ANGLIA RUSKIN UNIVERSITY

NEARWORK-INDUCED TRANSIENT MYOPIA IN MYOPIC AND NON-MYOPIC INDIAN SUBJECTS

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Abstract

This research project investigated the characteristics of near-work induced transient myopia (NITM) in asymptomatic myopes and non-myopes among Indian subjects and its variation with target size and contrast. NITM was defined as the post-task distance refraction minus the pre-task distance refraction. In the first two studies NITM magnitude was greater and the decay was faster among myopes for 5 minutes and 60 minutes of near task respectively. There was no influence of target size and contrast on NITM parameters. In the third study Zernike wave-front co-efficient values were measured using COAS (complete ophthalmic analysis system) before and immediately after 5 minutes of near task to investigate the effect of near task on higher order aberrations among myopes and non myopes. Aberration values did not show significant differences for pre and post 5 minutes of near task. In the fourth study axial length, corneal thickness, AC depth and lens thickness were measured with the Bio-graph (Allegro, wave light) instrument before and immediately after 5 minutes of near task to investigate the influence of near task on biometry readings among myopes and non-myopes. Axial length, corneal thickness, AC depth, lens thickness did not show significant differences following 5 minutes of near task. In the fifth study 31 myopes were recruited to assess the NITM parameters in pre and post Lasik refractive surgery. NITM magnitude was higher in pre-Lasik myopic subjects compared to post-Lasik myopic subjects. Most of the accommodative parameters especially the lag of accommodation and facility of accommodation improved following the surgery.

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Abbreviations

NITM: Near-work Induced Transient Myopia

NPC: Near Point of convergence

NPA: Near point of accommodation

NRA: Negative relative accommodation

PRA: Positive relative accommodation

AC/A: Accommodative convergence/Accommodation ratio

AF: Accommodative facility

EOM: Early onset Myopia

LOM: Late onset Myopia

COAS: Complete Ophthalmic Analysis System

EMM : Emmetropes

MYO : Myopes

PM : Progressing Myopes

SM : Stable Myopes

AL : Axial length

ACD : Anterior chamber depth

CT : Corneal thickness

LT : Lens thickness

Chapter One

Introduction

Myopia is a worldwide public health problem and it is estimated that 2.5 billion people will be myopic by the end of this decade (Pan, et al., 2012; Dolgin, 2015). Therefore, great efforts have been made to identify and understand the mechanisms underlying the development, progression and control of myopia. Various studies have been conducted to understand the exact aetiology, but still it is yet to be elucidated and presently it is believed to have a diverse aetiology from both genetic and environmental factors (Wu and Edwards, 1999; Saw, et al., 2001; Mutti, et al., 2002; Saw, et al., 2002; Saw, et al., 2005; Saw, et al., 2006; Huang, et al., 2014; Li, et al., 2015).

1.1 Definition and Classification of Myopia

Myopia is a refractive condition where parallel rays of light from a distant target are focused in front of the retina when the eye is in the un-accommodated or relaxed state. Though there are several classifications of myopia, broadly myopia is divided into two clinical types: 1) Pathological myopia, and 2) Physiological myopia (Curtin, 1979). Pathological myopia is considered to be congenital and physiological myopia is considered to be more environmental in nature. Another classification is based on the degree of myopia. Less than 3 diopters of myopia is considered as low, between 3 diopters and 6 diopters as moderate and greater than 6 diopters as high myopia (Grosvenor, 1987). Borish (Benjamin, 2006) classified myopia by cause as axial and refractive. There is an increase in axial length of the eye in axial myopia whereas in refractive myopia the focal length of the eye is abnormal. This abnormal focal length could either be due to excessive curvature of one of the refractive surfaces of the eye, especially the cornea (Curvature Myopia), or variation in the index of refraction of one or more of ocular media (Index Myopia).

Goldschmidt, (1969) classified myopia based on age as 1) early-onset myopia (EOM), where myopia develops prior to 15 yrs of age, and 2) late-onset myopia (LOM) where myopia develops after 15 yrs of age.

When an eye grows, the axial length of the eye is matched to the optical properties of the cornea and crystalline lens in order to make the image focus on the retina as part of the emmetropization process. Early onset myopia may be due to the failure of this emmetropization process where the axial length of the eye grows and is not compensated by the optical properties of the cornea and crystalline lens (Saw, et al., 2002). Late onset myopia may be more related to environmental factors such as excessive near work, urbanization, time spent outdoors and lighting (McBrien and Adams, 1997; Jorge et al., 2007; Ciuffreda and Vasudevan, 2008; Arunthavaraja, Vasudevan and Ciuffreda, 2010, Dolgin, 2015).

Myopes are also classified as stable myopes (SMs) and progressive myopes (PMs) based on the history of their refractive error. Any change in refraction of - 0.50D or more over the previous two years is termed as progressive myopia and if not as stable myopia (Abbott, et al., 1998). Based on their clinical appearance myopia has been described as follows: Simple myopia, where the eye is too long for its optical power and Degenerative myopia, where it is characterized by marked fundus changes such as posterior staphyloma (Abrams D, 1993; Benjamin William J, 2006).

1.2 Prevalence of Myopia

The prevalence of myopia in some East Asian countries is between 1.2% and 89.4% among children between 5 to 17 years of age (Pokharel, et al.,2000; Zhao, et al., 2000, He, et al., 2004; Fan, et al., 2004; He, et al, 2007;Sapkota, et al., 2008; Yuan, et al., 2013), and in non-Asian countries it has been found to be between 1.9% and 49.7% (Maul, et al., 2000; Villarreal, et al., 2000; Naidoo et al., 2003; William, et al., 2008; Vitale, et al., 2009; O'Donoghue, et al.,2010) among children between 5 and 15 years of age. In Singapore, myopia prevalence has been reported to be 36.7% among 7 to 9 year old children and 73.9% in 15-19 year old adolescents (Saw, et al, 2002; Quek, et al, 2004; Saw, et al, 2006). The variations in the prevalence of refractive errors were according to ethnicity and geographic regions (Foster and Jiang, 2014). Although the majority of studies defined myopia as spherical equivalent (SE) ≤ -0.50 D of myopia, a wide variety of definitions were adopted from ≤ -0.12 D to -1.00 D (Foster and Jiang, 2014). In addition the variation in prevalence can be accounted for by the sampling procedure and to some extent methods used for measuring refractive errors. Majority of the studies adopted cycloplegic auto-refraction (Zhao, et al., 2000; Saw, et al, 2002; Zhao, et al., 2002; Fan, et al., 2004; Lin, et al., 2004; Saw, et al., 2006; He, et al., 2007; Rose, et al., 2008; O' Donoghue, 2010), and few others cycloplegic retinoscopy and auto-refraction (Maul, et al., 2000; Pokharel, et al., 2000; Naidoo, et al., 2003; He, et al., 2004; Goh, et al., 2005) and the rest non-cycloplegic autorefractometer (Cheng, 2003; Quek, 2004; Xu, 2005; Williams, 2008).

In India, prevalence has been found to be between 2.8% and 19.39% among children between 5 and 15 years of age (Dandona, et al., 1999; Dandona, et al., 2002; Murthy, et al., 2002; Uzma, et al., 2009; Saxena, et al., 2015).The prevalence of myopia in Asian countries is tabulated in Table 1.1 and that of India in Table 1.2.

The prevalence of myopia has been found to be 22.9% and 19.4% among Chinese and Taiwanese adult populations of over 40 years of age (Cheng, et al., 2003; Xu, et al., 2005). Myopia occurs in epidemic proportions among adults from 85% to 90% in Asian cities (Yu, et al., 2011). In India, it is between 31% and 38% among the urban and rural adults over 39 years of age respectively. The higher prevalence among rural adults was attributed to the presence of nuclear cataract which causes myopic shifts in refraction (Raju, et al., 2004; Krishnaiah, et al., 2009).

Table 1.1 Prevalence of myopia in Asian Countries

Author(Year)/Sample size(N)/N per year (age)	Location	Age range(Years)	Prevalence (%)	Race/Ethnicity	Methods/Design	Myopia (D)
Pokharel, et al. (2000) N=5067 (5- 465, 6-444, 7-486, 8-439, 9-469, 10-500, 11-467, 12-481, 13-478, 14-452, 15-386)	Nepal(Sub-urban)	5-15	1.2	Nepalese (Mixed Mongoloid, Aryan and aboriginal ancestry)	Cluster sampling	0.5 or less
Zhao, et al. (2000)/N=5884 (5- 103, 6-199, 7-358, 8-595, 9-855, 10-824, 11-814, 12-704, 13-527, 14-486, 15-419)	China(Rural-North)	5	nil	Chinese ethnic groups	Cluster sampling	0.5 or less
		15(males)	36.7			
		15(females)	55			
Lin, et al. (2001)/N=10,889	Taiwan	7	20	Taiwanese aboriginals and Chinese	Stratified cluster sampling	0.25 or less
(7-924,8-915,9-890,10-945,		12	61			
11-944, 12-920,13-969,14-960,15-937,16-882,17-802,18-790)		15	81			
Saw, et al. (2002)/N=957	China	7-9	18.5	Chinese ethnic groups	Cross sectional	0.5 or less
Saw, et al. (2002)/N=957	Singapore	7-9	36.7	Chinese (Hokkien)	Cross sectional	0.5 or less
Zhao, et al. (2002)/N=4662 (5-92,6-189, 7-344, 8-571, 9-832, 10-793, 11-778, 12-672, 13-391)	China(Rural)	5-13	28.9	Chinese	Longitudinal Cohort Study	0.5 or less
Cheng, et al.(2003)/N=2045	Taiwan	65+	19.4	Chinese	Cross sectional	0.5 or less

He, et al. (2004) /N=4364	China(urban)	5	3.3	Chinese (Han)	Cluster sampling	0.5 or less
(5-271,6-295,7-326,8-394,9-398,10-415,11-427,12-454,		10	25.3			
13-498,14-510,15-376)		15	73.1			
Fan, et al. (2004)/N=7560	Hong Kong	7	28.9	Chinese	Longitudinal	0.5 or less
(7-1194,8-1210,9-1134,		8	37.5			
10-1267,11-1720)		11	53.1			
Lin, et al. (2004)/N=4125	Taiwan	7	5.8	Taiwanese aboriginals and Chinese	Stratified cluster sampling	0.25 or less
(7-260,8-265,9-263,10-268,11-263,12-266,13-265,14-264,15-257,16-576,17-604,18-574)		16	74			
Lin, et al. (2004)/N=10,878	Taiwan	7	21	Taiwanese aboriginals and Chinese	Stratified cluster sampling	0.25 or less
(7-924,8-915,9-890,10-945,11-944,12-920,13-969,14-960,15-937,16-882,17-802,18-790)		18	84			
Quek, et al.(2004)/N=946 (15-493, >15-453)	Singapore	15-19	73.9	Chinese-603, Malay-229, Indian-114	Cross sectional	0.5 or less
Goh, et al. (2005)/N=4674 (7-590,8-616,9-575,10-589,11-557,12-534,13-431,14-421, 15-321)	Malaysia	7-15	20.7	Malay-3257,Chinese-764,indian-412,others-201	Cluster sampling	0.5 or less
Xu, et al. (2005)/N=2414 (40-278,45-318,50-253,55-361,60-530,65-363,70-206,>70-106)	China	40-90	21.8	Chinese(Haidi,Yufa)	Cluster sampling	0.5 or less

Saw, et al. (2006)/N=1962 (7-851,8-630,9-481)	Singapore	7-9	36.3	Chinese, Indians, others	Cluster sampling	0.5 or less
Saw, et al. (2006)/N=1752 (7-581,8-601,9-570)	Malaysia	7-9	13.4	Malay, Chinese, others	Cluster sampling	0.5 or less
He, et al. (2007)/N=2454	China(Rural-South)	13	36.8	Chinese	Stratified cluster sampling	0.5 or less
(12-34,13-261,14-713,15-843,		15	43			
16-452,17-131,18-20)		17	53.9			
Rose, et al., (2008)/N=628	Singapore	6-7	29.1	Chinese (in Singapore)	Cross sectional	0.5 or less
Sapkota, et al.(2008)/N=4282	Nepal(Urban)	10	10.9	Aryan(2128),Mongol(1927),Tibetan(188),others(39)	Stratified cluster sampling	0.5 or less
(10-405,11-607,12-868,13-985,		12	16.5			
14-878,15-539)		15	27.3			
Yuan, et al. (2013)/N=395	China(urban)	7	39.3	Chinese	Cohort	0.5 or less
(8-92,9-107,11-30,13-103,		10	68.8			
15-23,17-40)		11-17	89.4			
Wu, et al. (2015)/ N=4798	China(urban)	16-18	80.7	Chinese(Han)	Cross sectional	1.0 or less

The prevalence of myopia was the highest among 19 year old males in Korea (96.5%) with 21.61% having high myopia (Jung, et al., 2012). Prevalence was found to increase with age in Taiwan (Lin, et al., 2004), Hong Kong (Lam, et al., 2012) and Singapore (Saw, et al., 2002). For instance, the prevalence increased for 18 years old compared to 7 years old young adults in Taiwan. In Hong Kong, the prevalence increased from 6 years old compared to 12 years old from 18.3% to 61.5% and in Singapore the prevalence increased from 7 years old compared to 9 years old from 29% to 53%.

The prevalence of myopia also varied among 16 to 25 year olds of different ethnic groups in Singapore. The prevalence was 69% in Indians, 65% in Malays and 82% in Chinese (Wu, Seet, Yap et al., 2001). The prevalence among Indians living in Singapore is high compared to Indians living in India; this could be due to the higher literacy rate among adults (96%) in Singapore compared to adults (63%) in India (Central Intelligence Agency, 2009; Census of India, 2011).

Table 1.2 Prevalence of myopia in India (India refers to nationality and not ethnicity/race)

Author(Year)/Sample size(N)	Location	Age range(Years)	Prevalence(%)	Methods/Design	Myopia (D)
Jain, et al. (1983)/N=10509	India (urban)	all ages	6.9	Survey	6D or less
Jain, et al. (1983)/N=12743	India(rural)	all ages	2.77	Survey	6D or less
Dandona, et al.(1999)/N=2321	India (urban)	<15	4.44	Stratified cluster sampling	0.5 or less
<15-N=663, >15-N=1658		>15	19.39		
Dandona, et al.(2002)/N=4074	India(rural)	7	2.8	Stratified cluster sampling	0.5 or less
(7-588,8-626,9-471,10-507,11-447		10	4.06		
12-534,13-358,14-285,15-258)		15	6.72		
Murthy, et al.(2002)/N=6447	India (urban)	5	4.68	Cluster sampling	0.5 or less
(5-552,6-556,7-590,8-690,9-599		10	6.95		
10-670,11-598,12-636,13-593,14-543,15-471)		15	10.8		
Raju, et al. (2004)/N=2508	India(rural)	39+	31	Cross-sectional	0.5 or less
40-49-1456,50-59-686, 60-69-302,>70-64					
Ahmed, et al.(2008)/N=4360	India(urban)	7-18	4.74	Survey	0.25 or less
10-1674,<15-1745,<22-941					
Krishnaiah, et al.(2009)/N=3642 (40-1416,50-1035,60-858,70-333)	India (urban)	40+	31.9	Cross-sectional	0.5 or less

	India(rural)		38		
Nazia, et al.(2009)/N=3314 (7-216,8-240,9-200,10-196,11-204,12-180,13-199,14-178,15-176)	India(urban)	7-15	51.4	Survey	0.5 or less
7-210,8-150,9-220,10-187,11-200,12-121,13-123,14-186,15-128	India(rural)		16.7		
Pavithra, et al.(2013)	India(urban)			Cross-sectional	0.5 or less
7-9	257	7-9	0.29		
10-12	384	10-12	1.16		
13-15	737	13-15	2.97		
Saxena(2015)/N=9884	India(urban)			Cross-sectional	0.5 or less
5-10 = 3163		5-10	8.4		
11-13 = 4651		11-13	15.3		
14-15 = 2070		14-15	15.3		
		Boys	12.4		
		Girls	14.5		
		Private School	17		
		Government school	7.9		
Shakeel and Mittal (2016)/N=3146	India(urban)			Cross-sectional	0.5 or less
5-7=472		5-7	0.44		
8-10=689		8-10	0.92		
11-13=877		11-13	1.43		
14-16=1108		14-16	2.16		

The prevalence of myopia in the United States has substantially increased in the last three decades across all races (Vitale, et al., 2009). It was 12%, 25.8% and 24.0% among black, white and mixed race children between 12 and 17 years of age, which increased to 31.2%, 34.5% and 33.9% in the same racial group. The reason for the increase in prevalence was hypothesized to be due to increase in the years of formal education among 12 years and above, though the authors were not able to substantiate this hypothesis. Also in the Aston Eye Study, higher prevalence of myopia was reported among British South Asians (Bangladeshi, Indian, Pakistani), where the prevalence of myopia increased from 10.8% (95% CI 6.6-15%) at 6-7 years of age to 36.8% (95% CI 27.45.8%) at 12-13 years of age (Logan, et al., 2011), and in the (Child Heart and Health Study in England) CHASE study, the prevalence of myopia among South Asians were found to be 25.2% among 10 -11 years of age (Rudnicka, et al., 2010). The reason reported for the increased prevalence of myopia among South Asians was increased axial length (0.44 mm; 95% CI, 0.30 to 0.57 mm). Similarly in Chile, myopia prevalence has been found to be 3.4% among children of 5 years of age, which increased to19.4% among male children of 15 years, and 14.7% among female children of the same age. Table 1.3 summarizes the prevalence of myopia in some of the non-Asian countries.

