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A Review of Infrared Laser Energy Absorption and Subsequent Healing in the Cornea

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ABSTRACT

The purpose of this review is to compile information on the optical and healing properties of the cornea when exposed to infrared lasers. Our long-term goal is to optimize the treatment parameters for corneal injuries after exposure to infrared laser systems. The majority of the information currently available in the literature focuses on corneal healing after therapeutic vision correction surgery with LASIK or PRK. Only a limited amount of information is available on corneal healing after injury with an infrared laser system. In this review we will speculate on infrared photon energy absorption in corneal injury and healing to include the role of the tear layer. The aim of this review is to gain a better understanding of infrared energy absorption in the cornea and how it might impact healing.

1. INTRODUCTION

Recently, there has been increasing interest in the use of infrared lasers with wavelengths from 1.4 microns to 2.0 microns. The reasons for this increased interest are many, including the ability to deliver these wavelengths efficiently via fiber optics and the increased power levels that are now available at these wavelengths. Manufacturers are advertising these lasers as "eye-safe."^{1,2} Lasers in this wavelength regime can be made with sufficient energy to cause corneal injury, so in some cases the phrase "eye-safe" may be misleading, and "retina-safe" may be more accurate.³ The absorption of energy in the cornea, resulting damage and healing processes have not been well explored for this wavelength regime. In this paper, we present a brief overview of the cornea layers of interest, a review of the absorption of 1.4 to 2 micron wavelengths and basic healing of infrared corneal injuries. This paper represents a step in our process of reviewing the available literature for cornea properties that can be utilized to help develop energy absorption and healing models.

2. BASIC CORNEA ANATOMY

When the human cornea is exposed to photons from a laser, those photons encounter a multi-layered tissue consisting of the following: tear film layer, epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium. No information on the specific absorptive properties of infrared light in each layer could be located. The anatomy of the rabbit cornea is important to discuss along with the human as the rabbit is typically utilized as an in-vivo model for human exposures.^{4,5} Although the tissues are similar, there are distinct anatomical differences between the two species. Figure 1 compares the anatomical differences between the cornea of the human and the rabbit.

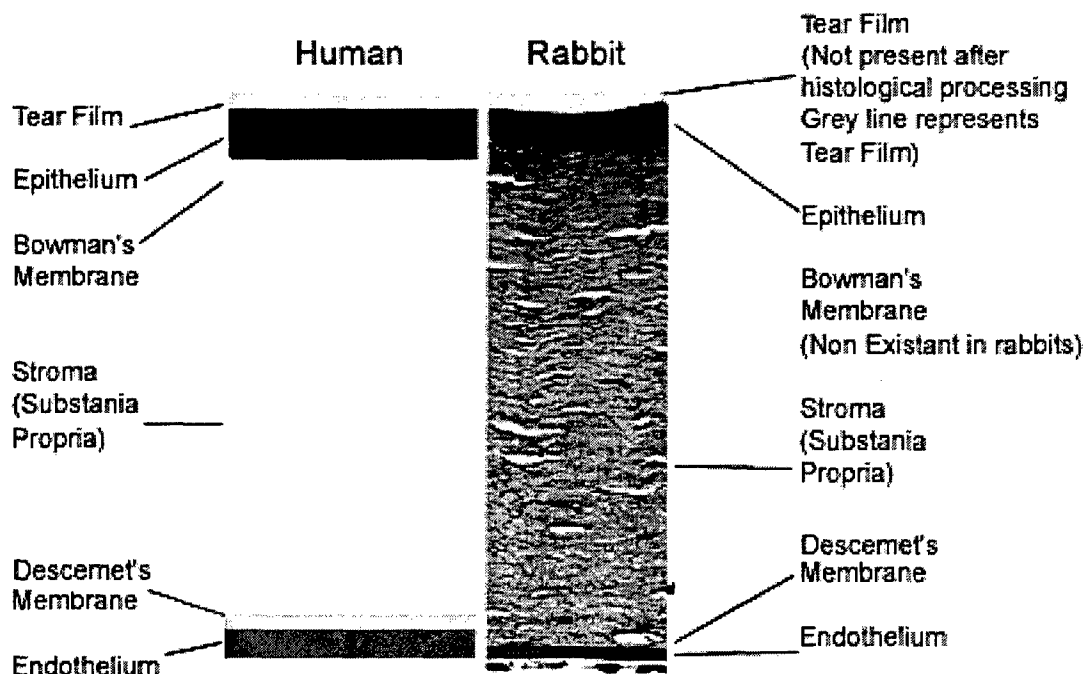


Fig. 1. Basic anatomic structures of the human and rabbit cornea. Not to scale.

