress biomarkers (415 – 455 nm).

• Blue–violet light induces high ROS production (H2O2, O2.–).

• Blue–violet light acts as a strong inhibitor of antioxidant mechanisms (glutathione, SOD, catalase).

• Blue–violet light directly impacts mitochondria: peri–nuclear clustering, globular shape, decreased respiration rate.

• Low–irradiance blue–violet light induces apoptotic cell death.

• … Accelerated retinal photo–ageing and AMD.
BLUE LIGHT HAZARD FUNCTION should be revised to a $B_2(\lambda)$ curve for cumulative hazard

$$B(\lambda) = [\text{Ham et al.'s 1976}] \text{ acute action spectrum on monkey eyes (acute)} \times \text{spectral transmittance of the human crystalline lens}$$

Photoprotection potency in vitro
Photoprotection benefits

1. A complete protection on front AND back sides

A 20% cut of noxious Blue-Violet light

*in vitro* quantification of protective effect

Decrease of 25% in average of the target retinal cell death over [400 nm ; 455 nm] compared to the *naked eye*

![Graph showing photoprotection benefits](image)

2. The UV protection on back side

A 25x higher protection compared to the *naked eye*
The first biological quantification of the effect of blue-cut optical filters \textit{in vitro}

\[ y = 6.5008x^3 - 6.3084x^2 + 2.3115x \]

\[ R^2 = 0.9196 \]
Blue-light – Part II

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LENS TECHNOLOGIES for BLUE-VIOLET FILTERING

interferential vs absorption ... or combined

- Antireflective coating
- Absorber in coating
- Nanostructure technologies
- Absorber in MASS

HMC system
HC system
Additional layer
Substrate

Filtering % (efficacy)
- low w. thin films
- high

Narrow band (selectivity)
++
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**SELECTIVITY of a BLUE-CUT LENS**

**Spectral selectivity**
* narrow-band ‘gutter profile’

**Target λ selectivity**
* cut the bad, leave the good

---

**1. The selectivity of the filter for the Blue-Violet light cut** [415-455] nm

**2. The selectivity of the filter for the chronobiological light** [465-495] nm

---

**Blue cut filter concepts**

- **retina cell protection**
- **chronobiology light**
Product performances: toward next generations of blue-cut lenses

- **AR efficacy** ($R_v > 2.5 = \text{not AR}$)
- **Visible transmission** ($T_v\% < 80\% = \text{Class 1}$)
- **ESPF: UV protection**
- **Blue-violet cut** ($400-455\text{ nm}$)
- **T blue-turquoise $\%$** ($465-495\text{ nm}$)
- **+ Yellow index ($b^*$)**
- **+ Lens aesthetics**
- **+ in vitro photoprotection potency**

Graph showing performance metrics for different products (Product A, Product B, Product C) with various transmission values and UV protection levels.
CONCLUSIONS

• Blue-violet light 380-455nm is a recognized risk factor in retinal ageing and maculopathies

• Opportunity and filtering level of blue-cut lenses to be discussed with ophthalmologists and optometrists:
  → advice vs individual risk and environmental exposure level
  → trade-off photoprotection vs photoreception

• Adopting relevant criteria for a blue-filtering lens:
  → blue-violet light filtering: T% in [380-455nm], T% in [415-455nm]
  → *in vitro* photoprotection potency (RPE cell model of AMD) – biology QC
  → chronobiology blue T% [465-495nm]
  → Tv(%), yellow index (b*), aesthetics
FUTURE RESEARCH NEEDED

• Prospective and controlled clinical studies to assess the benefit of blue-cut lenses to slow down retinal ageing and AMD
  → target population / filtering level / endpoint / follow-up 3+ years

• To what extent does blue-violet light contribute to pathogenesis? to disease progression?

• Blue-cut lenses and immediate benefits
  → what spectral determinant / what filtering dose-effect on eye fatigue, digital eye strain, glare, photosensitivity ...
A review of the evidence on the potential benefits and harms of blue-filtering lenses

Professor John Lawrenson

City University London
Declarations of Interest

• John Lawrenson has no proprietary interests in the development or marketing of any product mentioned in this lecture.
Seven cups of tea a day ‘raises risk of prostate cancer by 50%’

Oxford study claims slashing the official alcohol limit would save 4,500 lives a year

Would Diana have seen Kate as an ally or rival?