Table 1.3 Summary of prevalence of myopia in some of the non-Asian Countries

Author(Year)/Sample size(N)	Location	Age range (Years)	Prevalence (%)	Race/Ethnicity (%)	Methods/Design	Myopia (D)
Zadnik, et al. (1993)/N=530 (5-15,6-133,7-46,8-143,9-25,10-13,11-129,12-26)	United states	6-14	20	White-87.1, Hispanic-10.4, Asian-1.9, Black-0.6	Longitudinal	0.75 or less
Maul, et al. (2000)/N=5303	Chile(males)	5	3.4	Children from Chile	Cluster sampling	0.5 or less
(5-560,6-538,7-552,8-585,9-514,10-475		15	19.4			
11-502,12-435,13-432,14-315,15-395)						
Maul, et al. (2000)/N=2613	Chile(females)	5	3.4			
		15	14.7			
Villarreal, et al. (2000)/ N=1045	Sweden	12-13	49.7	Children from Sweden	Survey	0.5 or less
Naidoo, et al. (2003)/N=4890	South Africa	5	1.9	Indian/Asian: 9.4	Cluster sampling	0.5 or less
(5-339,6-458,7-469,8-471,9-469,10-551,		10	2.5	White-6.6, Mixed-1.4		
11-483,12-476,13-420,14-428,15-326)		15	9.0	African/Black-82		
Ip, et al. (2008) /N=2309	Australia	12	Urban:17.8	European caucasians-59.2, East Asians-15.11, Mixed-25.6	Survey	0.5 or less
			Sub-urb:6.9			
Vitale(2009)/N=4436	US(White)	12-17(1971-1972)	25.8	Black, White, Mixed	Survey	0.25 or less
N=8339	US(White)	12-17(1999-2004)	34.5	Black, White, Mixed	Survey	0.25 or less

O'Donoghue(2010)/N=392	Northern Ireland	6-7	2.8	Northern Irish Children	Cluster sampling	0.5 or less
O'Donoghue(2010)/N=661		12-13	17.7	Northern Irish Children	Cluster sampling	0.5 or less
Rudnicka, et al. (2010) N=1179	UK	9.8-<11 11-11.9	11.3 13.3	White European-22.73, Carribean black-23.75, South Asian-28.69, Asian other-6.87, others-17.9	Cross-sectional	0.5 or less
Logan, et al. (2011)/N=1700	UK	6-7	9.4	White European-70.35, Carribean black-6.12, South Asian-20.04, Asian other-6.87, others-3.49	Cluster sampling	0.5 or less
Logan, et al. (2011)/N=1200	UK	12-13	29.4	White European-70.35, Carribean black-6.12, South Asian-20.04, Asian other-6.87, others-3.49	Cluster sampling	0.5 or less
Pan, et al. (2013)/N=4430	US	45-84	White -31, Chinese-37.2, Black-21.5, Hispanic-14.2	White -37.6, Chinese-11, Black-27.8, Hispanic-23.6	Cross-sectional	1.0 or less
45-54-1280, 55-64-1506, 65-74-1196						
75+ - 448						

Figure 1.1 a: Prevalence of myopia in UK (Logan, et al., 2011)

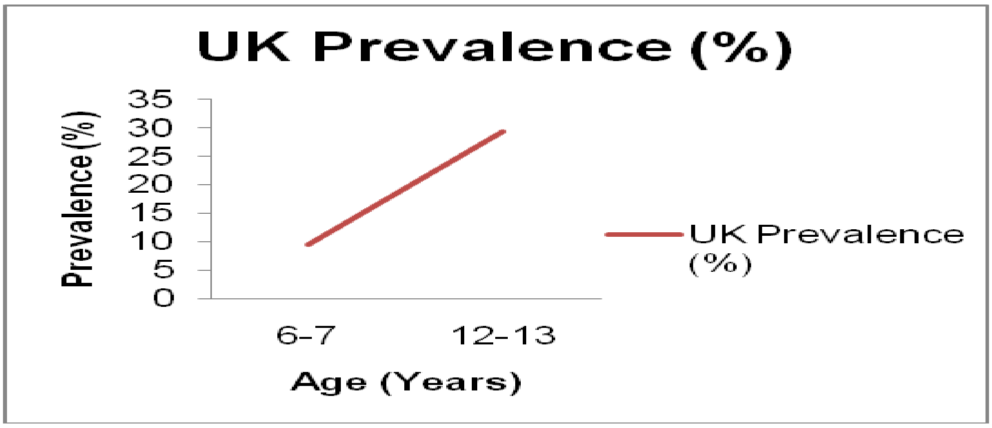


Figure 1.1 b: Prevalence of myopia in Ireland (O'Donoghue, 2010)

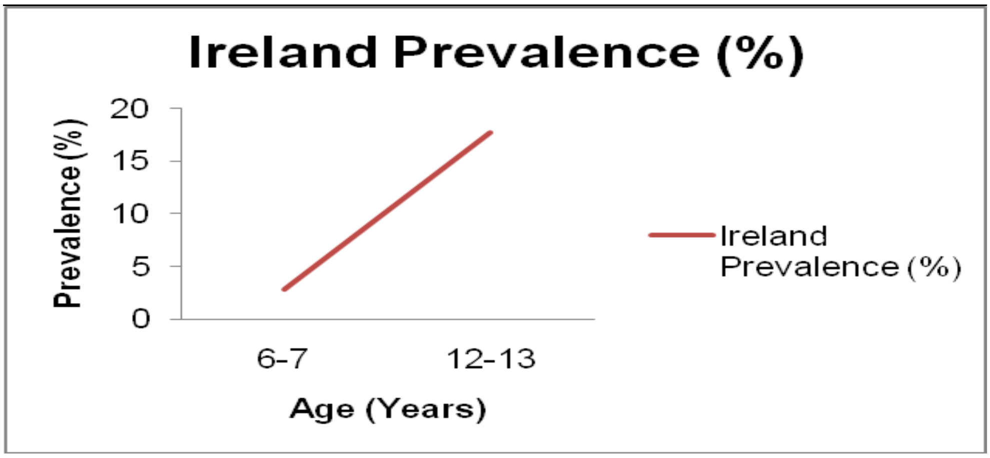
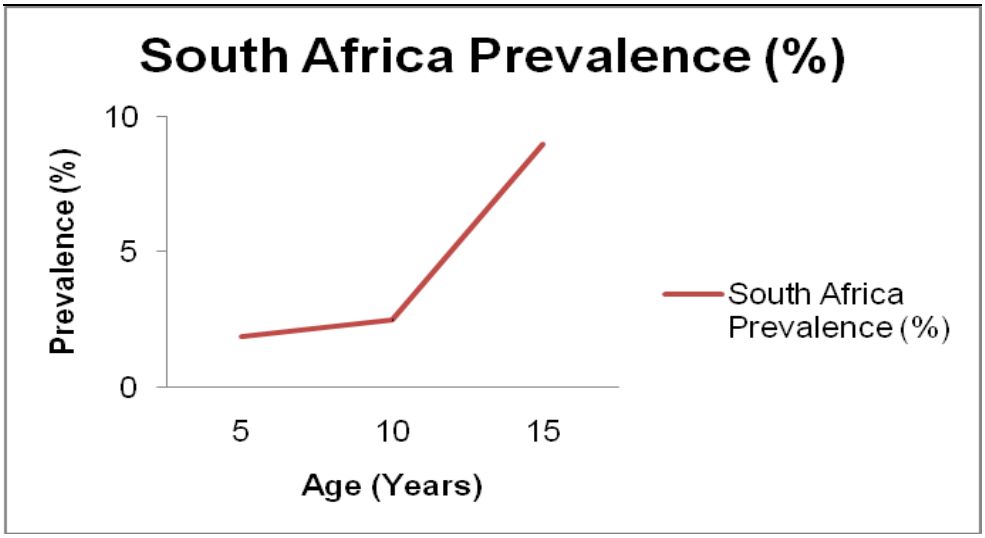


Figure 1.1 c: Prevalence of myopia in South Africa (Naidoo, et al., 2003)



The trend appears to be of myopia prevalence increasing with age globally (Figure 1.1 a,b,c). In countries like Taiwan, Singapore and China the rates of myopia prevalence are higher in the last two decades compared to India (Lam, et al., 2012, Morgan, et al., 2012). This increase in prevalence of myopia has been attributed to the rapid urbanization, and growing visual demand for near work (Jain, et al., 1983; Saw, et al., 2002; Dandona, et al., 2002; He, et al., 2004; Lin, et al., 2004; Quek, et al., 2004; Uzma, et al., 2009). Evidence has shown that children spend more hours on near work in countries where the prevalence of myopia is high. For instance, 15 year olds in Shanghai spend 14 hours per week on home work, compared with only 5 hours in the United Kingdom and 6 hours in the United States where the prevalence of myopia is relatively low (Dolgin, 2015).

1.2.1 Prevalence of myopia among Urban and Rural populations

Table 1.4 Summary of prevalence of myopia among Urban and Rural populations

Country	Age range (Years)	Prevalence (%)	
		Urban	Rural
China	5-15	38 (He, et al., 2004)	28.9 (Zhao, et al., 2002)
China	8-9	19.3 (Saw, et al. (2001)	6.6 (Saw, et al. (2001)
India	7-15	51.4 (Uzma, et al. (2009)	16.7 (Uzma, et al. (2009)

The prevalence of myopia among children in urban populations is higher than the rural population (Pan, et al., 2012). For instance, in China, the prevalence of myopia among urban children (5 – 15 yr old) was found to be 38% (He, et al., 2004). The prevalence of myopia among rural children of the same age group was 28.9% (Zhao, et al., 2002). Saw, et al. (2001) reported prevalence of myopia in rural and urban secondary grade school children in China. The prevalence of myopia was 19.3% among urban children and 6.6% among rural children. They also reported that the city school children spent 2.2 hours per day on reading and writing whereas the rural children spent only 1.6 hours. They reported an association between the higher prevalence of myopia with time spent on reading and writing among the city children. Similarly, Uzma, et al. (2009) assessed the prevalence of refractive errors in urban and rural Hyderabad, India and reported higher prevalence of myopia of 51.4% among urban children and 16.7% among rural children. The urban school children spent 4 hours reading and writing and 1 hour of computer class in school, and an average of 3 hours at home, whereas rural school children spent 3 hours reading and writing at school and an average of 1-2 hours at home.

Though the prevalence of myopia in India (Table 1.2) is low compared to China (Table 1.1), a similar trend of prevalence difference exists between rural and urban populations. Dandona, et al. (1999; 2002) reported prevalence of myopia among urban and rural school children less than 15 years was 4.4% and 3.1% and for children older than 15 years of age was 19.3% and 19.1%respectively. They also reported that myopia was common among males who completed their school education.

1.2.2 Socio-economic Status

Table 1.5 Relationship between socioeconomic strata and prevalence of myopia

(Ahmed, et al., 2008, Datta, Choudhury and Kundu, 1983)

Place/Country	Age range (Years)	Prevalence (%)	
		High Economic Strata	Low Economic Strata
Kashmir, India	6-22	2.67	8.6
Kolkatta, India	5-13	NA	56.35

Studies conducted in India have shown a higher prevalence of myopia among low socio economic strata than higher socio economic strata. A study conducted in Srinagar, a city in Kashmir, India, reported myopia prevalence of 2.67% and 8.60% among the high and low socio economic strata respectively (Ahmed, et al., 2008). Another study conducted in Kolkata, found the prevalence of myopia (-0.50 or less using cycloplegic retinoscopy) to be 56.35% among slum dwellers, who belong to low socio economic strata (Datta, Choudhury and Kundu, 1983). Usually higher prevalence of myopia is associated with higher economic strata and educational level, it is surprising that the above studies show more myopia among the low economic strata, but did not show the reasons for the higher prevalence of myopia among them. Though literature has shown an association between malnutrition and high prevalence of myopia, it was not well substantiated (Saw, et al., 1996).

From the above studies, it is clearly evident that the myopia development varies with ethnic origin and time spent on near work. Compared to Western populations, children from Asia especially those of Chinese ethnicity may be more susceptible. Though the prevalence of myopia in India is low, India is one of the fastest growing nations and 97.03% of children are attending schools in the age group of 6-13 years (Social and Rural Research Institute, 2014). Since near work demand is increasing, the tendency to follow other countries in terms of myopia progression is high.

1.3 Aetiology of Myopia

Family history of myopia is considered to be an important risk factor for myopia onset and its progression (Saw, et al., 2001; Saw, et al., 2005; Saw, et al., 2006; Kurtz, et al., 2007; Lam, et al., 2008). Studies have reported higher odds ratio for having myopia in children with one or both parents myopic when compared to those with no myopic parents (Zadnik, 1997; Wu and Edwards, 1999; Mutti, et al., 2002; Saw, et al., 2002; Liang, et al., 2004; Jones, et al., 2007; Lim, et al., 2014)

Lam, et al. (2008) evaluated the effect of parental history of myopia on eye growth in Chinese children and reported that the axial length growth and the myopic shift occurred more rapidly among children with a strong parental history of myopia than children with no myopic parents, but the exact mechanism which causes a breakdown of normal emmetropization and resulting myopia development is unknown. Saw, et al. (2006) reported a higher odds ratio for myopia development in children with one or two myopic parents than children with no myopic parent. Recently, Lim, et al. (2014) studied the impact of parental history of myopia on the development of myopia among school children in China and found a strong association between parental history and the genesis of myopia in offspring. They further reported that children with two myopic parents are at greater risk of developing higher degree of myopia than those with only one myopic parent. Also children with one myopic parent are at higher risk of developing myopia than those with no parental myopia. On the contrary, Fan, et al. (2005) and Iribarren, et al. (2005) did not show a difference in the degree of myopia and axial length between children with and without myopic parents. Fan, et al. (2005) did not report any difference possibly because they included children of six years and less, who might develop myopia later in life. Iribarren, et al. (2005) excluded high myopes (70%) and included only mild and moderate myopes (myopia lower than -6.00D) in their analysis, while comparing the degree of myopia between subjects with and without family history. Probably the exclusion of high myopes was the reason for not showing any relation between the degrees of myopia in the positive family history group.

Longitudinal studies which have assessed the rate of myopia progression have shown a higher myopic shift and axial elongation in children with one myopic parent or both myopic parents than children with emmetropic or hyperopic parents (Saw, et al., 2001; Saw, et al., 2005; Kurtz, et al., 2007; Lam, et al., 2008). The Orinda longitudinal study of Myopia (Zadnik, 1997) reported that though nature and nurture plays a role in the aetiology of myopia, positive parental history appears to play a predominant role. The COMET study, which evaluated the effect of progressive addition lenses and single vision lenses on juvenile onset myopia, reported that children with high myopia were more likely to have two myopic parents (Kurtz, et al., 2007). Mutti, et al. (2002) assessed the association between juvenile myopia and parental myopia, near work and school achievement and reported that heredity was the most important factor associated with juvenile myopia, with small contributions from near work, higher school achievement and less time in sports activity.

Although the genetic contribution in myopia is established, environmental influences do play a role (Midelfart, et al., 1992;Zylbermann, et al., 1993;McBrien and Adams, 1997) and hence understanding near work and myopia becomes important.

1.4 Near work and myopia

Studies have argued that sustained near work predisposes a child to myopia (Tan, et al.,2000; Hepsen, et al., 2001; Saw, et al., 2002a), other studies have found only a weak association (Saw, et al., 2001; Goldschmidt, et al., 2001; Saw, et al., 2005; Ip, et al., 2008).

Saw, et al., (2002a) reported a higher degree of myopia and longer axial length among children with higher near work activity than children with less near work activity. The limitation of this study was that information on whether the children wore their habitual spectacles while reading was not available, this could disrupt the normal refractive error development due to chronic hyperopic defocus (Ong, et al., 1999).

Norwegian textile industry workers who were engaged in carrying out quality control on textiles at a close working distance of 30 centimetres had 80% myopia prevalence whereas none of the others who were in sales, office or in production in the same factory were myopic (Simensen and Thorud, 1994). Seventy one percent of UK clinical microscopists had myopia and forty nine percent of them developed myopia after they started working as clinical microscopists (Adams and McBrien, 1992).

French, et al., (2013) studied the risk factors for myopia in Australian school children and reported that children who became myopic performed significantly more near work. A comprehensive questionnaire was used to determine the amount of time spent outdoors and near work activities per week at baseline apart from ethnicity, parental myopia and socio-economic status. They also reported that children of East Asian ethnicity (Chinese, Indians and Nepalese) had higher incidence of myopia and spent less time outdoors and more time on near work than those of European Caucasian ethnicity. Children from Australia had a lower prevalence of myopia. Such comparison of different ethnic groups in the same location indicates the strength of involvement of environment factors, especially less time spent outdoors and more near work, on refractive development. Thus myopic shifts were observed on exposure to near work over extended periods, though there could be recall bias with the use of a subjective questionnaire to measure various environmental activities.

In contrast, Saw, et al. (2001) and Ip, et al. (2008) did not show significant association between near work and myopia. The reason for not showing significant association may be due to the age group of subjects. Saw, et al. (2001) conducted a cross sectional study on Singapore military servicemen and assessed current close up work activity and at the age of seven years a through detailed questionnaire. It was found that though educational level was a risk factor for myopia, current near work activity was not. The reason could be that the exposure to close work activity was assessed during childhood when there was active growth of the eye. This study also mentioned that the accuracy of measures of near work activity were difficult to ascertain. Ip, et al. (2008) evaluated the impact of urbanization on childhood myopia in a population based sample of 12 year old Australian children. This study too used a questionnaire to evaluate the number of hours spent on near work, outdoor activities, environmental factors including ethnicity and parental education. The higher prevalence among urban children compared to suburban children were due to the differences in socio economic status and ethnic compositions among the groups. Also a greater proportion of parents had myopia. Also the studies mentioned used crude estimates of near work, like number of hours of near work in a day or in a week and number of books read in a week for analyses, except Mutti, et al. (2002) who calculated near work in terms of dioptre hours thus taking into consideration the accommodative demand required for near work activity. However, Mutti, et al. (2002) did not report whether higher dioptric demand was related to myopia progression.

Some of the longitudinal study results have provided better understanding of the effect of near work on myopia progression (Tan, et al., 2000; Saw, et al., 2001;Hepsen and Bayramlar, 2001; Loman, et al., 2002; Saw, et al., 2005; Saw, et al., 2006).

Results from Saw, et al. (2001), Loman, et al. (2002), Saw, et al. (2005), Saw, et al. (2006) showed no effect of near work on myopia progression, whereas Tan, et al. (2000) and Hepsen and Bayramlar, (2001) reported a significant correlation and more myopic shift and axial length elongation among children with more near work activity. One reason for the varied results could be that the former studies included subjects with parental myopia in their analyses, whereas the later studies did not include them.

Studies (Saw, et al., 2002b; Saw, et al., 2002c) have shown an association between myopia and near work but have not been able to demonstrate a cause-effect relationship. Also from the observation, environmental factors, genetics and their complex interactions could attribute to the regional and ethnic differences in the distribution of refractive errors.

Two theories that have attempted to describe the underlying mechanism of myopia development in relation to prolonged near work are the Incremental Retinal Defocus Theory (IRDT) and Hyperopic Defocus Theory. Incremental Retinal Defocus theory is based on the mechanism for the regulation of ocular growth, where following prolonged near work, decrease in retinal image defocus decreases the rate of proteoglycan synthesis decreasing scleral structural integrity and in turn the eye's axial length (Hung and Ciuffreda, 2003). The second hypothesis has emerged from consideration of animal experiments, where individuals who are engaged in near activities may experience prolonged periods of hyperopic retinal defocus, which may produce axial elongation (Gwiazda, Thorn and Held, 2005).

1.5 Outdoor activities and Myopia

While association between near work and myopia is contemplated, recent studies have shown beneficial effect of outdoor activities (Ip, et al., 2008; Dirani, et al., 2009; Wu, et al., 2010; Wu, et al., 2013; Mutti, et al., 2013).

