

## Blue-light Filtering Intraocular Lenses

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### Abstract

Blue-light filtering intraocular lenses are purported to reduce the incidence of potentially damaging UV and blue light on the retina. This article reviews their background, the proposed benefits on long-term eye health and the possible disadvantages on circadian rhythm, scotopic vision and colour vision.

### Keywords

Age-related macular degeneration, blue-light filtering, circadian rhythm, intraocular lenses, light hazard, retina, ultraviolet

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Cataract surgery is a commonly performed surgical procedure. The ageing population and the bilateral nature of the condition correlate with the increasing number of extractions. For example, in 2009, 345,000 cataract operations were performed in England. This is a substantial increase on the 230,000 procedures that were undertaken in 2000.<sup>1</sup>

In the early days of cataract surgery, intraocular lenses (IOLs) transmitted all incident radiation. Although the cornea prevented wavelengths less than 300nm from entering the eye,<sup>2</sup> all other radiation was transmitted to the posterior ocular structures. The incidence of ultraviolet (UV) light on the retina gave rise to symptoms of erythropia, with images having a red-tinged appearance.<sup>3</sup> To reduce erythropia, from the early 1980s onwards, UV filters were incorporated into the intraocular lens (IOL) material.<sup>4,5</sup> This gave benefits of preventing potentially damaging radiation from reaching the posterior eye and improving image quality without removing longer wavelengths used in vision and other biochemical process.<sup>6,7</sup>

The manufacturers of IOLs have now extended the concept of filtering radiation to include short-wavelength blue light (400–500 nm) from the visible spectrum. Blue-light filtering IOLs attenuate wavelengths up to 500 nm. They are readily available to surgeons but at a higher cost compared to standard UV-only blocking lenses. However, there has been controversy as to the extent of any benefit these IOLs provide and there are suggestions that they may have a detrimental effect on vision and the circadian rhythm.

### Light Hazard

With high oxygen levels and constant absorption of radiation in the form of light during waking hours, photo-oxidative reactions occur within the retina and choroid. UV and visible wavelengths up to 600 nm are capable of photochemically damaging the retina, with short-wavelength radiation being more damaging than long-wavelengths.<sup>2,3,8–10</sup> Photo-oxidative reactions are risk factors

for age-related macular degeneration (AMD), choroidal melanomas<sup>11</sup> and other posterior pole pathologies.

The eye attempts to limit the effects of phototoxicity by shedding photoreceptor outer segments, synthesising antioxidants such as lutein and zeaxanthin within the retina and producing light absorbing pigments such as melanin within the retinal pigment epithelium (RPE) and choroid.<sup>12</sup> The ageing eye is less likely to be able to sustain these protective mechanisms leaving the eye prone to phototoxic damage.<sup>2</sup>

Lipofuscin is a phototoxic pigment, which naturally accumulates within the retina as the eye ages. It has a peak absorption at 430 nm.<sup>13</sup> Photons absorbed by lipofuscin molecules are raised to an excited state and this results in the production of reactive oxygen species such as singlet oxygen and superoxides as well as free-radicals. Reactive species damage ocular tissue at a cellular level and this reduces the ability of the RPE cells to regulate photoreceptor cell turnover. Eventually the photoreceptors undergo permanent and atrophic damage.<sup>2,7</sup>

The crystalline lens provides some protection against phototoxicity. In the first three years of life the lens is clear, gradually becoming yellow over time. Pigments comprised of 3-hydroxyl kynurnine are deposited in the lens, particularly in the lens nucleus where UVA (315–400 nm) and UVB (280–315 nm) are absorbed.<sup>2</sup> These pigments, often referred to as chromophores, absorb light wavelengths between 300 and 400 nm preventing UVA, most UVB and some blue-light from reaching the retina. A 53-year-old healthy crystalline lens will allow 75 % of 470 nm blue light to be transmitted, whilst a 70 year old allows only 25 %.<sup>14</sup> Studies have shown that transmission of blue light through the crystalline lens decreases by 0.7–0.8 % per year because of chromophore deposition.<sup>15</sup> If the crystalline lens is removed this protective filter is lost. In an attempt to mimic the protective yellow pigments of the crystalline lens, some manufacturers include chromophores within the plastic polymer of the IOL. These yellow IOLs are marketed as imitating the ageing eyes' natural defence against short-wavelength light.

## Blue-light Filtering Intraocular Lenses and Age-related Macular Degeneration

Epidemic levels of AMD are occurring within the developed world, with the condition being the most common cause of severe sight impairment registration in the UK.<sup>16</sup> The theory that by reducing the amount of short wavelength light (UV and blue) entering the eye and consequently the phototoxic damage that leads to RPE dysfunction and ultimately retinal degeneration is a plausible one.<sup>17-20</sup> Therefore the possibility of reducing the risk of AMD by using short-wavelength filtering IOLs is attractive.

