In vivo confocal microscopy of the cornea in health and disease

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DECLARATION

I hereby declare that I am currently registered as a candidate for the degree of Doctor of Philosophy in Ophthalmology, University of Auckland. I am the sole author of this thesis: all references cited have been consulted by me; all studies were conceived and designed by myself. I performed the majority of data acquisition and entry and performed all analysis. This thesis and any research within has not been, is being, or will be submitted for any other higher degree at the University of Auckland or other education centre.

I, Dipika Patel, declare that the information is complete and accurate, that no relevant information has been withheld that I am aware of and believe that I have complied with all of the University requirements in the regulations associated with my degree.

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ABSTRACT

The cornea is the transparent structure forming the anterior eye. Principal functions include: transmitting and focusing light onto the retina, containing intraocular pressure, and providing a protective interface with the environment. The specialized microstructural organization of the cornea is key to these functions and maintenance of corneal integrity.

In vivo confocal microscopy enables examination of the living human cornea at the microstructural level. This technique, in combination with computerized topography, corneal aesthesiometry and other clinical assessments has been utilized in a series of inter-related studies of the human cornea.

Both slit scanning and laser scanning *in vivo* confocal microscopes were used and the attributes and performance of the two types of microscope were compared, demonstrating marked differences.

Quantitative analysis of the sub-basal nerve plexus in the normal cornea and the inherited ectatic condition of keratoconus was correlated with central corneal sensitivity, revealing that nerve density does not change with increasing age and that nerve density is positively correlated with corneal sensitivity. However, in keratoconus, central corneal sensation, sub-basal nerve density, and basal epithelial density are all significantly lower than normal.

A novel technique developed to map the corneal sub-basal nerve plexus enabled elucidation of the previously enigmatic architecture, revealing an overall radial pattern with a clockwise whorl at the area of convergence, inferior to the corneal apex. Keratoconic corneas demonstrated gross abnormalities of the nerve plexus even in mild cases. A two-dimensional reconstruction of the inferior limbus was also produced using this method.

Analysis of the corneal endothelium in posterior polymorphous dystrophy revealed that endothelial density does not correlate with the clinical severity of this dystrophy. Key observations included hyper-reflective endothelial nuclei and apparent aggregation of keratocytes around the endothelial lesions. Investigation of hyper-reflective corneal endothelial nuclei *per se,* revealed that these are not seen in the normal cornea but are associated with endothelial trauma, intraocular surgery or disease states that primarily affect the endothelium.

In conclusion, using *in vivo* confocal microscopy, these studies have provided important qualitative and quantitative data that add to our knowledge of the human cornea, at the microstructural level, in health and disease states.

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LIST OF ABBREVIATIONS USED IN THIS THESIS

BSCVA	best spectacle corrected visual acuity
CCD	charge-coupled device
CMTF	confocal microscopy through focusing
ECCE	extracapsular cataract extraction
HRT	Heidelberg Retina Tomograph
HSV	herpes simplex virus
ICE	iridocorneal endothelial syndrome
IOL	intraocular lens
LASIK	laser in situ keratomileusis
MPS	mucopolysaccharidoses
NAVIS	Nidek Advanced Vision Information System
NCCA	Non-contact corneal aesthesiometer
OCT	optical coherence tomography
OD	oculus dexter (right eye)
OS	oculus sinister (left eye)
OU	oculus uterque (both eyes)
PK	penetrating keratoplasty
PMMA	polymethyl methacrylate
PPD	posterior polymorphous dystrophy
PRK	photorefractive keratectomy
RCM	Rostock corneal module
SSCM	slit scanning *in vivo* confocal microscope
TSCM	tandem scanning *in vivo* confocal microscope
UAVA	unaided visual acuity
V	volts
W	watts

nm	nanometers
µm	micrometers
mm	millimeters
mbar	millibars
m/s	meters per second