Ip, et al. (2008) investigated the role of near work in myopia among 12- year old Australian children. They collected data on time spent on near work activity and outdoor activity per week. The duration of continuous reading and reading distances were collected using questionnaires. They found that near work at a close reading distance (<30 cms) and continuous reading (> 30 minutes) were associated with myopia development. They also reported that more time spent outdoors had a significant protective effect on myopia. Less time spent outdoors is considered a risk factor for myopia development (Rose, et al., 2008; Dirani, et al., 2009). Wu, et al. (2010) assessed the prevalence and risk factors of myopia among elementary school students in a rural area of Taiwan and suggested that outdoor activity was an important protective factor for myopia. Wu, et al. (2013) reported that outdoor activities during class recess had a significant effect on myopia onset and myopic shift. Mutti, et al. (2013) reported that emmetropic children with two myopic parents and who spent less than 5 hours per week outside had a 60% chance of becoming myopic, whereas for those who spent 14 hours per week outside, it reduced to 20%. Ngo, et al. (2014) evaluated an incentive based intervention to increase the time spent outdoors among children aged 6 to 12 years. They found an increase in outdoor time spent by children through this incentive based outdoor activity program after six months, though increased time spent outdoors was not sustained until the end of the study. Though this study did not assess changes in refractive error, it was a small exploratory trial and larger such trials to prevent and evaluate myopic shifts to reduce myopia incidence were recommended. Studies in China and Australia revealed that rate of progression of myopia was low among 10% of the children who were exposed to outdoor activities, compared to those who were not exposed (Dolgin, 2015).

Theories attempting to link a decrease in myopia progression and time spent outdoors believed that the brighter light outside may stimulate release of dopamine from the retina that inhibits the axial growth of the eye and also due to the intensity of light, the depth of focus could be larger, which would reduce image blur (Ip, et al., 2008). Increased Vitamin D level may have a beneficial effect on the ciliary muscle. It might prevent the stretch on the crystalline lens and prevent axial growth (Mccarthy, et al., 2007; Siegwart Jr, et al., 2012).

Also a recent study by Yazar, et al., (2014) found that myopes have lower vitamin D levels (measured serum concentration from their blood sample) compared to non-myopes.

Jones, et al. (2007) did not show any association between myopia progression with either near work or outdoor activity. This study assessed the time spent outdoors annually from parents and that could have under estimated the effect of outdoor activities due to recall bias.

1.6 Myopia and Education

There appears to be an association between myopia and the amount of near work involved with higher educational level (Tay, et al., 1992; Verhoeven, et al., 2013; Mirshahi, et al., 2014) as higher school achievement was one of the most important factors associated with juvenile myopia (Mutti, et al., 2002). Mirshahi, et al. (2014) analyzed the association between myopia and educational level in an adult European cohort and reported that higher levels of education were associated with myopia. Participants who had higher educational achievements were more often myopic than individuals with lower educational levels. Another study by Verhoeven, et al. (2013) reported that individuals who are at high genetic risk with only primary schooling were at a much lower risk of myopia development than those at high genetic risk with university level education. This study suggests that an individual's genetic risk of myopia may be affected by his/her educational level perhaps due to an increased amount of near-work. Results from the Gutenberg Health study on myopia and the level of education, also reported that higher levels of school and post-school education were associated with more myopic spherical equivalent compared to individuals with less education (Wolfram, et al., 2014).

1.7 Accommodation and its role on myopia development

Accommodation is a process whereby changes in the dioptric power of the crystalline lens occur so that an in-focus retinal image of an object of regard is obtained and maintained at the high-resolution fovea (Heath, 1956).

During near work, sustained accommodative effort is needed and many studies (Ebenholtz, et al., 1983; McBrien and Millodot, 1986b; Ip, et al., 2008) have investigated the role of accommodation in myopia development. Studies (McBrien and Millodot, 1986b; Bullimore and Gilmartin, 1987a; Gilmartin and Bullimore, 1991; Gwaizda, et al., 1993; Strang, et al., 1994; Allen and O'Leary, 2006) have shown that the accommodation responses are different for myopes compared to non-myopes.

1.7.1 Accommodation as a function of refractive group is described

1.7.1.1Amplitude of accommodation:

This is a measure of maximum accommodative response. The most common method of measuring amplitude of accommodation is the push-up technique using a near point rule. Studies (Maddock, et al. 1981; Fledelius, 1981; McBrien and Millodot, 1986a; Fisher, 1987; Mantyjarvi, 1987; Lekha, et al., 2005; Maheshwari, et al., 2011) have investigated if the amplitude of accommodation is different in myopes compared to other refractive groups and the results are not conclusive.

Few studies (Fledelius, 1981; Maddock, et al. 1981; McBrien and Millodot, 1986a; Lekha, et al., 2005; Maheshwari, et al., 2011) have reported that myopes have relatively high amplitudes of accommodation. Some others (Zhai and Guan 1988; Fong, 1997; Allen and O'Leary, 2006) have reported that myopes have relatively low amplitudes of accommodation. Other studies have shown no difference in amplitude of accommodation among refractive groups (Gawron, 1980; Fisher, Ciuffreda and Levine, 1987; Mantyjarvi, 1987). So from the above it is evident that the accommodative amplitude as a function of refractive state is equivocal. The differences between these studies may be attributed to distribution of age. Studies in which there was no difference in amplitude had age ranges covering a decade. These results could be attributed to the differing sample characteristics including that of the wider age and refractive error range. In addition, few studies have assessed monocular accommodative amplitude (McBrien and Millodot, 1986a; Fisher, Ciuffreda and Levine, 1987), few others have used RAF rulers (Lekha, et al., 2005; Allen and

O'Leary, 2006; Maheshwari, et al., 2011) and these methodological differences could also affect the outcome as higher amplitudes have been reported using the push-up method compared to other methods (Momeni-Moghaddam, Kundart, and Askarizadeh, 2014). Also some studies reported ocular accommodation and others spectacle accommodation and failed to consider the lens effectivity. Only a few studies have compensated for the lens effectivity (McBrien and Millodot, 1986a; Fisher, Ciuffreda and Levine, 1987; Allen and O'Leary, 2006). Failure to consider the lens effectivity of the spectacle power yields artificially inflated amplitudes of accommodation in myopes and relatively lower values in hyperopes. Though the exact mechanism underlying the differences in amplitude is not clear, McBrien and Millodot (1986a) suggested that myopes may have weak sympathetic or strong parasympathetic systems. This stronger parasympathetic system would give rise to higher amplitude of accommodation. Myopes who have high tonic accommodation tend to have lower amplitude of accommodation and so they use more of their accommodative reserve for near work (Fong, 1997).

1.7.1.2 Facility of accommodation

Facility of accommodation measures the speed of accommodative response (ability to rapidly alter accommodation) to blur (Zellers, Alpert and Rouse, 1984). Studies have shown reduced distance accommodative facility in myopes when compared to emmetropes (O'Leary and Allen, 2001; Allen and O'Leary, 2006; Pandian, Sankaridurg, Naduvilath, et al., 2006; Radhakrishnan, Allen and Charman, et al., 2007), but not for near accommodative facility. O'Leary and Allen, (2001) further suggested that the lowered (slower) distance facility could be one of the contributing factors to myopia progression as the prolonged period of blur could be a stimulus for axial elongation. Though the reason for the sluggish accommodative response among myopes is not clear, it could be due to deficit in autonomic innervations (both sympathetic and parasympathetic) (Chen, Schmid and Brown, 2003).

Allen and O'Leary, (2006), measured distance and near monocular and binocular facility and found that myopes had reduced (monocular) distance accommodative facility (15.95 $\pm$

4.91cycles/minute) compared to emmetropes (18.54 ± 5.40 cycles/minute). There was no difference in binocular distance, near monocular and near binocular facility values among myopes and emmetropes. They reported that accommodative facility (monocular distance accommodative facility) was a significant factor for myopia progression among young adults.

The authors reported an association of accommodative facility and myopia progression. However CAMS (Cambridge Anti-Myopia Study) did not report any association of accommodative facility and myopia progression. They stated that it could be due to low rate of myopia progression among the study cohort (Allen, et al., 2013).

Pandian, et al. (2006) reported reduced distance accommodative facility among myopes compared to emmetropes and hyperopes, but not for near.

While evaluating the dynamic changes in refraction during the accommodative facility test among myopes and emmetropes, Radhakrishnan, Allen and Charman, (2007) reported that subjective and objective facility measurements were lower in myopes when compared with emmetropes at distance but not at near. Velocity of disaccommodation was lower in myopes than in emmetropes at both distance and near. The lower accommodative facility shown by myopes could be due to the reliance on disparity cues (as the accommodative response is reduced, Gwiazda, et al., 1993) compared to emmetropes as individuals use a variety of monocular and binocular cues to guide their dynamic accommodative response.

Jiang and White, (1999) measured monocular accommodative facility to investigate the effect of refractive error on accommodative facility. They used ± 2.00 D flippers at a distance of 40 cm. Monocular facility rates were not significantly different for late-onset myopes (25 cycles per minute) and emmetropes (23 cycles per minute). When the data were analyzed separately for the positive (minus lens) and negative (plus lens) response time, positive response time was not significantly different, but negative response time was significantly different between myopes and emmetropes, with myopes having longer (slower) negative (plus lens) accommodation times. The authors suggested that this finding may indicate that myopes are less sensitive to hyperopic retinal defocus (blur).

Though accommodative facility and refractive error relationships were studied, still its role in myopia progression is not clear.

1.7.1.3 Accommodative (Stimulus) response

Studies have shown that accommodative responses among myopes, especially late onset and progressive myopes may be lower compared to early onset, stable myopes and emmetropes (McBrien and Millodot, 1986b; Abbott, et al. 1988; Rosenfield and Gilmartin, 1988; Gwiazda, et al., 1993; Gwiazda, et al., 1995; Jiang and White, 1999). However, Rosenfield and Gilmartin, (1987b) found no difference in accommodative response among late onset and early onset myopes and Rosenfield, et al. (2002) reported no difference between progressive and stable myopes.

McBrien and Millodot, (1986b) measured binocular accommodative response on 40 subjects and classified them into hypermetropes, emmetropes, late-onset myopes and early-onset myopes. They found that myopic subjects, especially late-onset myopes, exhibited a greater lag of accommodation at higher stimulus values compared to early-onset myopes, emmetropes and hypermetropes and at 4.00 and 5.00D accommodative demand, there was a statistical difference between late-onset myopes and non-myopes (emmetropes and hyperopes).

Gwiazda, Thorn, Bauer, et al. (1993), measured monocular accommodative response (lag) on 64 children between 5 to 7 years of age, from 4m to 0.25m. Myopes (0.78D) had lower accommodative response than emmetropic children (0.88D). The difference in accommodative response could be that myopes exhibit reduced blur sensitivity which may lead to myopes demonstrating larger lag of accommodation (or reduced accommodative response). Also the hyperopic retinal defocus resulting from this accommodation error may play a role in myopia progression (Rosenfield and Abraham-Cohen, 1999).

Abbott, Schmid and Strang, (1998) repeated the earlier study by Gwiazda, et al. (1993) on 33 subjects between 18 and 31 years of age. They found that accommodative responses of emmetropes, early-onset and late-onset myopes did not differ, but progressive myopes

(0.70D) had lower accommodative response than emmetropes (0.84D) and stable myopes (0.85 D) when accommodation was stimulated with negative lenses rather than a proximal target.

Buehren and Collins, (2006) reported that the accommodation errors are reduced when measured binocularly compared with monocular viewing conditions. This reduction could be due to the constriction of the pupil during binocular viewing, and reduced effects of spherical aberration and increased depth of focus. The authors further suggested that the increased depth of focus allowed the accommodative response to exert the minimum necessary accommodation amplitude to bring the stimulus into focus, resulting in a greater lag of accommodation. Also the role of convergent accommodation cannot be ignored when measured binocularly.

Furthermore, there seem to be differences in the pattern of refraction in the periphery of retina with myopes tending to show more hyperopia in the periphery. These differences are due to the prolate shape of the eye (Charman, 2005). Larger lags in accommodation could lead to degradation in the quality of retinal image by producing hyperopic defocus and may result in elongation of axial length of the eye and myopia. This hyperopic defocus which lies behind the prolate retina could stimulate axial growth of the eye towards the defocus (Gwiazda, et al., 1993; Gwiazda, et al., 1995; Jiang, 1997; Abbott, et al., 1998). It is not clear if lag of accommodation occurs as an accompaniment (Gwiazda, et al., 1985; 1998), prior (Goss, 1991, Portello, Rosenfield and O' Dwyer, 1997) or after (Rosenfield, Desai and Portello, 2002) the onset of myopia.

1.7.1.4 Accommodative convergence/Accommodation (AC/A) ratio

The association of near work and myopia not only involves the accommodative system, but also the vergence system. The interaction of accommodation and vergence described by accommodative vergence to accommodation ratio, (AC/A) is to be considered. It has been shown that myopes tend to have higher AC/A ratio compared to emmetropes (Rosenfield and Gilmartin, 1987b; Jones, 1990; Jiang, 1995; Gwiazda, Grice and Thorn 1998; Mutti, et al., 2000; Chen, et al. 2003; Allen, et al., 2013).

Rosenfield and Gilmartin, 1987b, assessed the response AC/A ratio on 17 early-onset, 17 late-onset myopes and 17 emmetropes. They found higher AC/A ratios among early-onset myopes (10.14 ∆ / D) than emmetropes (8.91 ∆ / D) and late-onset myopes (8.67 ∆ / D). Jiang, (1995) evaluated the response AC/A ratio on 33 emmetropes and 11 late-onset myopes, between 18 and 27 years of age. They found higher AC/A ratios among late-onset myopes and emmetropes who became myopic, compared to emmetropes who remained as emmetropes, and in progressive myopes compared to stable myopes. It was also noted that the response AC/A increased during myopia development and was suggested to be a risk factor for myopia development. Gwiazda, Grice and Thorn, (1999) found similar results in children and the reason for the elevated AC/A ratios among myopes was decreased accommodative response for near and increased accommodative convergence. Gwiazda, Thorn and Held et al., (2005) reported that elevated AC/A is present even before the onset of myopia. Allen and O'Leary, (2006) reported AC/A ratio to be a non-significant predictor for myopia progression. The reason for the variation in results could be due to the fact that Allen and O'Leary (2006) had included all accommodative functions as part of their study and possibly AC/A might be less predictive in the presence of more important accommodative functions.

1.7.1.5 Tonic accommodation

Tonic accommodation is the resting state of the accommodative system, where there is a state of equilibrium between sympathetic and parasympathetic inputs to ciliary muscle (Gilmartin and Hogan, 1985; Gilmartin, 1986). Studies have found lower dioptric levels of tonic accommodation among myopes compared to emmetropes and the variability in tonic accommodation and its adaptation (how it changes after active accommodation) reflects the differences in autonomic balance in the eye and therefore may play a role in the causation of refractive error (Maddock, et al.1981; McBrien and Millodot, 1987; Bullimore and Gilmartin, 1987a; Rosner and Rosner, 1989; Jiang, 1995; Gwiazda, et al., 1995b; Woung, et al., 1998; Zadnik, et al., 1999; Yap, et al., 2000).

McBrien and Millodot, (1987) assessed tonic accommodation on 62 subjects, between 19 and 25 years of age. They found that late-onset myopes (0.50D) had lower tonic accommodation than early-onset myopes (0.92D) and emmetropes (0.89D). Adams and McBrien, (1993), Jiang, (1995) and Yap, et al. (2000) reported that low level of tonic accommodation accompany, but do not precede the onset of myopia. Jiang, (1995) showed that late-onset myopes exhibited reduced tonic accommodation compared to emmetropes, but emmetropes who were in the process of developing myopia, displayed elevated tonic accommodation prior to the onset of myopia, which gradually lowered after the onset. So tonic accommodation values may depend on when it is measured. A high level of tonic accommodation in an emmetrope is considered to be a risk factor for the development of myopia (Ong and Ciuffreda, 1995). However Allen and O'Leary, (2006) did not find any association between tonic accommodation and myopia progression. They explained that the reason for the difference could be due to time delay between the measurement of stimulus and response in their experiment.

1.7.1.6 Near-work Induced Transient Myopia (NITM)

Near-work induced transient myopia (NITM) is operationally defined as the difference between pre and post task distance refraction, where the pre-task represents the baseline refraction and post-task represents the refraction immediately following near viewing (Ong and Ciuffreda, 1995).

Some studies (Ciuffreda and Wallis, 1998; Vera-Diaz, et al., 2002; Schmidt, et al., 2005; Vasudevan and Ciuffreda, 2008; Arunthavaraja, et al., 2010; Borsting, et al., 2010; Lin, et al., 2012) have assessed NITM under closed-loop natural viewing conditions. Figure 1.2 shows the experimental sequence of accommodative adaptation under closed-loop conditions.

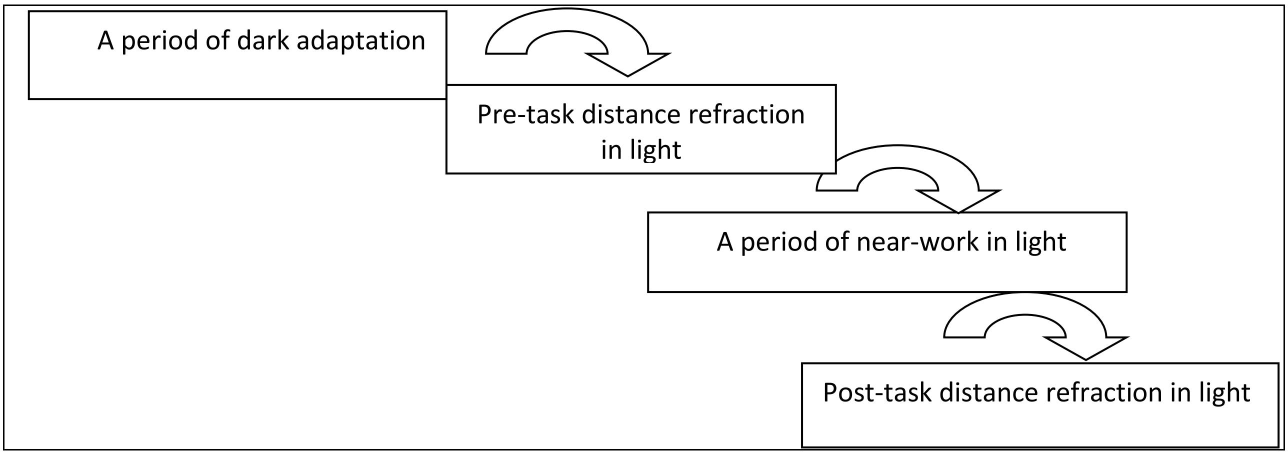


Figure 1.2 The sequence of accommodative adaptation under closed-loop conditions.

1.7.1.6.1Components of NITM

NITM is a temporary myopic shift for distance vision which normally occurs after prolonged near work (Vasudevan and Ciuffreda, 2008). Although the precise aetiology is unclear, Lancaster and Williams, (1914) suggested that it is likely to be lenticular in origin. There are two components (measures) of NITM, namely, magnitude and decay time constant. Magnitude means the maximum NITM achieved for a given task. Decay time constant or Decay is the time taken to reach the pre-task baseline refraction value.