Understanding the thickness and type of structures within the cornea is vital to understanding where and how energy is absorbed within that tissue. Models of corneal damage from infrared lasers require knowledge of the thickness of the cornea. Familiarity with differences in structure and thickness better equip theoreticians to produce accurate models. Table 1 lists the thickness of the human cornea and various structures within it. No specific information on individual layer thickness was located for the rabbit cornea. Data listed in Table 1 is preliminary rabbit data from our group.

	Human ⁶	Rabbit
	μm	(Preliminary data) μm
Tear film	~7	-
Epithelium	~50	30
Bowman's Membrane	10-30	N/A
Stroma	~480	300
Descemet's Membrane	5-10	-
Endothelium	~5	5
Overall thickness⁷	650	450

Table 1. Cornea Structure Thickness

The tear film layer is not simply a layer of water on the surface of the eye. It is comprised of three distinct layers; (1) thin superficial oily layer, 0.9 to 0.2 μm thick, (2) a watery layer 6.5 to 7.5 μm thick, and (3) a mucin layer 0.5 μm thick.

The epithelial layer of the human cornea is approximately five cells thick. Human epithelial thickness ranges from 50 to 60 μm . The rabbit corneal epithelium appears to be approximately 30 microns thick based on our preliminary measurements. This layer appears to be uniform across the rabbit cornea within the boundaries of the limbus.

Bowman's layer is found in humans, beneath the epithelium. It is approximately 8 to 12 μm thick and appears to be uniform across the cornea. Since the rabbit cornea lacks this structure, it makes it difficult to determine how it impacts the absorption of infrared photons.

The thickest layer of the cornea is the stroma. It is approximately 0.5 mm thick in humans. In rabbits, thickness appears to vary with location, being thickest in the central region of the cornea and thinner radially outward towards the limbus. Our preliminary measurements of rabbit stroma indicate that it is approximately 0.3 mm thick near the center of the eye.

Descemet's membrane lies immediately below the stroma and is 10 μm thick in humans.⁸ No specific measurement of this structure in a rabbit was found, but it appears to be similar in thickness. The endothelium for both species consists of a single cell layer below Descemet's membrane.

3. ABSORPTION COEFFICIENTS

When the absorption coefficient and the thickness of the cornea is known, predictions as to the distribution of absorbed energy can be postulated using basic mathematical models. Models of infrared energy absorption in the cornea frequently rely on the assumption that the properties of the cornea are identical to those of water.⁹ This appears to be a reasonable assumption for most wavelengths, but it must be used with care. Figure 2 shows that the human cornea absorbs light differently than water. No information was found regarding the absorption of infrared light in rabbit cornea, but monkey cornea appears to be an especially good model for human cornea infrared light absorption. The macromolecular structure of the cornea may contribute significantly to the optical property differences between the cornea and water.¹⁰

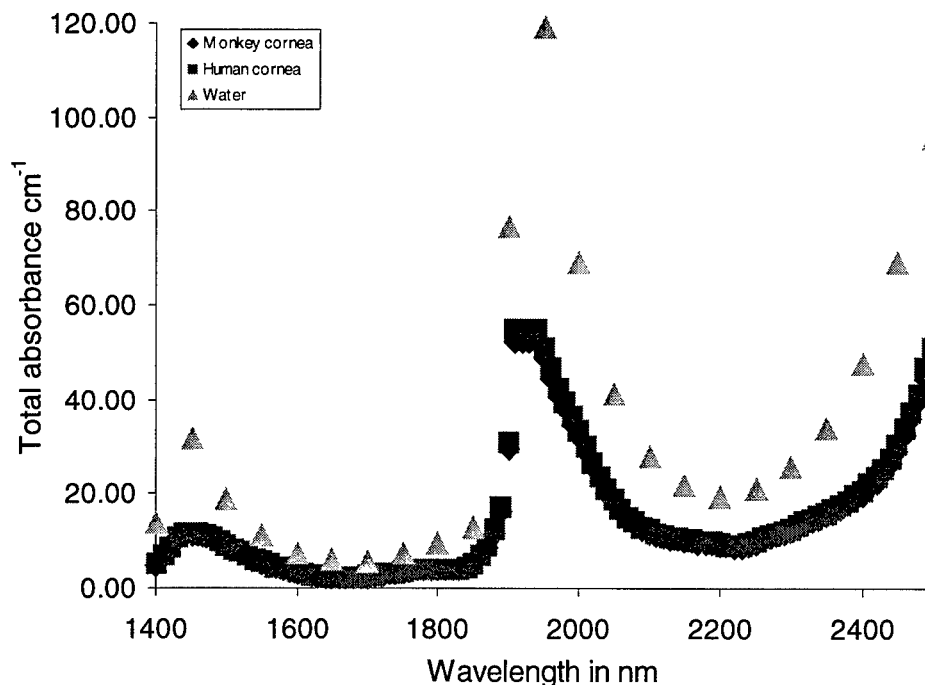


Figure 2. Absorption co-efficient for water and human and monkey cornea. Based on data from Maher¹¹ and Hale¹².