Six out of seven<sup>20-26</sup> studies that investigated short-wavelength light exposure and AMD, did not find a relationship. This could be due to the effect of confounding factors common to retrospective epidemiological studies. Difficulties in estimating lifetime UV exposure levels, along with the impact of other risk factors such as genetic, dietary and smoking histories may have affected the results. Although the concept is counterintuitive perhaps there is no link between short-wavelength light exposure and AMD. Evidence that the risk of AMD is not increased in pseudophakes suggests increased light exposure does not significantly affect the ageing processes of the macula.<sup>27,28</sup>

Mainster<sup>7</sup> suggested that more damaging short wavelength light passes through a blue-light filtering IOL than the crystalline lens of a middle-aged person. He has also posed the question that if old phakic patients are developing AMD with their own natural lenses, how can a blue-filtering IOL which allows relatively more short-wavelength light to reach the macular have any protective properties.<sup>29,30</sup> The counter argument is that while natural middle-aged crystalline lenses with their intrinsic short wavelength filtering properties may not prevent all occurrences of AMD, it may well be that some cases have been avoided or reduced in severity. To prove such an assumption, a prospective randomised controlled trial would be required, which is neither ethical nor practical when the safety implications, size and duration of such a study are considered.

## Concerns about Blue-light Filtering Intraocular Lenses

Henderson et al.<sup>31</sup> reviewed the literature regarding blue-light filtering IOLs. It was concluded that there is no evidence to suggest any negative effects on visual acuity, contrast sensitivity or colour vision. However, despite the potential benefits of blue-light filtering IOLs there has been some suggestion that they can disrupt the circadian rhythm, cause problems with colour discrimination and negatively affect scotopic vision.

### Effects on Circadian Rhythm

Circadian rhythm is an endogenously driven 24-hour biochemical and behavioural cycle that co-ordinates biological activities in humans, along with most other organisms.<sup>32</sup> Light is known to be an important contributor to the regulation of the circadian rhythm, although the process is highly complex with many mutually interacting circuits.<sup>33</sup>

Intrinsically photosensitive retinal ganglion cells (ipRGC) found within the inner retina project directly to the suprachiasmatic nucleus (SCN) a core zone of the hypothalamus. The ipRGC comprise between 0.2 and 0.8 % of all ganglion cells<sup>34</sup> and express a photopigment called melanopsin when exposed to light. Release of melanopsin is maximum at 480 nm.<sup>33</sup> The relative quantity of melanopsin expressed depends on light intensity and is communicated to several regions of the brain via

the SCN. This in turn affects the release rate of melatonin from the pineal gland. An increase in the melatonin release initiates a dark signal prompting sleep and relaxation. A suppression of melatonin release initiates waking and an increased alertness.<sup>33</sup> The intensity of day light-as measured by melanopsin and via the SCN thus causes the suppression of melatonin release.

Blue-light filtering IOLs, which absorb at 480 nm could theoretically decrease melatonin production and cause sleep disturbance. Furthermore, Mainster<sup>7</sup> has described the many important roles of melatonin in addition to circadian rhythm regulation. It is a free-radical eliminator, it may protect against oxidative stress,<sup>35</sup> it has anti-cancer effects<sup>36</sup> and limits tumour size<sup>37</sup> as well as acting as an anti-inflammatory.<sup>38</sup> Any disruption to melatonin control is therefore undesirable.

Augustin<sup>33</sup> proposed that the complex nature of the circadian rhythm would not be significantly influenced by blue-light filtering IOLs since they only filter light and do not totally block it. In the range 400–500 nm, blue-light filtering IOLs transmit 10 % at 400 nm light and 80 % at 500 nm. If this increase in transmission were approximately proportional to the increasing wavelength, this would provide transmission of approximately 60 % at 480 nm. In other words, wavelengths of 480 nm required by ipRGCs are attenuated but not absent when using blue-light filtering IOLs.

Mainster<sup>39</sup> theorised that blue-light filtering IOLs would result in 27–38 % less melatonin suppression than UV-only blocking IOLs. Augustin pointed out that Mainster did not directly measure melatonin suppression but extrapolated his findings, assuming a 1:1 ratio of 480 nm light filtering to melatonin suppression. This ratio has not been proven.<sup>40</sup> There is no definite measure of the extent to which blue-light filtering IOLs cause detriment to the control of melatonin and therefore any estimates of melatonin suppression are speculative.

In a healthy eye of a child, the crystalline lens will allow 70–80 % of 480 nm light to be transmitted. This decreases to 55 % with a 53-year-old adult crystalline lens.<sup>33,41</sup> One commonly used blue-light filtering IOL transmits 80 % at 480 nm.<sup>39</sup> In other words, blue-light filtering IOLs could transmit levels of 480 nm light greater than that transmitted in a child's eye.<sup>33</sup>

### Scotopic Vision

Scotopic vision is mainly facilitated by rod photoreceptors. When light levels drop to approximately  $3 \times 10^{-6}$  cd<sup>2</sup>, rods provide useful vision, with maximum sensitivity at 507 nm.<sup>33</sup> With a blue-light filtering IOL in place, the reduction in light transmission could potentially decrease the response of rods and therefore reduce the scotopic response of the eye.