1.7.1.6.2 NITM: Magnitude

The mean magnitude of NITM ranges from 0.12D to 1.30D with a decay period of 30 seconds or longer (Ong and Ciuffreda, 1995). Only certain individuals (whose target image is beyond their depth-of-focus) are aware of NITM with the remainder unaware of it, as the target image is still within the eye's depth of focus (± 0.55 ± 0.06D). However, certain individuals have abnormal NITM and experience symptoms of distance blur (Ciuffreda and Ordonez, 1995). Greater NITM has been found in myopes of both early-onset (<13yrs of age) and late-onset (>15yrs of age) but less so in emmetropes and hyperopes. More recent studies have found the typical NITM magnitude among myopes to range between 0.14 D–0.36 D (Ciuffreda and Wallis, 1998; Vasudevan and Ciuffreda, 2008), emmetropes to range between 0.09 D – 0.19 D (Ciuffreda and Wallis, 1998; Schmidt, et al. 2005; Lin, et al. 2012) and hyperopes to range between 0.01 D to 0.10 D (Ciuffreda and Wallis, 1998; Lin, et al. 2012). Lancaster and Williams (1914) measured NITM using retinoscopy following 45 minutes of near task. They reported a change in distance refraction (also referred as magnitude) of 1.30 D. They felt that the reason for the far point shift is that the subjects were unable to relax accommodation. As the subjects in this study were up to 60 years of age, the blur sensitivity and the difference in the accommodative characteristics (namely amplitude, response etc.) of the individuals could have affected the results.

Ciuffreda and Lee, (2002) extended the task duration to 4 hours. The distance refraction measurements were taken at the end of each hour of near task. EOM (if they received their first myopic correction before the age of 14 years) had the greatest amount of NITM followed by the LOMs (if they received their first myopic correction after the age of 14 years). Emmetropes were only moderately susceptible and the hyperopes had hyperopic shift. NITM values in this study were less than those found by Ciuffreda and Wallis, (1998), and the difference could be due to small sample size (16 subjects, 4 in each group). Further subjects were asked to do the near task at their habitual working distance and so there was no control of near accommodation demand.

1.7.1.6.3 NITM: Objective measurements

In 1987, Ehrlich, was the first to measure NITM objectively using an infrared optometer. Fifteen young adults between 18 and 30 years were given a continuous 2 hours binocular near task at 20cm. The task was to count the frequency of occurrence of a particular number in a table. They reported a post task myopic shift of 0.29D. They felt that this transient change could be due to the tonic accommodation level, i.e. subjects who had higher pre-task tonic accommodation levels had greater transient myopia (Pearson correlation r=0.64).

Owens and Kelly, (1987) measured monocular far point, accommodative stimulus/response function and tonic accommodation both prior and after a binocular near task. The task was to read text on a VDT screen or as a hardcopy at a distance of 20 cm for one hour. They reported a transient myopic shift for distance of 0.43 D.

1.7.1.6.4 NITM: Monocular VS Binocular

Monocular viewing of the near task was adopted in earlier studies (Fisher, Ciuffreda and Levine1987; Tan and O'Leary,1988) whilst later studies adopted more natural binocular viewing conditions. As reading involves accommodation and vergence, it is better to do the experiment under binocular viewing conditions. NITM experiments more recently have predominantly followed Ciuffreda and Wallis "NITM paradigm" for easy comparison. To test accommodative susceptibility between myopes (late-onset and early onset), hyperopes and emmetropes, they measured NITM parameters using an auto-refractor before and after 10 minutes of a near task at 20cm (Ciuffreda and Wallis, 1998). In their NITM paradigm, the mean spherical equivalent post-task data for each subject were divided into 10 second bins and the first ten second bin average is considered as initial NITM magnitude. They reported a mean initial NITM magnitude of 0.35 D and concluded that myopes are more susceptible to the effects of near work than hyperopes (0.01D) and emmetropes (0.09D) . They speculated that this change in accommodative susceptibility among myopes could be due to a small amount of retinal defocus that in turn causes axial elongation. When individuals look at a distant target following prolonged near work, there would be a transient increase in retinal defocus (due to transient myopia) and with time a cumulative effect may produce subsequent changes in axial length, thereby resulting in permanent myopia. Similarly decay time constant was defined as the time elapsed between the end of the closed-loop task and the point at which the closed-loop accommodative response decayed to 63.2% of the pre-task baseline. An exponential equation was used to calculate the decay time constant: $y_n = y_0 e^{-xt}$ where y_0 is the starting value, and e positive real constant.

1.7.1.6.5 NITM: Decay

Lancaster and Williams, (1914) reported decay to pre-task baseline value within 15 minutes. Ehrlich, (1987) reported that even after 1 hr, the subjects did not reach the pre-task baseline values. Ciuffreda and Wallis, (1998) reported a decay of 35 seconds in the early onset myopic group and 63 seconds in the late onset myopic groups and attributed this decay difference to reduced sympathetic activation. Emmetropes and hyperopes showed hyperopic effect (decay time not calculated). The differences in the above studies could be attributed to the methodology, where the decay was measured subjectively by asking the subjects to report the clarity of the letters in the chart whereas the latter study used objective measurements using an open-field auto-refractor which are considered to be more reliable (Sheppard and Davies, 2010).

1.7.1.6.6 NITM and cognitive demand

Rosenfield and Ciuffreda, (1994) compared measurements of the far point of accommodation obtained following 10 minutes of sustained near-work involving low (subjects were asked to read single digit numbers), moderate (subjects were required to add pairs of single digit numbers) or high (subjects were required to add a series of 4 two-digit numbers) cognitive demand . All measurements were taken using open-field infrared optometer. Though they observed significant myopic shift for all the conditions, there were no significant differences between the three cognitive levels. They thus concluded that the degree of myopic shift was related to the within-task accommodative response rather than the variations in the cognitive demand during the course of the near task. Later, Wolffsohn, Gilmartin, Thomas and Mallen (2003) also showed that there was no change in accommodation while the subjects were asked to perform summation tasks. Neither study found an effect of cognitive demand on NITM.

1.7.1.6.7 NITM: Stable versus Progressive Myopia

Vera-Diaz, et al. (2002) measured NITM during myopia progression, where a total of 41 subjects (13 progressing myopes, 14 stable myopes and 14 emmetropes) participated in the study. They defined progressing myopes as subjects whose refractive error had increased more than 0.50 D over the past two years. They reported 0.33 D of initial NITM magnitude in the progressive myopic group and 0.17 D in the stable myopic group. Progressing myopes had a greater lag (0.40D) of accommodation for a 4.00 D near task and also greater lead (0.35D) for a 0.25D at distance compared to stable myopes and emmetropes. They concluded that NITM was greater in progressive myopes than stable myopes. They also attributed the increase in NITM during myopia progression to the retinal defocus. Moreover they reported that the stable myopes and emmetropic groups decayed faster than progressive myopes.

1.7.1.6.8 Is NITM Additive (cumulative) in nature?

To investigate whether NITM is additive in nature, Vasudevan and Ciuffreda, (2008) measured NITM after 1 and 2 hours of reading in 15 EMMs, 15 EOMs and14 LOMs. Only stable myopes were considered. Subjects were made to sit in the dark for 5 min to permit dissipation of potential transient accommodative after-effects and then the distance refractive error was measured. Subjects read lecture notes during the 2-hour test period. They were instructed to maintain the text in focus at all times at a distance of 35 to 40 cm and not to gaze into the distance. Reading activity was periodically monitored, and reading distance was reassessed every 15 minutes. The distance refractive status was measured after the first 1 hour of reading. They were asked to continue reading for an hour and again distance refractive state was measured. Initial NITM magnitudes for the emmetropes after the first and second hours were 0.14 ± 0.02 D and 0.15 ± 0.02 D respectively. In the LOMs, they were 0.14 ± 0.02 D and 0.20 ± 0.03 D after the first and second hours, respectively, whereas they were 0.22 ± 0.03 D and 0.29 ± 0.03 D after the first and second hours in the EOMs. Additivity was seen in myopes and emmetropes at the end of 2 hours. However the number of subjects who showed an increase in NITM after the second hour was more in the myopic group (70%) than in the emmetropic one (47%). Also the additive effect was more in progressive myopes (PMs) but not in stable myopes after the first hour of reading. They also found that the decay duration after the second hour was significantly longer for EOMs than other groups after the first hour. The decay duration was more in progressing myopes than in stable myopes. For emmetropes, it was 20 seconds after the first hour and 50 seconds after the second hour and for LOMs it was 20 and 60 seconds after the first and second hour respectively. It was 28 seconds and 87 seconds after the first and second hour respectively for EOMs. They attributed the longer decays to baseline to impaired sympathetic function and also speculated that NITM may play a role in the aetiology of permanent myopia. 46% of myopes did not decay to the pre-task baseline even after the 120 second of the experiment period.

However, Arunthavaraja, Vasudevan and Ciuffreda, (2010) reported no additive effect after three trials of continuous near task but with a break of five minutes in between the trials. The earlier work of continuous near work without interruption resulted in an additive effect for myopes and in the later study there was no additive effect for myopes after continuous near task for one hour with a break in-between the task for 5 minutes. Details of the various NITM studies are provided in Table 1.6. A majority of these investigations demonstrated the presence of NITM under various testing conditions. Myopes showed longer decay time compared to non-myopes.

Table 1.6 Summary of Near-work Induced Transient Myopia studies

Summary of NITM studies						
Investigator Year	**N/age (yrs)**	**Apparatus**	**Near task paradigm**	**Target/instructions**	**Transient Myopia(D)**	**Decay(s/min/hr)***
Lancaster & Williams (1914)	Children to 60	Subjective measurement	At near point for 45 minutes	Small object/maintain clarity	1.30	<15 min
Ehrlich(1987)	15/18-30	Dioptron II infrared optometer	Binocular at 20cm (5D) for 2 hrs	Number table(6/9)/visual search	0.29	>1 hr
Owens & Kelly(1987)	28/17-22	Polarized vernier optometer	Binocular at 20cm (5D) for 1 hr	Text on hardcopy or VDT/reading	0.43	>20 min
Ciuffreda & Wallis (1998)	44/21-30	Infrared autorefractor	Binocular at 20cm (5D) for 10 min	Black numbers on white background	0.35	35/63s
Vera-Diaz (2002)	41/18-27	Infrared autorefractor	Monocular near task at 25cm(4D) for 10 min	High contrast black numbers on white background	0.33PM, 0.17SM, 0.28EOM, 0.21LOM, 0.16EMM	NA
Schmid(2005)	53/18-25	SRW-5000 Shin-Nippon autorefractor	6 different reading targets (3 print sizes,2 contrasts)/25cm for 3 min	Text sizes N4,N6 and N8, with two print contrasts 60% and 90%	0.37	15.12s

Vasudevan(2008)	44/21-34	Canon infrared autorefractor	Binocular for 2 hrs at 35-40 cm	Optometry lectures	EMM-0.14/0.15, LOM-0.14/0.20, EOM-0.22/0.29 after 1hr/2hr	EMM-4/12s, LOM-5/22s, EOM-8/34s after 1hr/2hr
Borsting(2010)	24/18-22	WAM-5500 open field autorefractor	Binocular for 10 min at 20cm	Story	0.19 - High discomfort, 0.41- Low Discomfort	NA
Arunthavaraja(2010)	15/18-28	Canon infrared autorefractor	Monocular near task at 12cm (8D) for 10 min	Horizontal and vertical black lines on a white background	0.32/0.29/0.31 group mean trial 1,2,3/EOM-0.28, LOM-0.35	EOM-17.02s,LOM-44.40s
Lin(2012)	386/8.4-14.2	WAM-5500 open field autorefractor	Binocular for 5 min at 20cm	Test card - black & white pictures on a grey background	0.18, 0.09 & 0.10 - MYO/EMM/HYP	50s,30s,20s – MYO/EMM/HYP
Lin(2013)	43/9-28	WAM-5500 open field autorefractor	Binocular at 20cm for 5 min	Test card -12 pairs of complex pictures	0.21,0.15 D - more myopic/less myopic	108.4s,87s - more myopic/less myopic

*s-second,min-minute,hr-hour

1.7.1.6.9 Effect of text size and contrast on NITM

To investigate the effect of text size and contrast on NITM, Schmid et al (2005) measured NITM in young adults between 18 and 25 years, They hypothesized that as the contrast level of the accommodative stimulus reduces, then accommodation drifts to its tonic level. They were classified based on the refractive errors and history as emmetropes (n=20), progressing myopes(n=18) and non-progressing myopes (n=18). Three print sizes (N4, N6, N8) and two print contrasts (90%, 60%) were used and in total there were six different targets. All the subjects were asked to read each target for 3 minutes at 25 cm. Though they found a significant effect of target size (larger target size with low contrast) on NITM, it was not clinically relevant (and not statistically significant) as the differences were small. When averaged across all six targets, the initial NITM (0.37D, 0.36D) and decay (16.06s, 14.18s) was more in stable myopes and progressive myopes respectively compared to emmetropes (0.19D and 7.10s). There was no impact of target size and contrast on the NITM magnitude and decay time. To the best of our knowledge, there has been no repeat study done to confirm this finding. Also in India, there is a practice of taking copies with varying degrees of contrasts from the original version especially at the schools and colleges – so the current study aims to investigate this further.

1.7.1.6.10 NITM and Anisometropia

In a study (Lin et al., 2013) to investigate NITM in anisometropia under binocular viewing conditions, a comprehensive eye examination was undertaken for 43 subjects with anisometropia greater than 1.00D. NITM was measured objectively using an open-field auto-refractor (Grand Seiko WAM-5500). Subjects binocularly viewed a test card with 12 different pairs of complex pictures, at a distance of 20 cm (5 D) during the 5-minute near task period. NITM magnitude and decay time were calculated for each subject. The more myopic eye exhibited increased initial NITM and decay time, when compared to the less myopic eye. Therefore NITM may play an important role in the development of inter-ocular differences in myopia. However this requires further study to confirm. Probably this suggests NITM among subjects undergoing Lasik treatment might have different accommodative response before and after refractive surgery. This thesis will investigate if this hypothesis is true.

1.7.1.6.11 Effect of Vision Therapy on NITM

To test whether training of accommodation and vergence reduces NITM and improves accommodative dynamics (Ciuffreda and Ordonez, 1995), five myopic optometry students who reported transient blur in the distance for 3 seconds or more following 15 minutes or less of near work were tested and trained. On average, they received 8 weeks of home-based optometric vision training. The subjects performed this training 5 days each week, and then returned to the laboratory every 7 to 10 days for symptom assessment. They performed accommodative lens flippers (± 2D) at 40cms and the Hart chart at distance and near, under both monocular and binocular viewing conditions for 3 minutes per procedure for a total of 18 minutes per day. They averaged a total of 12 hours of training over the 8-week period. Following training, the initial NITM magnitude did not change; it remained at approximately 0.43D. There were consistent and progressive improvements in both the Hart chart and lens flipper rates in each individual. Further studies will be required to confirm these findings in a larger population. On the other hand the training may not have any impact on NITM and there could be other components other than accommodation and vergence dynamics which need to be evaluated.

In contrast to the above, not all myopes are symptomatic following the completion of sustained near work, however, they typically exhibit increased initial NITM, with extended decay durations. Presence of either or both of these factors would result in increased retinal defocus as compared to an individual having less NITM and rapid decay. Any residual, non-decayed NITM may add to the subsequent near accommodative response, if this occurs, it would increase the risk of myopia and/or myopic progression.

Summary

Though the aetiology of NITM is unclear, it is believed to be innervational in origin and the accommodation does not relax fully to the baseline far point. The accommodative system receives dual innervations from the autonomic nervous system, primarily a parasympathetic and secondarily a sympathetic system. The parasympathetic system is responsible for accommodation, by the action of acetylcholine on muscarinic receptors and the main function of the sympathetic component is inhibition which results in decreased or negative accommodation and is mediated by the action of noradrenaline on adrenoceptors (Ong and Ciuffreda, 1995). It was suggested that due to the dysfunction of inhibitory sympathetic component, there is increased activation of accommodation (in EOMs (more axial as this occurs much early in life and LOMs (more refractive as this occurs much later in life) through the parasympathetic system which would result in an increased myopic shift (Vasudevan and Ciuffreda, 2008). Gilmartin, Mallen and Wolffsohn, (2002) have shown that only 30% of the myopic individuals had access to sympathetic innervation and if the access to sympathetic system is blocked, an increase in NITM was demonstrated. However, it is not clear whether this dysfunction of the sympathetic system is linked to myopia development. Hung and Ciuffreda, (2007) suggested that the elongation of the axial length is controlled by the change in retinal blur rather than by just the presence of retinal blur alone which gives no directional cue. Repeated cycles of NITM may lead to repeated periods of retinal-image defocus due to incomplete decay of NITM, this could result in reduced rate of proteoglycan synthesis (as mentioned above as per IRDT theory 1.4) and decrease in scleral structural integrity which could in turn result in increase in axial growth.

1.8 Optical aberrations and myopia development

An optical system provides a perfect formation of a point image if all the rays meet in a single point. However, such an ideal condition is never fulfilled in practice. Like any optical system, the eye also suffers from failure to comply with ideal image formation. These deviations from the ideal are called aberrations.

These optical aberrations play a major role in the image quality formed on the human retina. There are various aberrations which consist of lower and higher order. Ninety two percent of vision correction is achieved by correcting the lower order aberrations (Defocus and Astigmatism), whereas 8% are still uncorrected and consist of higher order aberrations like coma, trefoil and spherical aberrations (Jesson, Arulmozhivarman and Ganesan, 2004; Lawless and Hodge, 2005). There are several aberrometers available to measure aberrations by using different techniques involving Ray tracing, Tschering and Shack Hartmann. Atchison, et al. (1995) while measuring monochromatic ocular aberrations of human eyes, observed that the subjects showed a trend towards negative spherical aberration (central rays are bent more than peripheral rays) with accommodation. Hazel, et al, (2003) have also observed that there was an increase in negative spherical aberration with increase in accommodative stimulus.

Beck, (2010) studied the effect of reading on peripheral aberrations among myopes and emmetropes before and after one hour of continuous reading. The spherical aberration, vertical coma, horizontal coma, vertical trefoil and horizontal trefoil (30^0) were found to be different among myopes compared to emmetropes. Though these differences were found between myopes and emmetropes, they felt that these differences may not play a role in myopia development as the differences were small. Buehren, Collins and Carney, (2003) investigated the effect of eyelid pressure on corneal shape and aberrations after reading. They found that there was an effect of eyelid pressure and due to which there was a change in vertical coma and trefoil along 30^0.

Paquin, et al. (2002) showed that aberrations increase with the degree of myopia, especially coma and spherical aberration. Studies have shown increased corneal aberrations after prolonged near work (Buehren, Collins and Carney, 2003; 2005). While the above studies show differences in aberrations among myopes and non-myopes, few other studies (Cheng, et al., 2003; Llorente, et al., 2004) did not reveal any differences in aberrations among myopes and non-myopes.

1.9 Axial length and myopia development

While trying to understand the influence of accommodation on ocular structures, Shum, et al. (1993) have shown that the axial length increases along with changes in anterior chamber depth during accommodation (due to changes in lens thickness). Mallen, et al. (2006) reported that the axial length increases in emmetropic (0.03 mm) and myopic (0.05 mm) subjects during short periods of accommodative stimulation. Transient increases in axial length were observed in myopes more than in emmetropic subjects. Bayramlar, et al. (1999) while measuring axial length without cycloplegia, observed an increase of 0.17 mm and with cycloplegia an increase of 0.18 mm. Since there was an increase in axial length during near fixation both with and without cycloplegia, the authors attributed the increase in myopia to accommodative convergence rather than accommodation itself. The authors hypothesized that much use of convergence during reading could result in elongation of the vitreous chamber causing myopia.