The absorption coefficients for individual layers of the cornea are largely unknown. Despite this, it has been stated that the tear layer is responsible for absorbing the majority of CO₂ laser radiation.¹³ While

histological evidence may confirm that this is true, it would be useful to know how photons are absorbed in individual layers to predict the extent and type of damage expected from infrared lasers.

4. HEALING PROPERTIES

Each layer of the cornea has distinct healing properties. Predicting where laser energy is absorbed, how damage develops, and the seriousness of the resultant injury will have an impact on treatment. The tear film layer is an important factor in the cornea healing process. The epidermal growth factor (EGF) and transforming growth factor- α (TGF- α) are key to healing of the cornea and are contained within the tear film. After corneal injury, EGF expression is increased, and together with reflex tearing, this appears to assist greatly in the healing process¹⁴. Direct application of EGF to corneal injuries has been attempted in-vivo but conclusive results have been elusive (Dellaert et al. 1997).

Bowman's membrane, when disrupted, remains retracted and does not rejoin. Thus, any changes to this particular structure might be considered permanent.¹⁵ The stroma does have the ability to regenerate, but the corneal epithelium must be present before stromal wound healing will occur.¹⁶ The reason for this requirement is uncertain, but a stimulatory influence of epithelial cell upon keratocytes during healing has been proposed.¹⁷ Little information was found regarding the healing properties of Descemet's membrane and the endothelial layer, except that both appear to have a low regenerative capacity.¹⁸

5. DISCUSSION

Some thermal models assume that the cornea approximates water in absorption and thermal properties. The action of individual photons using a simplified Beer's law model has been used by Roach et al¹⁹ and McCally et al.²⁰ Assuming the cornea does indeed absorb photon energy in the same manner as water, the depth of to which 63% of the energy is absorbed ($1/e$) is calculated in Figure 3.

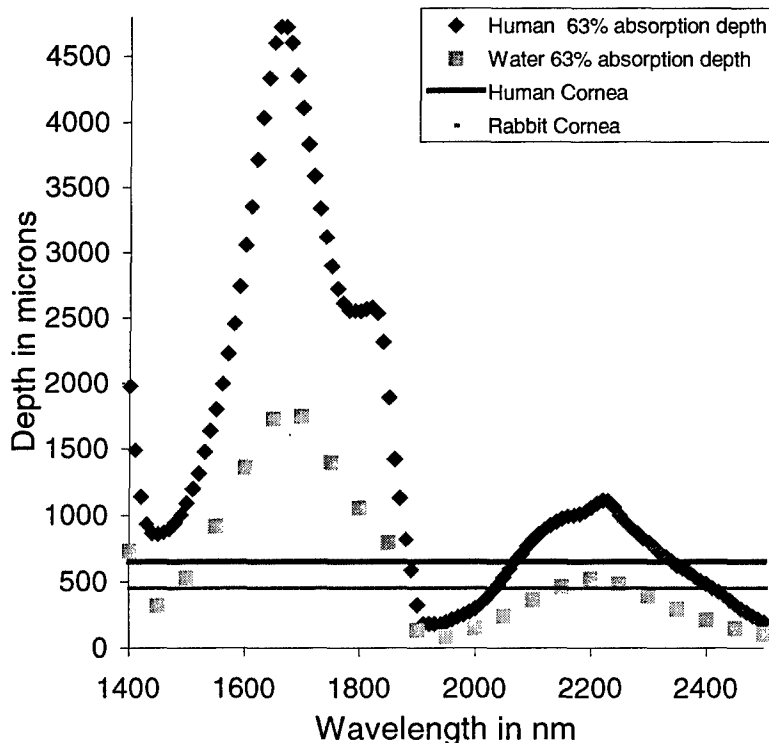


Figure 3. Depth to 63% photon absorption based on coefficients in Fig. 2.

Note that we expect significantly greater depths needed to obtain 63% absorption than the thickness of human or rabbit corneas for many of the wavelengths of interest for this paper. The thickness of human cornea required to absorb 63% of incoming photons is significantly greater than that of water. Since it is well established that retinal injury does not occur for this wavelength regime, simply using the absorption coefficients does not fully explain the observed phenomena. It is possible a portion of the incident photons are reflected and not available for absorption in the cornea or they are diffusely scattered in the cornea.