The reduction in scotopic sensitivity when comparing a 20 dioptre (D) and 30 D blue-light filtering IOL to a UV-only filtering IOL is 14 and 21 % respectively.<sup>12</sup> The effect of this loss is difficult to measure clinically, although Jackson<sup>42</sup> reported that pseudophakes fitted with blue-light filtering IOLs have reduced scotopic vision in violet and blue light. This could impair the ability of night time driving.<sup>7,43</sup> There is also an increased risk of falls with reduced scotopic vision which can lead to other health problems.<sup>44</sup> These negative effects on scotopic vision may be greater for those with compromised retinal function due to AMD or diabetic retinopathy.<sup>7</sup>

Blue-light filtering is not the only source of reduced scotopic vision. It is known that rods degenerate with age, as does neural efficiency and the integrity of the magnocellular pathways.<sup>45</sup> These age related changes decrease scotopic contrast sensitivity prior to any consideration of the filtering effects of IOLs.<sup>33,46</sup>

Muftuoglu and Duman<sup>47</sup> compared contrast sensitivity under scotopic conditions for UV and blue-light filtering IOLs. The results showed decreased contrast sensitivity and increasing glare sensitivity with age but no relationship between type of IOL and contrast sensitivity.

The potential effects of blue-light filtering IOLs on scotopic vision can be examined in terms of transmission of light at 507 nm as this is the wavelength which maximally activates rod cells. A child's crystalline lens transmits 90 % at 507 nm and an adult lens 60 %. A commonly used blue-light filtering IOL transmits 85 % at 507 nm which would provide a post-operative improvement to almost childlike levels of transmission.<sup>18,41</sup> Detrimental effects of blue-light filtering IOLs on scotopic vision are unlikely.

## Colour Vision

Cone receptors in the eye respond to luminance of 3–30 cd/m<sup>2</sup>, with three cone types responding to short (s), medium (m) and long (l) wavelengths. The reduction in wavelength predominately activating the s-cones by a blue-light filtering IOL could potentially affect colour vision.

Standard colour vision tests such Farnsworth D15 and Farnsworth-Munsell 100-hue test cannot discern a change in colour vision when comparing UV to blue-light filtering IOLs.<sup>4</sup> However, Rubin et al.<sup>48</sup> did detect a slight colour vision anomaly in patients fitted with blue-light filtering IOLs when using a Moreland anomaloscope.<sup>3</sup> However, discovering a colour vision defect with an anomaloscope, which is rarely used in practice when more widely used and clinically accepted tests find no colour defect, gives this finding an academic rather than a clinical importance.

With colour vision being modulated by three different cone types, the effect of filtering some s-cone activating blue-light is offset by the

residual activation of the unaffected m- and l-cone cells. Adaptations to subsequent neural processing will counteract any change to perceived colour and the patient should not appreciate a noticeable difference to their colour vision.<sup>33</sup> Bharrachorjee<sup>49</sup> found a blue-light filtering IOL resulted in colour vision similar to that provided by a natural crystalline lens, whereas a UV only blocking IOL gave an inferior performance.<sup>33,49</sup> From these observations it can be seen that blue-light filtering IOLs should have no detrimental effect on colour vision.

## Violet-light Filtering Intraocular Lenses

Recent thinking has led to the availability of violet-light filtering IOLs. These filter below 440 nm and therefore avoid potential effects on melanopsin, melatonin suppression and scotopic sensitivity. Violet-light filtering IOLs attenuate wavelengths that are known to excite lipofuscin and therefore the formation of reactive oxidative species and free radicals should be reduced and phototoxic damage of the photoreceptors and RPE avoided. The balance between photoprotection and photoreception appears to be addressed by the use of violet-filtering IOLs,<sup>7</sup> although further research is required.

## Conclusion

When considering the potential benefits of blue-light filtering IOLs, the possibility of preventing phototoxic damage to the eye is an important potential advantage. Although studies have failed to firmly establish a link between short-wavelength light and AMD, the scientifically based assumption that blue-light is in part responsible for macular degenerative changes is plausible.

Deciding on whether a blue-light filtering IOL should be recommended involves balancing relative risks and merits. Analysis of the patient requirements should be considered on an individual basis. If the patient has a strong family history of AMD and spends a substantial period of time in bright sunlit conditions, a blue-light filtering IOL may be sensible. However, until there are more definite answers to the questions that surround the use of blue-light filtering IOLs, it would be unwise to use them for all patients. Further work on the benefits and use of violet-light filtering IOLs would be helpful. ■

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