1.10 Lasik and NITM

The number of people undergoing refractive surgery is increasing worldwide (Kerry, et al., 2009) and Laser in situ keratomileusis (LASIK) is considered to be a safe procedure for the correction of myopia (Doyle, et al., 1999). Although the procedure is considered to be safe, there are sporadic reports of binocular vision impairment like intermittent esotropia, increase in AC/A ratio, diplopia and decrease in fusion and stereopsis (Godts,Tassignon and Gobin, 2004).

Prakash, et al. (2007) have reported a change in AC/A ratio following LASIK surgery. They stated that the increased AC/A ratio could be due to the improvement in the accommodative effort of the emmetropic state. Wang, et al. (2012) reported an increase in lens thickness and decrease in anterior chamber depth following LASIK surgery. They concluded this was due to the residual accommodation. To the best of our knowledge there is no literature on NITM among myopes following LASIK surgery. We do not know whether

LASIK corrected myopes will respond to the accommodative stimulus like an emmetrope or show similar NITM magnitude as a myope pre-surgery. This is important for us to understand as the difference in NITM magnitude may be manipulated by the physical changes like corneal curvature, thickness etc. post-operatively. This would lead to an original contribution to knowledge regarding the origins of NITM.

1.11 Rationale for proposed research

Studies showing NITM to be greater in myopes compared to emmetropes and hyperopes were in populations where the prevalence of myopia is high. However there is no literature on NITM characteristics in populations where the prevalence of myopia is low. The prevalence of myopia in India among school children in early studies was found to be 4.1 % - 7.4 % (Jain and Mohan, 1983; Dandona and Srinivas et al, 2002; Dandona, Srinivas, Sahare et al, 2002; Murthy, Gupta et al, 2002), whereas recent studies show a prevalence of 14% (Das, Dutta, Bhadur et al, 2007; Basu, Das et al, 2011). Though the prevalence of myopia is not as high as found in other Asian countries, it warrants a study to investigate the factors that might be causing an increasing trend. The prevalence of myopia among private school children has been found to be 17% (Saxena, et al., 2015), and in addition, with more urbanization and as the demand for near work is increasing, understanding NITM characteristics and its association with near work becomes especially important as accommodative parameters such as amplitude of accommodation was found to vary among the Indian population compared to other populations (Chattopadhyay, 1984). As mentioned, there is a practice of taking copies at the schools and colleges and the effect of these has not been evaluated.

Therefore this study aims to understand NITM characteristics among myopes and non-myopes in Indian cohorts.

This study was also carried out to understand the NITM characteristics before and after LASIK among myopes.

1.12 Objectives of proposed research

Objectives:

1. To investigate the effect of target size and contrast on NITM magnitude and decay time. I hypothesise that the decreased text size and decreased contrast would induce a greater NITM magnitude and decay.
2. To quantify accommodative parameters associated with NITM.
3. To quantify the concurrent changes in optical and biometric parameters during NITM. I hypothesise that there would be an increase in negative spherical aberration and an increase in axial length with increase in lens thickness following reading.
4. To quantify the NITM measurements pre and post Lasik procedure. I hypothesise that there would be a greater NITM magnitude and decay prior to the Lasik surgery but not following the surgery as there is a change in refractive state (myopia to emmetropia).

This thesis will address the following questions:

- Does the NITM magnitude and decay differ between different refractive groups in an Indian cohort?
- Is NITM influenced by different target sizes and contrasts?
- Do the pre and post task aberration parameters vary and do they correlate with the induced NITM (if any)?
- Do the pre and post task biometric parameters vary and do they correlate with the induced NITM (if any)?
- Does the NITM magnitude and decay differ following Lasik procedure?
- Is there an association between NITM and vergence/ accommodation parameters?

Chapter Two

Methodology

2.1 Procedures

To test the hypotheses in Chapter 1, accommodative responses were measured (monocularly) under various conditions during sustained binocular viewing in a group of myopic and emmetropic subjects between 12 - 35 years of age.

The following procedures were conducted:

1. A comprehensive eye examination which included detailed history, visual acuity, slit lamp examination, intra-ocular pressure and fundus examination was performed for all the subjects.
2. In addition, binocular vision parameters which included near point of convergence, near point of accommodation, negative relative accommodation, positive relative accommodation, accommodative facility were measured (for studies 1 (5 minutes near task),3 (aberration measurements),4 (biometry measurements) and 5 (pre and post LASIK)).
3. NITM was measured using the methods of Ciuffreda and Wallis (1998), using the Grand Seiko WAM 5500 open-view auto-refractor (Ajinomoto Trading Inc., Tokyo, Japan) before and after a near-vision task and the NITM magnitude and timescale for decay of NITM calculated (for studies 1 (5 minutes near task), 2 (60 minutes near task) and 5 (pre and post LASIK)).
4. Optical parameters (wavefront aberrations and pupil diameter) were assessed using the COAS-HD wavefront analyzer (Wavefront sciences, Albuquerque, New Mexico, USA) before and after the near vision task (for study 3).
5. Biometric parameters (corneal curvature, anterior chamber depth, axial length) were assessed using the Wave-light Allegro Biograph before and after the near vision task (for study 4).

Details of the procedure

2.1.1 Comprehensive Eye Examination – Visit 1

A detailed history was taken to enquire about any previous medical and surgical intervention. General health, including allergy to any medications was noted.

CLINICAL REFRACTION:

RETINOSCOPY: Static retinoscopy was performed at 0.66m by asking the subjects to view a 6/60 target with a working distance lens of +1.50D. The examiner's right eye for subject's right eye and left eye for the left eye was used.

SUBJECTIVE REFRACTION: With the gross retinoscopy value, removal of the fogging lens was performed in 0.25 steps. The Jackson cross cylinder was used to refine the cylindrical axis first and then the power. A duo-chrome test was performed to refine the final sphere in refraction. Binocular balancing was done in +0.25 D steps until 6/6 letters were blurred but 6/9 letters were easily resolved. By alternately occluding each eye, subjects were asked to compare alternate views of the 6/9 line of letters. A lens of +0.25 D was added to clear the target until both were equally blurred. Binocularly plus was reduced until the 6/6 line became readable (Benjamin, 2006).

Following subjective acceptance, a pupillary evaluation (dim room illumination), and slit lamp examination, including an IOP measure using an applanation tonometer (Goldmann), were performed. All the subjects were dilated using 1 drop of 1% cyclopentolate applied twice at 5 minutes interval (Negrel, et al., 2000). Objective refraction using an open-field auto-refractor (WAM-5500) was performed after 30 minutes.

2.1.2 Visit – 2: Orthoptic Evaluation

STEREOPSIS

Stereopsis was assessed using a Randot Stereo test. Polaroid glass was worn over the habitual correction. The subjects were asked to identify the six figures in the eight rectangular targets at 40 cm. Following this they were asked to identify the smallest set of targets that appeared closest. Subjects who appreciated stereopsis on the first target were instructed to go to the next one and repeated until they gave two consecutive incorrect answers.

OCULAR MOTILITY

The purpose was to assess the subject's ability to perform conjugate eye movements in all nine cardinal positions. Subjects were instructed to follow the target (pen torch) at 40 cm without moving his/her head. During eye movements, smoothness, accuracy and extent of movements were noted.

COVER TEST

The purpose was to assess the presence and magnitude of a phoria or a tropia. The test was done for both distance and near with the habitual correction.

COVER-UNCOVER TEST

The purpose was to differentiate a phoria from a tropia. One eye was covered and any movement of the uncovered eye was observed for the presence of a tropia. If there was no movement, the cover was removed and the movements in the just covered eye were noted for the presence of a phoria.

ALTERNATE COVER TEST

The purpose was to measure the total deviation, where the cover was placed alternately in front of each eye several times to dissociate the eyes and to maximize the deviation. Prisms were used to neutralize the deviation accordingly. The amount of the prism power used was taken as the measure of the deviation.

NEAR POINT OF CONVERGENCE (NPC):

The purpose was to determine the subject's ability to converge the eyes while maintaining fusion. With the subject's habitual correction, the accommodative target (6/9 reduced Snellen linear target) was moved towards the subject who was asked to report when the target appears double (subjective) or until the examiner observed one eye losing fixation (objective). The distance was noted and taken as the break point. The target was moved away from the subject's eyes and the distance at which the subject regains fusion and reports the target as single was noted as the recovery point. A NPC of 6-8 cm was considered as normal (Scheiman and Wick, 2008).

NEAR POINT OF ACCOMMODATION (PUSH-UP METHOD):

The purpose was to measure the amplitude of accommodation in dioptres. The test was done both monocularly and binocularly with the habitual correction in place. The subject was directed to a row of letters one line larger than their near visual acuity. The subject was instructed to keep the letters clear. The chart was moved slowly towards the subject who was asked to report the first sustained blur. That distance was measured from the subject's spectacle plane in cm. This linear measurement was referred as the near point of accommodation. This value was converted into dioptres and represented as the subject's amplitude of accommodation (AA).

NEGATIVE RELATIVE ACCOMMODATION (NRA) AND POSITIVE RELATIVE ACCOMMODATION (PRA)

The purpose was to determine the range of accommodation with the fixation distance constant. The near vision target was held at 40 cm in front of the subject. While wearing their habitual correction he/she was asked to fixate the N6 target. Plus lenses were slowly added binocularly in 0.25 dioptres steps until the subject reported the first sustained blur. This was taken as the negative relative accommodation. The same procedure was repeated with negative lenses and noted as the positive relative accommodation (Scheiman and Wick, 2008).

NEGATIVE FUSIONAL VERGENCE AND POSITIVE FUSIONAL VERGENCE (NFV/PFV)

The purpose was to measure fusional vergence by the step vergence method. A vertical line target was shown at a distance of 6m. A prism bar was placed in front of one eye, base in first, subjects were asked to report when the target was blur/double/single, which represented blur/break and recovery respectively. The same was repeated for near and values were recorded in prism dioptres.

ACCOMMODATIVE FACILITY

The purpose was to measure the subject's ability to make rapid and accurate accommodative changes under monocular and binocular conditions using ± 2.00 D accommodative flippers. The subjects were asked to hold the near vision card at 0.4m and were asked to fixate a N6 target. They were instructed to hold the flipper close to the eye (plus lens first) and flip the lens upon clearing the target. The numbers of flips made in 1 minute were noted. A full cycle consisted of clearing both plus and minus lens (es). Any difficulties clearing the plus and minus lenses were noted. If AF was less than 10 cycles/minute, the subject was likely to be symptomatic (Zellers, Alpert and Rouse, 1984).

VERGENCE FACILITY

The purpose was to test the ability of the subject's fusional vergence to respond to rapid changes in disparity over time. The test was done with the subject's habitual correction in place. The near target was held at 0.4m. A 12 BO/ 3 BI standard vergence flipper was used for all subjects. The subject was instructed to hold the vergence flipper close to the eyes (base in prism was introduced first) and was flipped when the print became single and clear. The numbers of flips made per minute were noted. A full cycle consisted of both base-in and base-out prisms. A VF of 7 to 10 cycles/minute range was considered as normal (Gall and Wick, 2003).

ACCOMMODATIVE CONVERGENCE/ACCOMMODATION RATIO (AC/A RATIO)

To calculate the response AC/A ratio the subject was positioned on the WAM-5500 with the contact lenses worn throughout the procedure. A Maddox rod was placed horizontally in front of left eye and the subject was asked to look at a modified Thorington card placed at 4m. The subject was instructed to report the distance of the red line from the centre. When the subject reports the position of the red line, simultaneously the joystick of the WAM-5500 was pressed to record the accommodative response. Similarly, a MIM card was placed at 0.4m and the accommodative response was recorded while simultaneously measuring the near phoria. Response AC/A ratio was calculated by the following equation (Figure 2.1) adapted from Gwiazda, et al. (2005).

Figure 2.1 Response AC/A calculation

Response AC/A ratio= [(IPDXNAS)-(FP - NP)]/NAR-FAR

Where:

IPD=interpupillary distance in centimetres

NAS =near accommodative stimulus in dioptres

FP = far phoria in prism dioptres

NP = near phoria in prism dioptres

NAR = near accommodative response in dioptres

FAR = far accommodative response in dioptres

Study protocol

2.2 Study subjects

Subjects were recruited from the Elite School of Optometry, Chennai, India for studies 1 to 4 and subjects for study 5 were recruited from patients presenting at the Sankara Nethralaya tertiary eye hospital, Chennai, India. All the subjects gave written informed consent for taking part in the study, which followed the tenets of the Declaration of Helsinki. This study was approved by the institutional review board (Vision Research Foundation, Chennai, India) and ethics committee, in 2011. Figure 2.2 shows the schematic representation of the study procedures. Figure 2.3 shows the flow chart of the study protocol.

Figure 2.2: Study Procedures

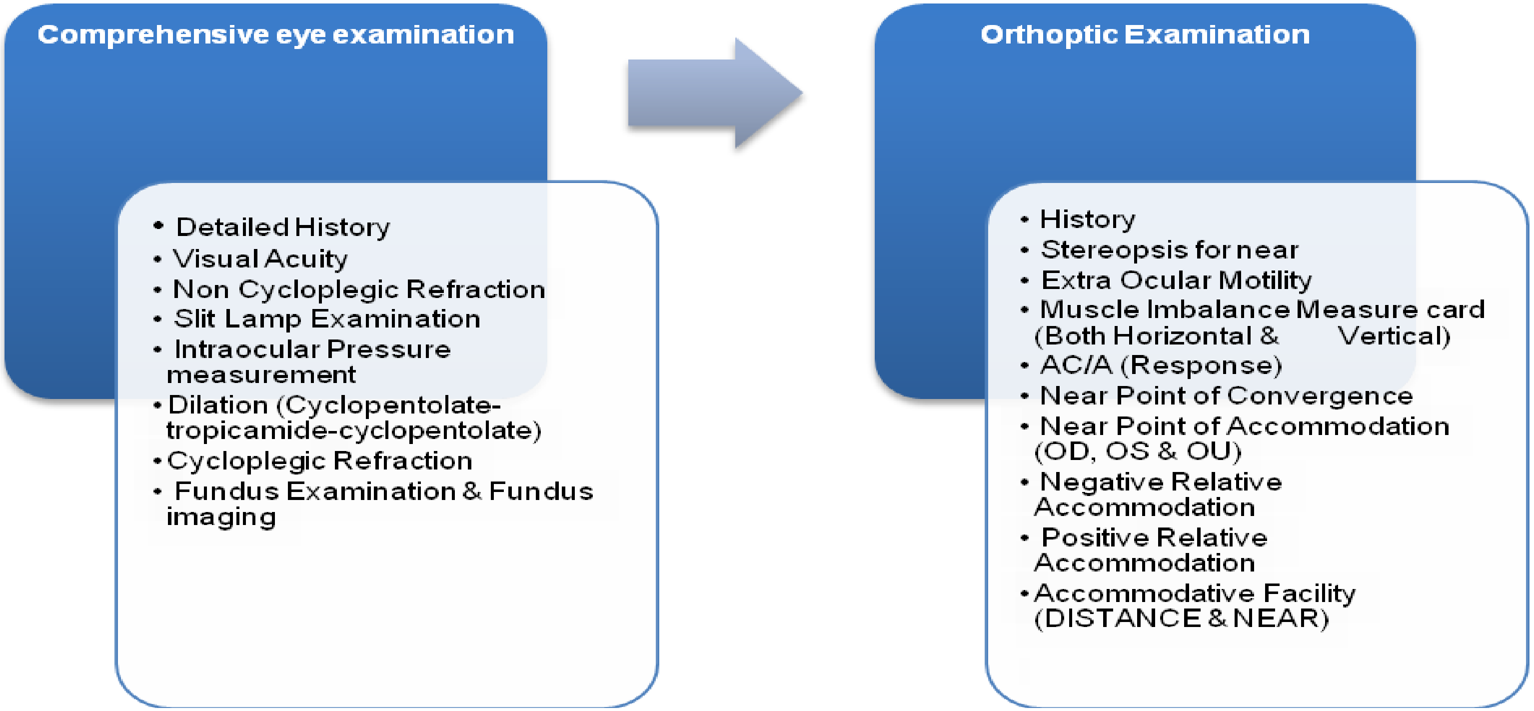
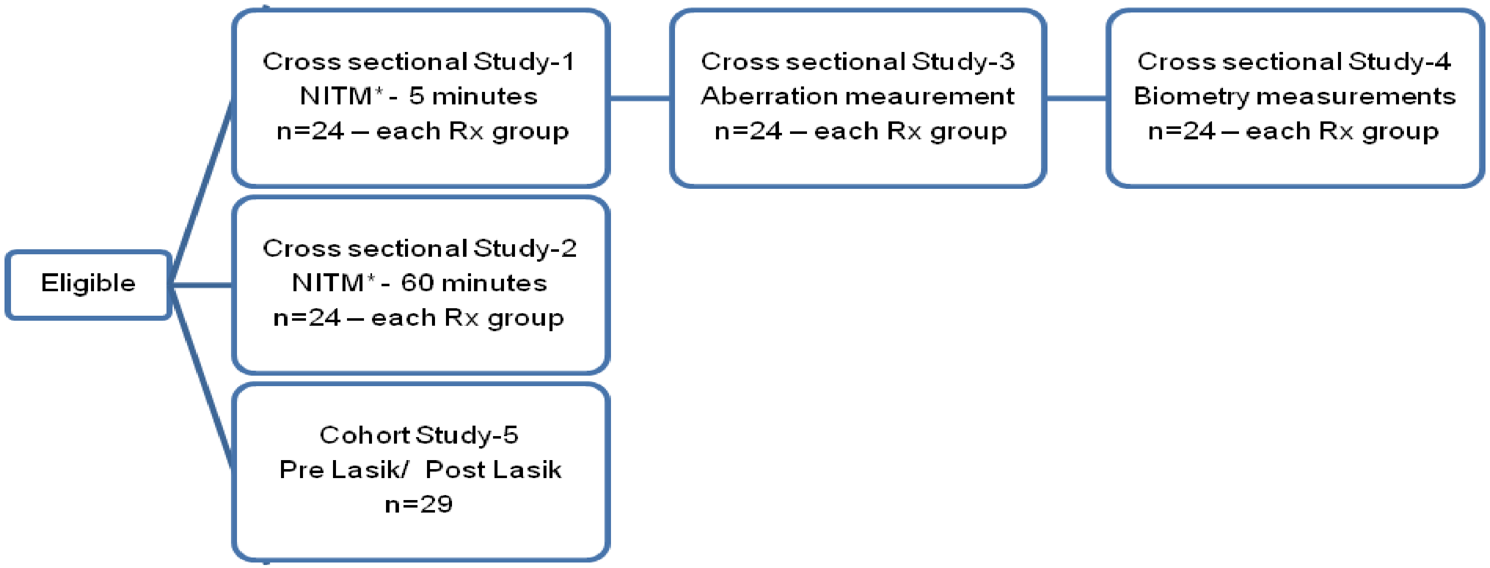


Figure 1.3 Schematic presentation of study protocol

(*NITM - Near Induced Transient Myopia)



2.2.1 Inclusion criteria

- Age 12-35 (for studies 1 – 4)
- Age 21-35 (for study 5)
- Myopia (spherical equivalent refractive error <-0.50D) (for study 1-5) or emmetropic (±0.50D)
- Astigmatism ≤1.00DC
- Best corrected visual acuity at least 6/9 in each eye
- Willing and able to give consent for the study procedures

2.2.2 Exclusion criteria

- Manifest squint
- Amblyopia (defined as reduction in the quality of central, corrected vision resulting from a disturbance in retinal image formation during the first decade of human life (Friendly, 1987)
- Diabetes
- Any significant ocular pathology (e.g. glaucoma, retinal detachment)
- Taking systemic medications known to affect accommodation (anticholinergic drugs e.g. Dicyclomine (Bentyl)
- <2D of Hofstetter minimum expected amplitude

2.2.3 Sample size

A power calculation based on the results of Schmidt et al. (2005) gave an effect size for NITM of 1.1D among refractive error groups. This gives a group size of 18 for α = 0.05 and power of 90%. The following equation was used: $n = (Z_{\alpha/2}+Z_{\beta})^{2} * 2 * \sigma^{2} / d^{2}$, where $Z_{\alpha/2}$ is the critical value of the Normal distribution at α/2, Z_{β} is the critical value of the Normal distribution at β, σ^{2} is the population variance and d is the difference to detect.