6. CONCLUSION

Where photon energy is absorbed and how it is absorbed are key factors in developing models for infrared cornea injury. If predictions can be made as to where and how infrared energy is absorbed in the cornea, the structures of the cornea that are at risk of permanent injury can be better identified. Current models are general in nature and do not focus on the individual structures in the cornea. Rather than looking at the overall absorption of photons in the cornea, a more fundamental understanding is sought of how individual photons are absorbed by structures, and perhaps even macromolecules.

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REFERENCES

- ¹ Leica Vector advertisement/flyer dated 1997
- ² NASA Facts FS-2001-07-042 DFRC, 2001
- ³ W. T. Ham and H. Mueller, "Ocular effects of laser radiation," *Journal of Laser Applications* 3, p. 19, 1991.
- ⁴ W.T. Ham, H.A. Mueller, *Ocular effects of laser infrared radiation*, Research Report to Bell Telephone Laboratories, Virginia Commonwealth University, Virginia, 1989.
- ⁵ C.B. Bargerion, O.J. Deters, R.A. Farrell, R.L. McCally, "Epithelial Damage in rabbit corneas exposed to CO₂ Laser Radiation," *Health Physics*, Vol 56, No. 1, pp. 85-95, 1989.
- ⁶ W. S. Snyder, M .J. Cook, E. S. Nasset, L.R. Karhausen, G.Parry Howells, I. H. Tipton, Report of the Task Group on Reference Man. *International Commission on Radiological Protection* 23, 221-222, 1975.
- ⁷ Smolin G. and R.A. Thoft. 1994 *The Cornea: Scientific Foundations and Clinical Practice* 3rd ed. Little Brown and Company, Springfield IL.
- ⁸ R.S. Snell, M.A. Lemp, *Clinical Anatomy of the Eye*, Second edition, Blackwell Science Inc, Malden MA. 1998
- ⁹ R.L. McCally, C. B. Bargerion, Epithelial damage thresholds for multi-pulse exposures to 80 ns pulses of CO₂ laser radiation. *Health Physics*, Vol. 80, No. 1, p. 41-46, 2001.
- ¹⁰ Cintron C, Hassinger LC, Kublin CL, and Cannon DJ: Biochemical and ultrastructural changes in collagen during corneal wound healing. *J Ultrastruct Res* 65:13, 1978.
- ¹¹ Maher, E.F. Transmission and Absorption Coefficients for Ocular Media of Rhesus Monkey. USAF School of Aerospace Medicine, Brooks AFB, SAM-TR-78-32, 1978
- ¹² Hale, G.M., Query, M.R., Optical Constants of water in the 200 nm to 200 um wavelength region, *Applied Optics*, Vol. 12, No. 3, p.555-563, 1973
- ¹³ R.L. McCally, C. B. Bargerion, Epithelial damage thresholds for multi-pulse exposures to 80 ns pulses of CO₂ laser radiation. *Health Physics*, Vol. 80, No. 1, p. 41-46, 2001.
- ¹⁴ Minna Vesaluoma, Ann-Maija Teppo, Carola Grönhagen-Riska, Timo Tervo, Increased release of tumour necrosis factor- α in human tear fluid after excimer laser induced corneal wound. *British Journal of Ophthalmology* 81, 145-149, 1997.

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- ¹⁵ Chris Steele, Corneal Wound Healing. *Optometry Today*. 29-32, 1999.
- ¹⁶ Gasset AR and Dohlman CH: The tensile strength of corneal wounds. *Arch Ophthalmol* 79:595, 1968.
- ¹⁷ Dunnington JH and Weimer V: Influence of the epithelium on the healing of corneal incisions. *Am J Ophthalmol* 45:89, 1958.
- ¹⁸ Heather C. Balwin and John Marshall, Growth Factors in Corneal Wound Healing Following Refractive Surgery: A Review. *Acta Ophthalmologica Scandinavica* 80, 238-247, 2002.
- ¹⁹ W. P. Roach, B. Ketzenberger, M.B. Burton, T.E. Johnson, Corneal Injury from 1318-nm Single Laser Pulses, *Proceedings of SPIE*, Vol. 3, No. 9, p. 30-40; 2002.
- ²⁰ R.L. McCally, C. B. Barger, Epithelial damage thresholds for multi-pulse exposures to 80 ns pulses of CO₂ laser radiation. *Health Physics*, Vol. 80, No. 1, p. 41-46, 2001.