Don’t drink more than 3 glasses of wine a week

Wouldn’t drink lots of tea more likely to raise prostate cancer risk, experts warn, and that those who drink five or six cups a day may increase their risk of cancer by 20%-40%.

HRT can double risk of breast cancer

Experts warn of danger in pre-cooked frozen foods

Cancer risk in portion of chips

Eating lots of meat and cheese in middle age is ‘as deadly as smoking’
Have you seen the (blue) light?

Did you know that some blue light, from smartphone screens to sunshine, can affect your eyes? Luckily Boots Opticians can help

Living in the modern world has lots of exciting advantages, not least the fact that we now have computers small enough to fit in our pockets, so we can stay in touch anywhere and everywhere.

But did you know that there are lots of factors in your daily life that could be affecting your – and your family’s – eyes? Many modern gadgets, whether it’s a fancy LED TV or your smartphone, as well as sunlight and energy-saving light bulbs, give off a certain kind of blue light that can cause your retinal cells to deteriorate over time.

There’s no need to issue a ban on technology or spending too much time in the sun. But did you know that there are steps you can take to protect your eyes? Visit your local Boots Opticians and ask for advice on how to help protect your eyes from blue light damage.

Call 0345 125 3753† or go to Boots.com/opticians to make an appointment for your eye health check in one of more than 600 practices nationwide.
Have you seen the (blue) light?

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'Misleading' Boots eye advert banned

© 28 October 2015  |  Health

Smartphones are a source of "blue light"

An advert for Boots Opticians has been banned for "misleading" claims that blue light, emitted from smartphones and other gadgets, damages eyesight.

The Advertising Standards Authority said there was insufficient evidence to prove a direct link between blue light and retinal damage.
ASA Ruling

‘Boots did not provide evidence that a modest 20% reduction in the amount of harmful blue light entering the eye would lead to a significant reduction in the amount of retinal damage caused by exposure, as implied by the ad. In the context of an ad which purported that harmful blue light was damaging to retinal cells and implied that the majority, if not all, harmful blue light was filtered out by Boots’ lens coating before it reached the retina, we did not consider the evidence was adequate to support the implied claim made. We therefore concluded the ad was misleading.’
Questions for the Optometrist

• Should we worry about exposure to blue light in our natural visual environment?
• Do computers, tablets and smartphones pose a serious risk to ocular health?
• Is there a case for photo-protection and if so how can this be achieved?
Is blue light harmful?

Radiance
Radiant power emitted into a solid angle
\( W m^{-2} sr^{-1} \)

Luminance
Luminous power as perceived by a human standard observer
\( cd m^{-2} \)

Is blue light harmful?

Is blue light harmful?
Is blue light harmful?

Role of the Pupil

Natural protective filter

Lens transmission aged 5, 50, 80 years

Natural protective filter

Figure 1  Blue light hazard action spectrum.

Sunlight and AMD

Is sunlight exposure a risk factor for age-related macular degeneration? A systematic review and meta-analysis

Guo-Yuan Sui,1 Guang-Cong Liu,1 Guang-Ying Liu,2 Yan-Yan Gao,1 Yan Deng,1 Wen-Ying Wang,1 Shu-Hui Tong,1 Lie Wang1

Sunlight and AMD

http://bjo.bmj.com/content/97/4/389.abstract
In the low exposure group 20 people out of 1000 developed late AMD over 75 years, compared to 27 (95% CI 22 to 34) out of 1000 for the high exposure group.
Sunlight and AMD

The **number needed to harm** (NNH) indicates how many patients on average need to be exposed to a risk-factor over a specific period to cause harm in a patient who would otherwise not have been harmed.