2.2.4 Overview of the procedures:

Elite School of Optometry students were recruited for studies 1, 3 and 4 after informed consent. A separate cohort was recruited from subjects presenting at LASIK clinic (Sankara Nethralaya tertiary eye hospital) for study 5.Twenty-four emmetropes and twenty-four myopes participated in studies 1, 2, 3 and 4. The same subjects participated in studies 1, 3 and 5, a separate cohort of 24 emmetropes and 24 myopes were enrolled in study 2. 29 myopes participated in study 5. Demographic details are included in each study chapter.

2.2.5 Instrumentation and study setup

All the myopic subjects had their refractive error corrected using Pure-Vision (Bausch and Lomb) disposable silicone hydrogel contact lenses. Over refraction was performed to ensure that the contact lens correction was optimal (+/- 0.25 D) and where necessary the contact lenses were changed. All the lenses were centred properly in all positions of gaze and the visual acuity was assessed. The contact lenses were worn throughout the study.

An infrared open-field auto refractor (Grand Seiko WAM-5500, Tokyo, Japan) (Figure 2.4) was used to measure the accommodative response. Once the subject’s pupil was centrally aligned, aided by the visual display screen, an infra-red ring image was focused on the retina. The size and shape of the ring target was digitally analyzed in multiple meridians to calculate the sphero-cylindrical refractive error. In the dynamic mode, continuous measurements of the refractive state were obtained, five times per second (5 Hz). Hi-speed mode allowed more dynamic measurement of the refractive status of the eye and the software recorded the results, including time (in seconds), pupil size and mean spherical equivalent. The output is generated in Microsoft Excel (Comma Separated Values (csv) file) (Sheppard and Davies, 2010).

The spherical dioptric range of the Grand Seiko is ± 22 D and ± 10 D of cylindrical refractive error, which can be measured in increments of 0.01 D, with an axis resolution of one degree (Sheppard and Davies, 2010). The auto refractor has a noise level of 0.005 ±

0.0005D in the dynamic mode (Sheppard and Davies, 2010), and the post task accommodation measurements above this value were considered for analysis. To achieve consistency in the above mentioned readings, the instrument was calibrated regularly.

Figure 2.4 Refraction measurements before and immediately after reading tasks were measured through the open-field auto-refractor while viewing a 3m logMAR chart.

This instrument has been shown to produce valid and reliable measurements of refraction (Sheppard and Davies, 2010).

A COAS (Complete Ophthalmic Analysis System, WaveFront Science, Inc., Albuquerque, NM), based on the Shack-Hartmann principle, was used to measure the higher-order aberrations from the light reflected off the retina. By analyzing the position of each of the dots captured by a camera, the wavefront shapes affected by both lower order (refractive error) and higher-order aberrations were measured. Salmon and Van de pol, (2005) measured the lower-order and higher-order aberrations on 28 pilots and reported that the accuracy, repeatability and instrument myopia (-0.2 D) were similar to conventional auto-refractors for lower-order aberrations and for higher-order aberrations (0.03 μm for third order aberrations and fourth order 0.02 μm for fourth order aberrations). The instrument was found to be more reliable especially for the third and fourth order aberrations, namely coma and spherical aberration respectively.

The Allegro Biograph (Wave-light AG, Erlangen, Germany) was used to take biometry measurements. This system works on partial coherence interferometry, where a dual beam of infrared light is reflected at the corneal surface and the retinal pigment epithelium (RPE). The interference signal received can be precisely measured, allowing the optical length between corneal surface and retina to be determined. Buckhurst, et al., (2009) evaluated the validity and repeatability of a Biograph on 112 subjects, and reported that corneal curvature, anterior chamber depth measurements were comparable to an IOL master and overall the biometric measurements were found to be repeatable (Corneal curvature (-0.04±0.2D), anterior chamber depth (0.1±0.4mm), crystalline lens thickness (0.16± 0.83mm), axial length (0.01±0.02mm)).

2.2.6 NITM assessment for studies 1, 2 and 5

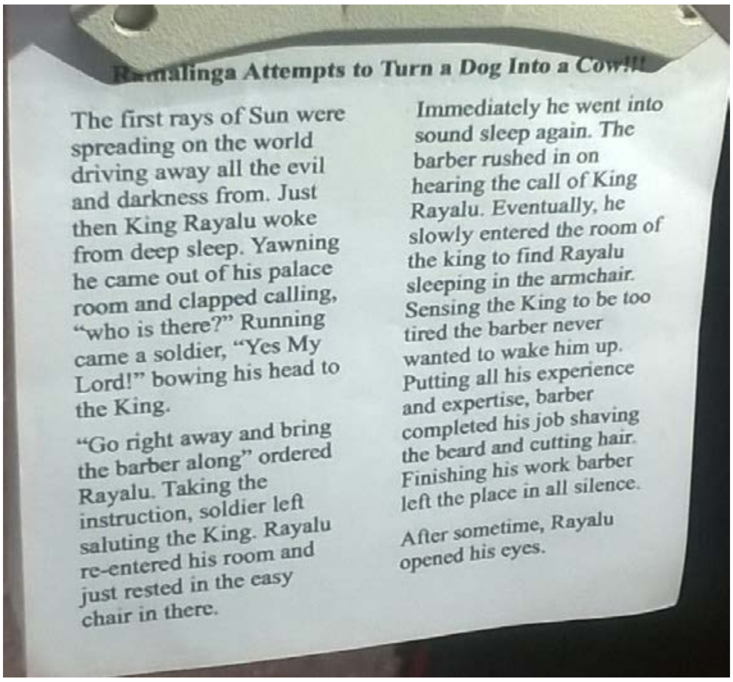
Pre-task

To dissipate any pre-existing transient accommodative effects (Ong and Ciuffreda, 1995) subjects sat in a completely darkened room for 5 minutes. Subjects were asked to look towards a distant target and refraction readings were recorded for 1 minute for the right eye and averaged. Following this period of dark adaptation, subjects were then asked to look binocularly at a +0.2 logMAR letter on an externally lit 3m logMAR chart under subdued room illumination (approx. 21.53 lux). The chart illuminance was 485 lux. The baseline distance refraction was measured continuously for 60 seconds for the right eye only. The mean spherical equivalent was calculated and used as the pre-task distance refractive state. The tonic accommodation value was taken as the difference between the average of the far refraction readings in the dark and the pre-task distance baseline reading.

2.2.6.1 Study 1: 5 minutes reading task

The pre-task assessment was followed by a 5-minute near task performed binocularly. The near targets comprised text from a collection of Tennalirama stories. Tennalirama was a 16th century Indian poet who wrote witty tales for the king's court. The text targets were viewed along the midline at a distance of 0.2m (5D). There were four text targets in total (Figure 2.5). Two targets were N8 of 50% contrast (N8-50) and 90% contrast (N8-90), and the other two were N12 at 50% contrast (N12-50) and 90% contrast (N12-90) respectively. Corel draw was used to achieve accurate contrast levels of the targets. The four targets were presented in a randomized order using a random number generator, with a 5 minute interval in complete darkness between each presentation. The subjects were periodically reminded to keep the target in focus throughout the reading task.

Figure 2.5–Example of near target used for 5 minutes of reading



Ramalinga Attempts to Turn a Dog Into a Cow!!!

The first rays of Sun were spreading on the world driving away all the evil and darkness from. Just then King Rayalu woke from deep sleep. Yawning he came out of his palace room and clapped calling, "who is there?" Running came a soldier, "Yes My Lord!" bowing his head to the King.

"Go right away and bring the barber along" ordered Rayalu. Taking the instruction, soldier left saluting the King. Rayalu re-entered his room and just rested in the easy chair in there.

Immediately he went into sound sleep again. The barber rushed in on hearing the call of King Rayalu. Eventually, he slowly entered the room of the king to find Rayalu sleeping in the armchair. Sensing the King to be too tired the barber never wanted to wake him up. Putting all his experience and expertise, barber completed his job shaving the beard and cutting hair. Finishing his work barber left the place in all silence.

After sometime, Rayalu opened his eyes.

2.2.6.2 Study 2: 60 minutes reading task

The pre-task assessment was followed by a 1-hour near task (without any break) performed binocularly at 0.2m. The near targets comprised text from optometry lectures, similar to the N12-90 target used in study 1. The subjects were again periodically reminded to keep the target in focus throughout the task.

Post-task

Immediately after reading, the subject's distance refractive state was measured continuously for 120 seconds. Continuous refractive data for each subject were divided into 10-second bins. The average difference between the pre-task and post-task distance refractive state in the first 10 second bin represented the initial NITM dioptric magnitude. Data were analyzed with respect to initial NITM magnitude and decay time constant.

2.2.6.3 Study 3: Effect of near task reading on ocular aberrations

Protocol:

All subjects were asked to look towards the distant target to dissipate any residual accommodation for 5 minutes in dark.

Pre-task: Following this, subjects were asked to place the chin in the chin rest of COAS (see Figure 2.6), and forehead against the headrest and were instructed to look at the fixation target located inside the instrument, that is optically projected to infinity. The instrument myopia has been reported to be -0.03 D (Salmon and Van de pol, 2006).

An average of 3 measurements was taken for the right eye. A rescaled 5 mm pupil diameter was considered for analysis as the noise level of the instrument would increase with a larger pupil diameter and decreases with small pupils (Salmon and Van de pol, 2005).The baseline measurements were carried out under subdued illumination. The root mean square and spherical aberration were the parameters of interest (see chapter - 5).

Figure 2.6 Aberrations measurements before and after the reading task were measured using the COAS Wavefront Analyzer.

Task: After the pre-task measurements were taken, the subjects were asked to read N12 target (Tennalirama story) with 90% contrast for 5 minutes at 20cms.

Post task: Immediately after the conclusion of the 5 minutes of reading task, the lights were extinguished and subjects were asked to place the chin back on the chinrest of the COAS and aberration measurements were taken again.

2.2.6.4 Study 4: Effect of near task reading on biometry parameters

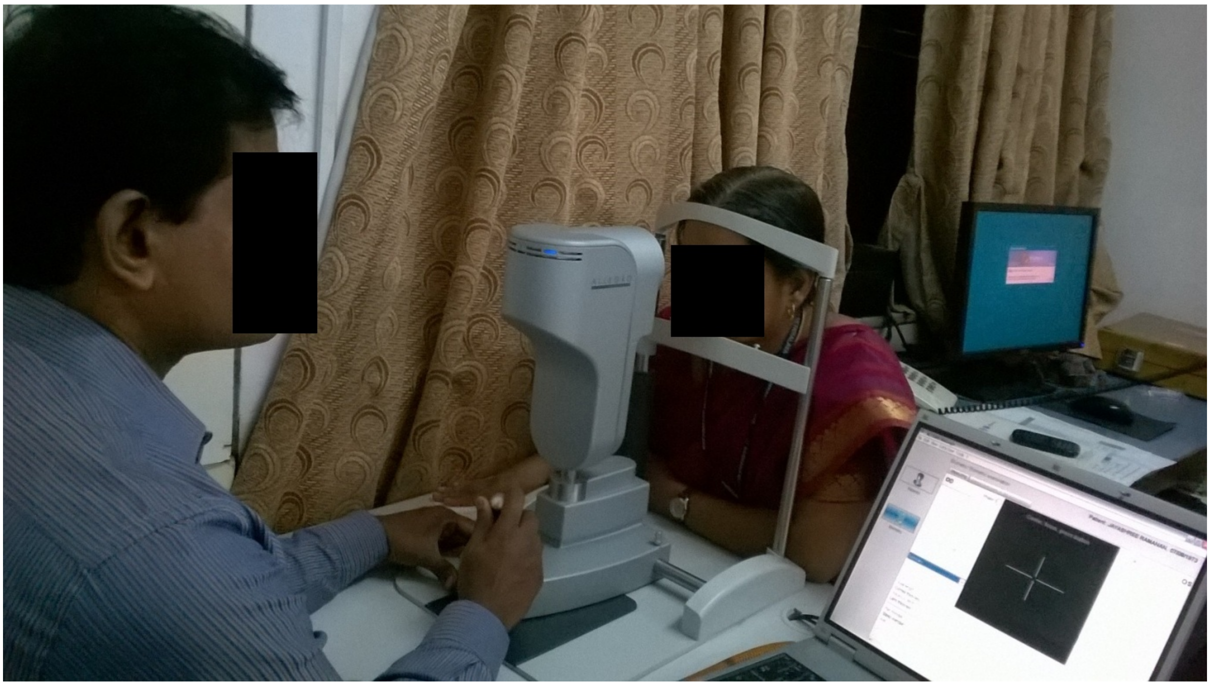
Protocol:

All subjects were asked to look at a far 6/9 Snellen optotype in the dark to dissipate any residual accommodation for 5 minutes.

Pre-task: Following this, subjects were asked to place their chin in the chin rest of the Biograph (see Figure 2.7), and aligned in such a way that the following measurements were taken through the centre of the pupil.

Baseline measurements of axial length, anterior chamber depth, corneal thickness and lens thickness were captured on the right eye only, but all measurements were performed in a natural binocular state. Three measurements of each parameter were taken for the right eye and the average of these measurements were considered for analysis.

Figure 2.7 Biometry measurements before and after reading task were measured using Allegro Biograph.



Task: The subjects read N12 target (Tennalirama story) with 90% contrast for 5 minutes at 20cms.

Post task: Immediately after the conclusion of the near task, all of the above biometry measurements were repeated.

2.2.6.5 Study 5: NITM parameters in LASIK subjects

Protocol: The above NITM paradigm used in study 1 (5 minutes - near task) was followed.

In this study, myopic subjects were recruited from the Sankara Nethralaya tertiary eye hospital, Chennai. They viewed a N12 target with 90% contrast for 5 minutes with pre- and post- refractive state measurements assessed objectively as mentioned above with the

Grand Seiko WAM-5500 open-field auto refractor. Additionally, the NITM measurements were repeated one month after refractive surgery. NITM was defined as the post-task distance refraction minus the pre-task distance refraction. A binocular vision assessment (section 2.1.2) was carried out pre and post one month of refractive surgery.

2.3 Statistical methods

Immediately after completion of each period of reading, the subject's distance refractive state was re-measured continuously for 120 seconds. The data (mean spherical equivalent) for each subject were divided into 10 second bin intervals and averaged. Mean values for the pre-task 60 seconds and the post task 120 seconds were calculated. The initial NITM magnitude was calculated as the difference between the first ten second bins (averaged over the duration of the interval with outlier data points of more than 2 SD removed) and the pre task baseline refraction as described above. Decay time was the time taken from the initial magnitude to dissipate to the baseline distance refraction value. Decay time constants were calculated for the post task accommodative response with an exponential fit (Ciuffreda and Wallis, 1998). Initial NITM magnitude and decay times were calculated for each subject and were averaged for each target presentation. Statistical analyses were performed using SPSS version 15.

2.3.1 Study-1.

Comparisons were made between emmetropes and myopes using repeated measures ANOVA to calculate the effect of target size and contrast on NITM initial magnitude and decay.

2.3.2 Study-2.

Independent t-tests were performed in order to compare the initial magnitude and decay duration between emmetropes and myopes. Normality was tested using a Shapiro-Wilk test and independent-samples t-tests were conducted for the data if normally distributed and Mann-Whitney U test if not normally distributed.

2.3.3 Study-3.

Repeated measures MANOVA was used to examine the change in spherical aberration (Z_4^0) and Higher order root mean square (HORMS), pre and post 5 minutes of near task.

2.3.4 Study-4.

Repeated measures MANOVA was used to compare the biometry measurements pre and post reading task axial length, anterior chamber depth, lens thickness and corneal thickness were the parameters of interest.

2.3.5 Study-5.

Paired t-tests were used to compare the NITM magnitude and a range of binocular vision parameters in pre and post LASIK subjects.

Chapter Three

Results of study 1: 5 minute reading task under different font size and contrast conditions

3.1 Introduction

Near work induced transient myopia (NITM) refers to the myopic shift in distance refractive error immediately after a prolonged near vision task (Ong and Ciuffreda, 1995). Evidence has shown that NITM magnitude and decay vary in different locations among myopes (especially progressive myopes) compared to non-myopes (Ong and Ciuffreda, 1995; Ciuffreda and Wallis, 1998; Vera-Diaz, 2002; Schmidt, et al., 2005; Vasudevan and Ciuffreda, 2008; Arunthavaraja, Vasudevan and Ciuffreda, 2010; Borsting, et al., 2010; Lin, et al., 2012, Liang, et al., 2013). There is no literature on NITM in an Indian population. So this experiment aims to understand the NITM characteristics among myopes and non-myopes in an Indian cohort.

Few studies (Fledelius, 1981; Maddock, et al. 1981; McBrien and Millodot, 1986a; Lekha, et al., 2005; Maheshwari, et al., 2011) have reported that myopes have relatively high amplitudes of accommodation. Some others (Zhai and Guan 1988; Fong, 1997; Allen and O'Leary, 2006) have reported that myopes have relatively low amplitudes of accommodation. Other studies have shown no difference in amplitude of accommodation among refractive groups (Gawron, 1980; Fisher, Ciuffreda and Levine, 1987; Mantyjarvi, 1987). Emmetropic children who became myopic were found to be more esophoric at near with elevated AC/A ratio compared to those who remained emmetropic (Jiang, 1995). Myopes tend to have higher AC/A ratio compared to emmetropes (Rosenfield and Gilmartin, 1987b; Jones, 1990; Jiang, 1995; Gwiazda, Grice and Thorn 1998; Mutti, et al., 2000; Chen, et al. 2003; Allen, et al., 2013). Studies have shown reduced distance accommodative facility in myopes when compared to emmetropes (O'Leary and Allen, 2001; Allen and O' Leary, 2006; Pandian, Sankaridurg, Naduvilath, et al., 2006; Radhakrishnan, Allen and Charman, et al., 2007; Allen, et al., 2013), but not for near accommodative facility. Studies have found lower dioptric levels of tonic accommodation among myopes compared to emmetropes (Maddock, et al.1981; McBrien and Millodot, 1987; Bullimore and Gilmartin, 1987a; Rosner and Rosner, 1989; Jiang, 1995; Gwiazda, et al., 1995b; Woung, et al., 1998; Zadnik, et al., 1999; Yap, et al., 2000).

3.2 Methods

All subjects underwent a detailed ocular examination including objective and subjective examination, slit lamp examination and fundus examination. Also binocular vision parameters which included near point of convergence, amplitude of accommodation, tonic accommodation, response AC/A ratio and accommodative facility for distance and near.

The subjects sat in the dark for 5 minutes to dissipate any pre-existing transient accommodative effects (Ong and Ciuffreda, 1995). Following this, they were asked to look at a 3m logMAR chart and far refraction readings were recorded under subdued illumination for 1 minute for the right eye and averaged. Four different targets (see Table 3.2) were presented along the midline at a distance of 20cm with the subjects reading each target for 5 minutes. Immediately after each period of reading, post task continuous measurements were taken for 120 seconds. Between each target presentation (Figure 2.5 – Chapter-2) subjects viewed a 6/9 Snellen optotype target at 3m logMAR in the light.

Comparisons were made between and within emmetropes and myopes using repeated measures ANOVA to calculate the effect of target size and contrast on NITM initial magnitude and decay. Independent t-tests were performed in order to compare the binocular vision parameters between emmetropes and myopes.

3.3 Results

The experiment subjects were 18 to 25 years of age. The average spherical equivalent in the emmetropic group was 0.10D and -3.32D in the myopic group. There was no significant difference in gender or age between refractive groups (Table – 3.1).

Table – 3.1: Demographic details of participants: 5 Minutes reading task

	5 minutes reading task		
	Emmetropes (n=24)	**Myopes (n=24)**	**p Value**
Age (years)	20 ±1.3	19.63±2.1	0.46
Male : Female	7 :17	4:20	0.49*
Refractive Error(SE) (mean± SD)	0.10±0.09	-3.32±2.76	< 0.01

*Chi-square

3.3.1 Initial NITM

Initial NITM magnitudes for both refractive groups with all target types are shown in Table 3.2 and variations in post-task NITM for different targets are plotted in Figures 3.1 and 3.2.

Table 3.2: NITM magnitude (in dioptres) for emmetropes and myopes for four different targets following the 5-minute reading tasks. Two targets were N8 of 50% contrast (N8-50) and 90% contrast (N8-90) and two were N12 at 50% contrast (N12-50) and 90% contrast (N12-90). A positive value indicates a myopic shift in refractive error.

NITM 5m	**N8 – 50 (Mean±SD)**	**N8 - 90 (Mean±SD)**	**N12 - 50 (Mean±SD)**	**N12 - 90 (Mean±SD)**
Emmetropes	-0.08±0.15	-0.09±0.22	-0.07±0.22	-0.01±0.20
Myopes	0.22±0.27	0.25±0.24	0.16±0.21	0.23±0.26

Figure 3.1: Post task shift in refractive error (D) for emmetropes following the 5 minute reading tasks. Error bars indicate±1 SEM.

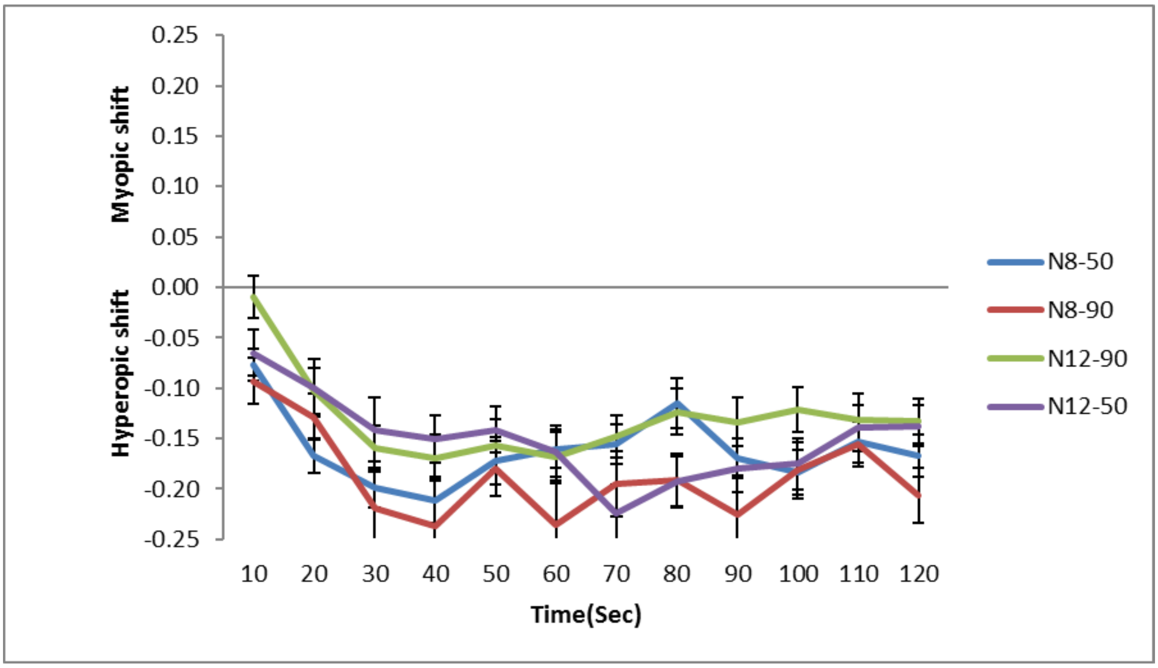
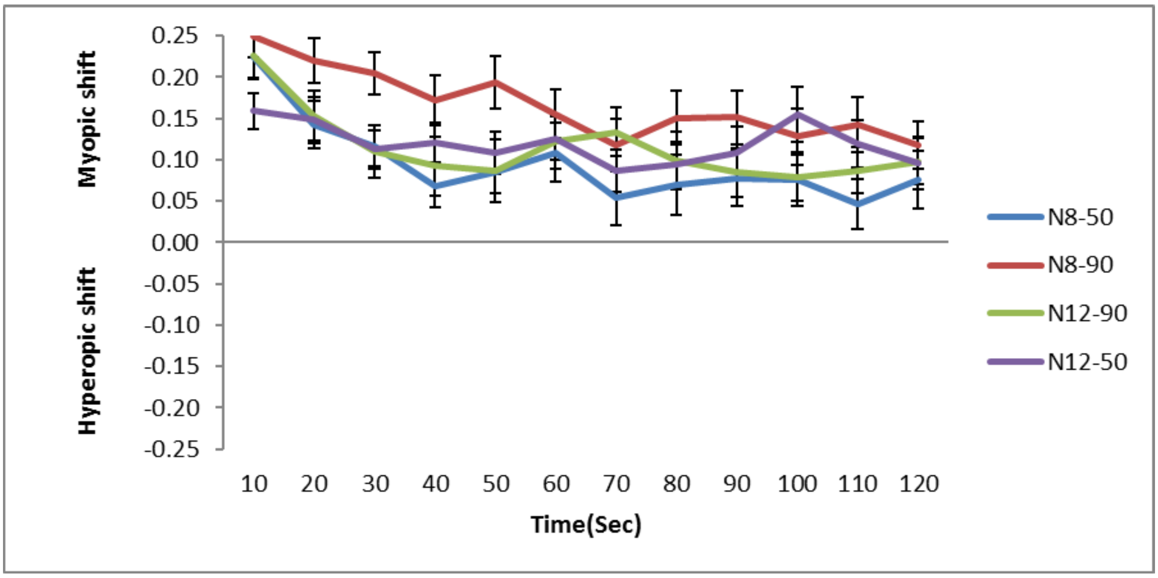


Figure 3.2: Post task shift in refractive error for myopes following the 5 minute reading tasks. Error bars indicate ±1 SEM.



When averaged across all targets, myopes displayed a mean myopic shift of 0.21D after five minutes of reading whereas the emmetropes displayed a hyperopic shift of 0.07D. Analysis of variance revealed a statistically significant main effect of refractive error group ($F_{1,\ 46}$ = 28.07, p < 0.001) on NITM indicating a significant difference in NITM between myopes and emmetropes. There was no significant interaction between refractive error group and target type, and Mauchly's test indicated that the assumption of sphericity had been violated, χ^2 (5) = 18.65, p=0.002, therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (Ɛ=.8). The results show that there was no significant effect of target type on NITM ($F_{2.42,\ 111.3}$ = 1.9, p=0.14) (Table-3.2).

3.3.2 Decay time constant

When averaged across all targets, decay time constant was 6.07 seconds for the myopic group. As there was hyperopic shift for the emmetropes the decay time constant was not calculated. There was no significant interaction between target type and refractive group, and Mauchly's test indicated that the assumption of sphericity had been violated, χ^2 (5) = 15.78, p=0.007, therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (Ɛ=.83). Analysis of variance showed that there was no significant effect of target type on decay time constant in myopes ($F_{2.51,\ 115.6}$ = 0.91, p=0.42) (Table-3.3).

Table 3.3: Decay time constant (seconds) for myopes for different targets following the 5 minute reading tasks.

Time constant 5m	**N8 with 50% contrast** **Mean(±SD)**	**N8 with 90% contrast** **Mean(±SD)**	**N12 with 50% contrast** **Mean(±SD)**	**N12 with 90% contrast** **Mean(±SD)**
Myopes	6.82± 8.35	7.58±10.03	5.44 ± 5.85	4.44±4.20

3.3.3 Binocular vision parameters

There was a significant difference between myopes and emmetropes in amplitude of accommodation (AOA) (t (46) = 2.03, p=0.04), accommodative facility for near (AF) (t (46) = -2.25, p=0.03), tonic accommodation (TA) (t (46) = 2.2, p=0.03) and response AC/A ratio (t (46) = 5.75, p<0.01). There was no significant difference between myopes and emmetropes in near point of convergence (NPC) (t (46) = -1.49, p=0.14), accommodative facility for distance (AF) (t (46) = 1.85, p=0.07), and vergence facility (VF) (t (46) = -1.70, p=0.09). The mean binocular vision parameters for emmetropes and myopes are shown in Table – 3.4.

Table – 3.4: The mean and standard deviation of binocular vision parameters for emmetropes and myopes.

	Emmetropes (N=24)	**Myopes (n=24)**	**p value**
NPC(cm)	6.60±1.19	7.46±2.54	0.14
AOA(D)	12.05±2.20	14.03±3.80	0.04
AF-Distance (Cycles/sec)	12.98±3.58	11.17±3.19	0.07
AF-Near (Cycles/sec)	10.00±2.73	12.13±3.72	0.03
VF-(Cycles/sec)	10.29±2.73	12.06±3.82	0.09
Response AC/A(PD)	4.66±0.86	6.49±1.3	<0.01
TA(D)	0.08±0.06	0.21±0.29	0.03

3.4 Discussion

To the best of our knowledge, this was the first study that has documented NITM magnitude and decay time constant among an Indian cohort. This study demonstrated that initial NITM magnitude of Indian myopes was more than Indian emmetropes following 5 minutes of a near task. It also showed that there was no effect of different targets size and contrast on the NITM magnitude. The average decay time constant (recovery to baseline) was found to be 6.07 seconds among the myopes.

Initial NITM was found to be in the range of 0.18D to 0.41D among different locations (Table 3.5). In the present study, NITM ranged between 0.16D to 0.25D for different target sizes and contrasts. Initial NITM for the N12 low contrast target was 0.16D and for the N12 high contrast target was 0.23D. Similarly, the initial NITM for the N8 low contrast target was 0.22D and for the N8 high contrast target it was 0.25D, whereas, in an Australian population, Schmidt, et al.(2005), reported that after 3 minutes of a near task the initial NITM was 0.36D for both high and low contrast N8 targets. Interestingly, Schmidt, et al. (2005), also found that target contrast had no effect on NITM and that target size produced only a small change in NITM that was not clinically significant. The NITM magnitude in this experiment on Indian subjects closely resembles that of the Australian population and our results agree with those of Schmidt, et al. (2005), in that target types had no significant effect on NITM.

People are exposed to different text characteristics, both size of the letters (N8, N12 etc.) and contrast when performing near task. The text size and contrast are reduced when students photocopy the lecture notes. Though there was no effect of target size and contrast on NITM statistically, NITM magnitude of 0.07D and 0.03D was observed in this study for N12 and N8 targets with higher contrast respectively.

Table 3.5: Studies showing NITM magnitude and decay in myopes following the 5 minute near tasks. Target size and contrast was kept constant across all studies shown.

Studies (location)	NITM(D) Mean±SD	Decay(Sec) Mean±SD	Task Duration – Task Distance
Lin et al. (2012) (China)	0.18±0.16	50 (20, 90)	5 minutes – 20 cms
Lin et al. (2013) (China)	0.21±0.16	108.4±63	5 minutes – 20 cms
Present Experiment (India)	0.22±0.25	6.07±7.11	5 minutes – 20 cms

The emmetropic group demonstrated mean NITM magnitude between 0.00D and 0.09D (Hyperopic shift), whereas in other studies emmetropes had myopic shift (Ciuffreda and Wallis, 1998, Lin, et al., 2012). Since the data for emmetropes showed hyperopic shift and since physiologically we would expect all the individuals to be myopic during and immediately after near work, we can hypothesise that the decay was faster. Unfortunately the data from this study is not able to support the hypothesis that decay in emmetropes was faster than myopes, as it was not possible to calculate the decay from emmetropes data.

The NITM decay time constant describes the decay dynamics of accommodation. The decay duration in this experiment for myopes was faster (6.07 seconds) than other studies (Table 3.5). We initially investigated NITM after a 5-minute near work task and found that the magnitude was comparable with other ethnicities but the decay was faster. So to verify this, we wanted to extend the experiment by lengthening the near work task to 60-minutes. The results of this experiment are presented in chapter 4.

3.4.1 Binocular vision parameters-Emmetropes and Myopes

3.4.1.1 Amplitude of accommodation

This study measured amplitude of accommodation and found that the myopes had significantly higher amplitude of accommodation compared to emmetropes. Though the exact mechanism underlying the differences in amplitude is not clear, myopes may have weak sympathetic or strong parasympathetic system (McBrien and Millodot, 1986a). This stronger parasympathetic system would give rise to higher amplitude of accommodation among myopes.

3.4.1.2 Facility of accommodation

This study measured facility of accommodation for distance and near and found that the facility of accommodation for near among myopes was greater (12.13 ± 3.72 cycles/minute) compared to emmetropes (10.00 ± 2.73 cycles/minute), but not for distance accommodative facility. Allen and O' Leary, (2006), measured distance and near monocular and binocular facility and found that myopes had reduced (monocular) distance accommodative facility (15.95 ± 4.91cycles/minute) compared to emmetropes (18.54 ± 5.40 cycles/minute). There was no difference in binocular distance, near monocular and near binocular facility values among myopes and emmetropes. They reported that accommodative facility (monocular distance accommodative facility) was a significant factor for myopia progression among young adults. The authors reported an association between accommodative facility and myopia progression. However CAMS (Cambridge Anti-Myopia Study) did not report any association between accommodative facility and myopia progression. They stated that this could be due to low rate of myopia progression among the study cohort (Allen, et al., 2013).

Pandian, et al. (2006) reported reduced distance accommodative facility among myopes compared to emmetropes and hyperopes, but not for near. The authors further suggested that, though the exact reason for the lower accommodative facility shown by myopes is not clear, it could be a feature of progressive myopia.

3.4.1.3 Accommodative convergence/Accommodation (AC/A) ratio

This study measured response AC/A and found higher AC/A ratios among myopes (06.49 ∆ / D) compared to emmetropes (04.66 ∆ / D). Jiang, (1995) noted that the response AC/A increased during myopia development and was suggested to be a risk factor for myopia development. Gwiazda, Grice and Thorn, (1999) found similar results in children and the reason for the elevated AC/A ratios among myopes was decreased accommodative response (lag) for near and increased accommodative convergence. Allen and O'Leary, (2006) reported AC/A ratio to be a non-significant predictor for myopia progression. The reason for the variation in results could be due to the fact that Allen and O'Leary (2006) had included all accommodative functions as part of their study and possibly AC/A might be less predictive in the presence of more important accommodative functions.

3.4.1.4 Tonic accommodation

This study measured tonic accommodation and found higher dioptric levels of tonic accommodation among myopes (0.21D) compared to emmetropes (0.08D). A high level of tonic accommodation in an emmetrope is considered to be a risk factor for the development of myopia (Ong and Ciuffreda, 1995). However Allen and O' Leary, (2006) did not find any association between tonic accommodation and myopia progression. They explained that the reason for the difference could be due to time delay between the measurement of stimulus and response in their experiment.

3.5 Conclusion

NITM magnitude in Indian myopes was comparable with other studies. However Indian emmetropes in this study showed hyperopic shift unlike reported in existing literature. The decay time for myopes in this study was faster compared to other ethnicities. There was no significant effect of target size and contrast on NITM for both myopes and emmetropes among these study subjects. There was a significant difference between myopes and emmetropes in amplitude of accommodation, facility of accommodation for near, tonic accommodation and response AC/A ratio.

Chapter 4

Results of study 2: 60 minute reading task

4.1 Introduction

Study 1 showed that following a 5 minute reading task NITM magnitude was higher for myopes compared to emmetropes and the decay duration was faster for myopes compared to other studies (Ong and Ciuffreda, 1995; Ciuffreda and Wallis, 1998). Emmetropes demonstrated a small hyperopic effect. The parasympathetic system is responsible for (positive) accommodation and sympathetic system is responsible for disaccommodation (Ong and Ciuffreda, 1995). This suggests that the sympathetic response may be faster in these study subjects (study 1). Moreover, the amplitude of accommodation was found to be lower among the Indian population compared to other populations (Chattopadhyay, 1984). Vasudevan and Ciuffreda (2008) have shown that with increase in task duration, there was an increase in NITM magnitude and have also shown that with repeated cycles of near task, NITM magnitude are additive and could lead to permanent myopia. So the aim of this study is to see whether NITM magnitude increased with prolonged reading (especially in myopes) and to understand the effect of prolonged reading on decay time constant. In this study the task duration was extended from 5 minutes to 60 minutes. Studies mentioned in Table 4.3 have been shown to vary in NITM magnitude and decay due to methodological differences like target distance, classification of myopes etc. NITM has been found to be highly influenced by near task duration (Vasudevan and Ciuffreda, 2008). In general, studies which have been done at 20cm or less, have found to have greater NITM magnitude and longer decay. However, this study wanted to measure NITM at a realistic working distance, not one that would elicit a maximal response that people don't actually use. We were conscious of the training effects that can occur with studies investigating accommodation (Ciuffreda and Vasudevan, 2008) and as a consequence recruited a new cohort of participants.