**NNH=135**

In the low exposure group 20 people out of 1000 developed late AMD over 75 years, compared to 27 (95% CI 22 to 34) out of 1000 for the high exposure group.
Cataract Extraction and AMD

Cataract Extraction and AMD

Relative Risk = 3.05; CI 2.05 - 4.55

Cataract Extraction and AMD

Benefits versus side effects of blue-filtering IOLs

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Photoprotection</td>
<td>• Altered colour perception</td>
</tr>
<tr>
<td>• Improved contrast sensitivity</td>
<td>• Reduced scotopic sensitivity</td>
</tr>
<tr>
<td>• Reduced cyanopsia</td>
<td>• Impact on sleep and circadian rhythms</td>
</tr>
</tbody>
</table>

Benefits of Blue Light

On Seeing Yellow

The Case for, and Against, Short-Wavelength Light–Absorbing Intraocular Lenses

Matthew P. Simunovic, MB, BChir, PhD

Blue-Blocking IOLs: A Complete Review of the Literature

Bonnie An Henderson, MD, and Kelly Jun Grimes, MS

Blue-blocking IOLs Decrease Photoreception Without Providing Significant Photoprotection

Martin A. Mainster, PhD, MD, FRCOphth, and Patricia L. Turner, MD

Ultraviolet or blue-filtering intraocular lenses: what is the evidence?

SM Downes

Blue light–filtering intraocular lenses: Review of potential benefits and side effects

Fiona M. Cuthbertson, FRCOphth, Stuart N. Peirson, PhD, Katharina Wulff, PhD, Russell G. Foster, PhD, Susan M. Downes, FRCOphth, MD

Edward Lai, Benjamin Levine, and Jessica Ciralsky
Based on the evidence the authors of this perspective disagreed on the IOL they would choose should they need cataract surgery in the future!

• MAM opted for a UV-only blocking IOL to provide maximal UV protection and to wear sunglasses in bright environments, which can be removed for optimal vision in dim environments.

• JRS opted for a UV+ blue blocking IOL to provide the same protection against phototoxicity and scotopic sensitivity as a 50 year old crystalline lens and to wear sunglasses in bright environments, which can be removed for optimal vision in dim environments.
Smartphone overuse may 'damage' eyes, say opticians

Opticians say people are so addicted to smartphones they may be increasing their risk of eye damage.
Low-energy light bulbs, computers, tablets and the blue light hazard

Dr John O’Hagan
Group Leader, Laser and Optical Radiation Dosimetry Group
Public Health England

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) ‘rule of thumb’ is that detailed risk assessments within spectral range 380-780 are not required for luminance values \(<10^4 \text{ cd m}^{-2}\).

The ICNIRP blue light weighted radiance exposure limit for long-term viewing in range 300-700nm is \(100 \text{ Wm}^{-2} \text{ sr}^{-1}\).

<table>
<thead>
<tr>
<th>ID</th>
<th>Luminance \text{ cd m}^{-2}</th>
<th>% of ICNIRP (10^4 \text{ cd m}^{-2}) limit</th>
<th>Blue light weighted radiance \text{ Wm}^{-2} \text{ sr}^{-1}</th>
<th>% of blue light exposure limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet computer screens N=9</td>
<td>155.8 (± 57.9)</td>
<td>1.4 % (0.4-2.4)</td>
<td>0.14 (±0.06)</td>
<td>0.1% (0.03-0.2)</td>
</tr>
<tr>
<td>Smartphone screens N=5</td>
<td>292.6 (± 97.8)</td>
<td>2.9% (1.8-4.1%)</td>
<td>0.26 (±0.09)</td>
<td>0.3% (0.2-0.4)</td>
</tr>
</tbody>
</table>

Blue light weighted spectral radiance:
- clear day in June = 10.4 Wm$^{-2}$ sr$^{-1}$
- cloudy day in December = 3.4 Wm$^{-2}$ sr$^{-1}$

These exposures represent 10.4% and 3.4% of the exposure limit.

<table>
<thead>
<tr>
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Filtering the Blue

Blue light hazard peaks at 440nm

5 yr old versus 50 yr old lens

Filtering the Blue

UV versus blue filtering IOL

Filtering the Blue
Filtering the Blue

Summary

• Blue light has the potential to cause retinal phototoxicity although blue light also plays a role in scotopic sensitivity and circadian entrainment.
• Blue light sources encountered indoors are unlikely to approach exposure limits, even for extended viewing times.
• The eye possesses natural defences to mitigate blue light damage.
• Photoprotection could be considered in ‘at risk’ individuals.