4.2 Methods

The pre-task assessment was followed by a 60 minute near task performed binocularly at 0.2m. The subjects were again periodically reminded to keep the target in focus throughout the task. The near targets comprised text from optometry lectures, similar to the N12-90 target used in study 1 as this is the most real life type stimulus they would experience normally. Immediately after reading, the subject's monocular distance refractive state was measured continuously for 120 seconds. A review of NITM studies (Ong and Ciuffreda, 1995) revealed no apparent relationship between the magnitude of NITM and viewing conditions (monocular versus binocular). Continuous refractive data for each subject were divided into 10-second bins. The average difference between the post-task and pre-task distance refractive state in the first 10 second bin represented the initial NITM dioptric magnitude. Data were analyzed with respect to baseline NITM magnitude and decay time constant.

4.3 Results

The study subjects were between 17 and 27 years of age. Mean spherical equivalent for the emmetropes was 0.13D and -2.75D for the myopes.

The study subjects in study 1 were between 18 and 25 years of age. Mean spherical equivalent for the emmetropes was 0.10D and -3.32D for the myopes. The baseline characteristics (age, gender and refractive error) of the cohorts (study 1(Lines 1462-63)) and study 2) were similar. There was no significant difference in age (p=0.07), gender (p=0.82) or refractive error (p=0.55) among the myopes.

Characteristics of the study 2 cohort are presented in Table 4.1.

Table 4.1: Demographic details of participants in study 2: 60 Minute reading task

	Study 2		
	Emmetropes(n=24)	**Myopes(n=24)**	**P**
Age (years)	22.04±1.9	20.71±2.4	0.21
Male : Female	8:16	5:19	0.33*
Refractive Error (mean+ SD)	0.13±0.09	-2.75±1.89	< 0.01

*Chi-square

The initial NITM magnitude and decay time following the 60 minute reading task are given in Table 4.2.

Table 4.2: NITM magnitude (diopters) and decay time constant (seconds) for emmetropes and myopes following the 60 minute near task. A positive value indicates a myopic shift in refractive error or NITM.

NITM 60 min	**NITM Mean(±SD)**	**Decay constant Mean(±SD)**
Emmetropes	0.00±0.16	4.90±5.09
Myopes	0.31±0.15	8.16±10.83
P	<0.01	0.45

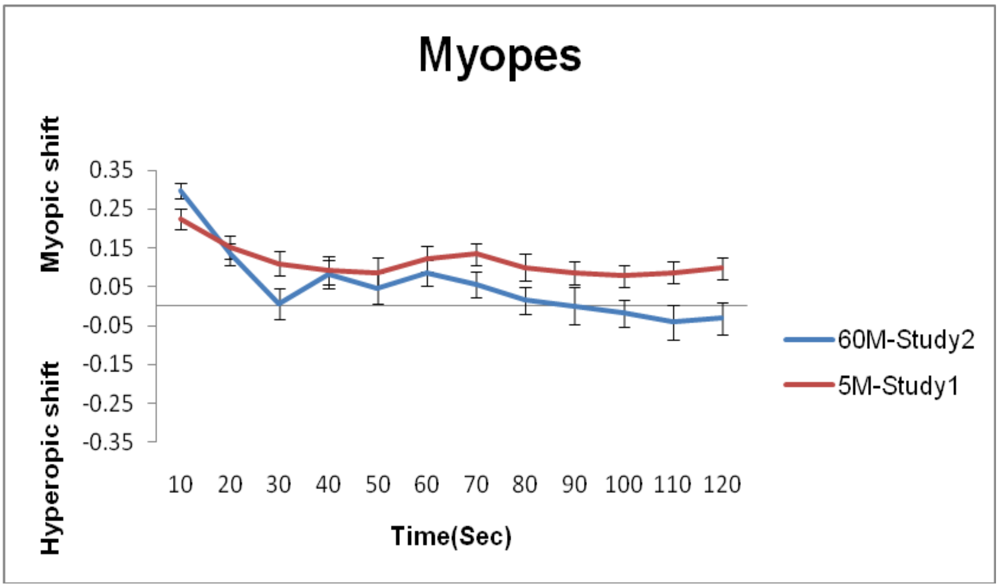
NITM data was normally distributed (Shapiro-Wilk, p=0.93) but decay time constant was not normally distributed (Shapiro-Wilk, p<0.01).

Independent samples t-tests were carried out to compare the initial NITM for emmetropes and myopes. There was a statistically higher mean NITM magnitude in myopes (M=0.31, SD=0.15; t(46)=6.69, p<0.01) compared to emmetropes (M=0.00, SD=0.16).

Mann-Whitney U test were performed to compare the decay time constant for emmetropes and myopes. There was no significant difference in decay time constant for myopes (M=8.16, SD=10.83) and emmetropes (M=4.90, SD=5.09; U=251.5, p=0.45) and this might have been masked by the increase in SD range. Though the difference was not statistically significant, the myopes showed delayed decay compared to emmetropes. Emmetropes had an apparent decay of 4.90 (S) and this could be due to the variation in NITM standard deviation. Myopes tend to have a larger lag of accommodation for near viewing (e.g. Gwiazda, et al., 2003). This may have caused a high standard deviation among myopes for the decay time constant.

Figure 4.1 and 4.2 shows the post task shift for myopes and emmetropes following 60 minutes task in comparison to 5 minutes task respectively. Figure 4.3 shows the post task shift for myopes (EOMs and LOMs) following 60 minutes and 120 minutes (Vasudevan and Ciuffreda, 2008).

Figure 4.1: Post Task Shift (D) for myopes at 5 minutes and 60 minutes for N12 with 90% contrast. Error bars indicate ±1 SEM.



Myopes had an initial NITM of 0.23D after 5 minutes and 0.31D after 60 minutes of near task for N12 with 90% contrast. When normality tests were performed for NITM among myopes for 5 minutes and 60 minutes of near task, the data were not normally distributed (Shapiro-Wilk, p= 0.04). Mann-Whitney U test was performed to compare NITM magnitude among myopes for 5 minutes and 60 minutes of near task. There was a significant difference in NITM (U=184, p=0.03).

Figure 4.2: Post Task Shift (D) for emmetropes at 5 minutes and 60 minutes for N12 with 90% contrast. Error bars indicate ±1 SEM.

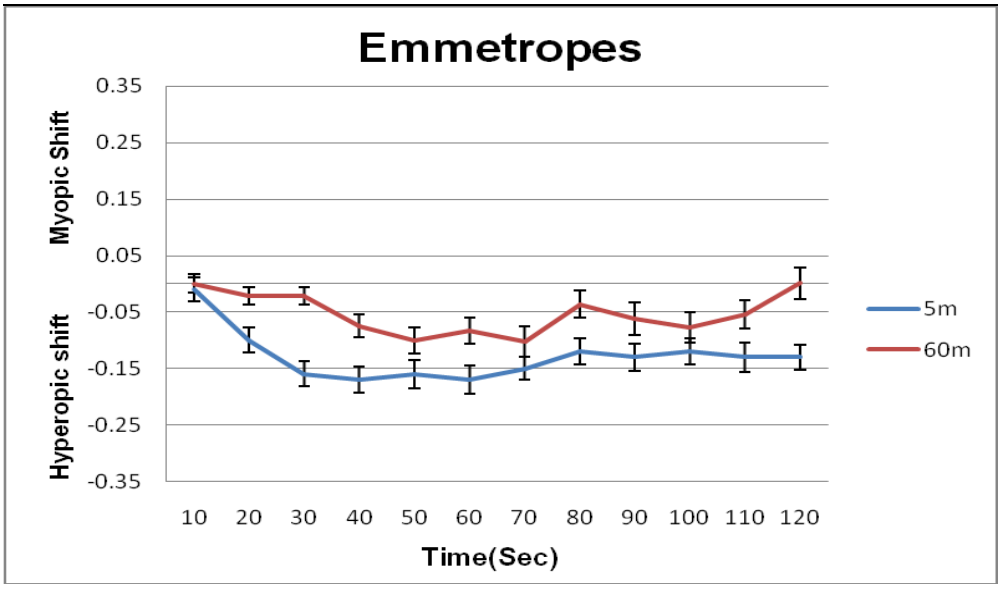
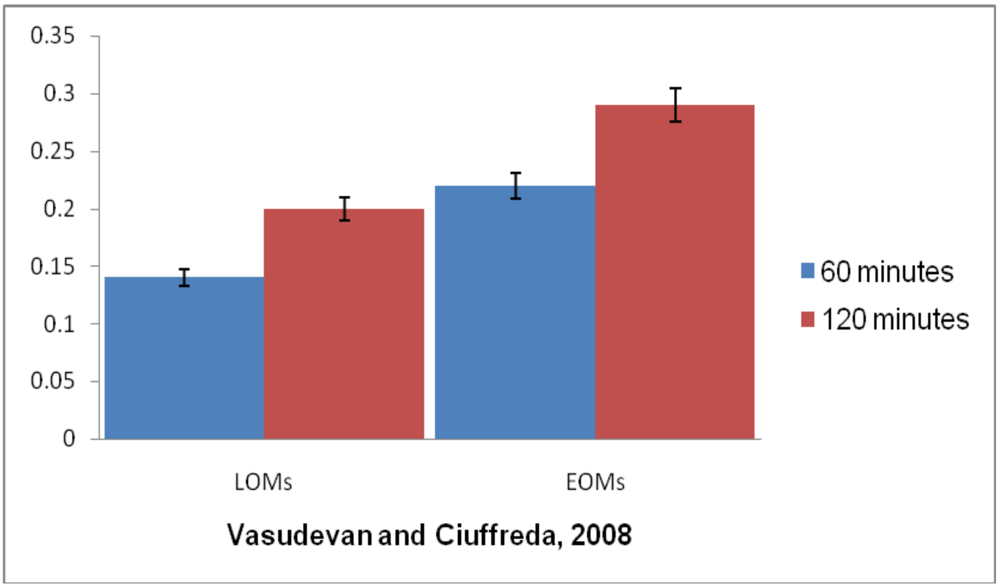


Figure 4.3: Post Task Shift (D) for myopes (EOMs and LOMs) at 60 minutes and 120 minutes (Vasudevan and Ciuffreda, 2008).



Emmetropes had -0.01±0.20D of hyperopic shift after 5 minutes and 0.00D after 60 minutes of near task for N12 with 90% contrast. When normality was performed for NITM among emmetropes for 5 minutes and 60 minutes of near task, the data were normally distributed (Shapiro-Wilk, p= 0.92). An independent-samples t-test was performed to compare NITM magnitude among emmetropes for 5 minutes and 60 minutes of near task. There was no difference in NITM (t (45) =-0.2, p=0.98).

4.4 Discussion

When Indian subjects period of near work was extended from 5 minutes to 60 minutes, myopes once again demonstrated a larger initial NITM magnitude (0.31±0.15D) compared to emmetropes (0.00±0.16D). The baseline NITM magnitude in this study after 60 minutes of near task was also well within the expected magnitude of NITM found in Caucasian myopes (Table 4.3). For the extended task duration of 60 minutes, Owens and Kelly, (1987), reported NITM magnitude of 0.43 D for myopes whereas Vasudevan and Ciuffreda, (2008), reported 0.14 D and 0.22 D for the LOMs and EOMs respectively for the same period of task duration. When the task was extended to 120 minutes, Vasudevan and Ciuffreda, (2008), reported 0.20 D and 0.29 D for the LOMs and EOMs respectively (Figure 4.3). It is interesting to note that the NITM magnitude increased after extended near task in this study too. There was an increase in magnitude of 0.06D for LOMs and 0.07D for EOMS in Vasudevan and Ciuffreda, (2008) study, and in this study there was an increase in magnitude of 0.10D for myopes after extended near task. NITM has been found to be additive in nature (Vasudevan and Ciuffreda, 2008). That is, following second hour of reading NITM was significantly greater than found after the first hour especially for myopes. Though Vasudevan and Ciuffreda, (2008) tested on a Caucasian population, where the prevalence of myopia is relatively high, and the present study was tested in Indian subjects, where the prevalence of myopia is relatively low, myopes were particularly susceptible to NITM compared to emmetropes. This study did not classify myopes as EOMs or LOMs as the prevalence studies (Dandona, et al., 1999; Dandona, et al., 2002; Murthy, et al., 2002;

Saxena, et al., 2015) did not reveal significant changes over time in the prevalence of myopia with respect to age of myopia onset. In contrast, Ciuffreda and Lee, (2002), found lower NITM of 0.12 D and 0.13 D for the LOMs and EOMs after 4 hours of a near task when tested at the subject's habitual working distance. The lower NITM magnitude found could be due to the dissipation of accommodation as the subjects were allowed to take rest between reading tasks. In the present study, subjects read the near task for 60 minutes continuously without break.

Table 4.3: Studies showing NITM magnitude and Decay in different locations with differing task duration.

Study (Year/locations)	NITM(D)	Decay(s/m/h)	Task duration/distance
Ehrlich (1987/UK)	0.29	> 1hr	2 hrs / 20 cms
Owens & Kelly (1987/US)	0.43	>20 min	1 hr/ 20 cms
Ciuffreda and Lee (2002/US)	EMM = 0.09, LOM = 0.12, EOM = 0.13, HYP =0.44 (hyperopic shift)	EOMs, LOMs -1 min	4hr/ habitual working distance (> 20 cms)
Vasudevan & Ciuffreda (2008/US)	EMM = 0.14/0.15, LOM = 0.14/0.20, EOM = 0.22/0.29 after 1hr/2hr	EMM-4/12s, LOM-5/22s, EOM-8/34s after 1hr/2hr	2hrs/35-40 cms
Current Study (2015/India)	0.31	8.16s	1 hr/ 20 cms

EOM-Early onset myopia, LOM- Late-onset myopia

The decay duration for myopes (8.16s) and emmetropes (4.9s) in this study was faster than found in Caucasian population (Ehrlich, 1987; Owens and Kelly, 1987; Arunthavaraja, 2010). The difference in the values of decay between the present study and that of Arunthavaraja, (2010), for the 10 minutes of repeated near task, with 5 minutes of break between tasks duration, suggests a faster relaxation to the baseline in the Indian subjects, as all the studies in Table 4.3, have stated that there could be an autonomic imbalance, especially impaired sympathetic system, resulting in delayed decay. The longer/incomplete decay over time could lead to permanent myopia (Vasudevan and Ciuffreda, 2008). This requires some consideration. We can speculate that, may be due to a genetically-driven difference in lens structure that may allow some subjects to relax their accommodation more quickly after near work (Ong and Ciuffreda, 1995). Alternatively, Indian subjects may have a faster sympathetic response compared to other ethnic groups. It has been well-documented that the accommodative system receives dual innervations, consisting primarily of a parasympathetic (cholinergic) and secondarily a sympathetic (adrenergic) component. An increase in parasympathetic stimulation results in an increase in accommodation. Prior investigation has demonstrated that the sympathetic system is slower in onset (40 secs) and smaller in effect than the parasympathetic system (Ciuffreda, 1991). Gilmartin (1986) and Mallen et al. (2005) have suggested that a deficit in this system in myopes may slow the decay of NITM. The longer decay time found in previous studies compared to the present study may be attributed to differences in parasympathetic stimulation between our subjects and those of different ethnicity (Ciuffreda, 1991). Therefore, the sympathetic response efficiency in Indian subjects compared to other ethnicities with a higher prevalence of myopia should be further investigated particularly as the prevalence of myopia (4-7%) in Indian populations is lower compared to other populations where decay duration is longer (Ciuffreda and Wallis, 1998). The difference in NITM decay time may indicate a reduced susceptibility to myopia development in this population. Unfortunately, our study did not attempt to measure the progression of myopia among our subjects, so was not able to investigate the relationship between their NITM characteristics and their rate (if any) of myopia progression. The underlying reason for a lower prevalence of myopia in India is yet to be determined. While both the countries have a large population of young children and adults who perform significant magnitudes of near work during the day, the prevalence of myopia in the Chinese population is much higher than that of Indian. Aside from the genetic predisposition, Indian children and adults living within the cities study using both English and native Indian language characters that might have a different spatial content in the text compared to that of the Chinese language characters. As myopia seems to be multi-factorial, it is difficult to differentiate between the genetic influence and other factors such as environmental influence. More research would help us understand the apparent protective mechanism present in the Indian population that enables a lower prevalence of myopia, and could possibly serve as a potential treatment option for countries with high myopia. Our data also show faster decay dynamics which may possibly explain why the presenting NITM does not persist which may in turn lead to lower myopia prevalence. This needs to be investigated further.

To confirm the above hypothesis, Vasudevan, Ciuffreda and Gilmartin, (2009), assessed the effect of near work in young Caucasian adults following one hour of reading. All the subjects received timolol maleate to block the sympathetic nervous system and betaxolol as a control agent. NITM magnitude and decay duration was increased in subjects who received timolol. They further stated that the decay duration among myopes was more prolonged than emmetropes suggesting a possible role of impaired sympathetic system in myopia development. This difference in NITM decay time in this study subjects may indicate a reduced susceptibility to myopia development in this population.

Though the subjects in this study were age matched with that of study 1, they were a different cohort. This is one of the limitations of this study.

4.5 Conclusion

Myopes demonstrated larger NITM magnitude compared to emmetropes when the task was extended to 60 minutes. The decay time constant was faster even after 60 minutes of near task compared to other study populations though one study showed similar results as the present study.

Chapter 5

Results of study 3: Ocular aberrations before and after 5 minutes of reading

5.1 Introduction

An optical system provides a perfect formation of a point image if all the rays meet in a single point. However, such an ideal condition is never fulfilled in practice. Like any optical system, the eye also suffers from failure to comply with ideal image formation. This failure to form an ideal image formation is attributed to aberrations. These aberrations are of two types namely, lower and higher order aberrations. Lower order aberrations, which include myopia, hypermetropia and astigmatism, account for approximately 92% of the overall aberrations in the eye (Jesson, Arulmozhivarman and Ganesan, 2004). Higher order aberrations include spherical aberration, coma and trefoil. These contribute to the remaining 8% of the total aberrations in the eye. In bright light conditions, the pupil constricts blocking the more peripheral rays thereby minimising the effect of spherical aberration. Most eyes show positive spherical aberration (marginal rays are focused closer than the paraxial rays) in an unaccommodated state, with a tendency towards negative spherical aberration (paraxial rays are focused closer than the marginal rays) on accommodation (Atchison, et al., 1995; He, et al., 2000; Ninomiya, et al., 2002; Ghosh, et al., 2011). The reason for this change could be that some of the ocular structures, especially, the shape, position and refractive index of the crystalline lens change during accommodation (Garner and Smith, 1997; Koretz, Cook and Kauffman, 2002; Dubbleman, Heijde and Weeber, 2005; Kasthurirangan, et al., 2011), although this is dependent on pupil size, corneal shape and retinal topography (Paquin, et al., 2002; He, et al., 2003; Buehren, Collins and Carney, 2003; 2005; Zhou, et al., 2015).

Although studies have shown changes in spherical aberration with accommodation, the nature of the change has varied. He, et al. (2000) reported negative spherical aberration with accommodation for all subjects whereas Atchison, et al. (1995) reported negative spherical aberration in only half their sample. With small sample sizes, it becomes difficult to comment about this variation critically, though it could also be due to the use of different measurement techniques. Atchison, et al. (1995) measured aberrations on 15 subjects whose refractive error ranged between +1.00D to -2.00D by Howland aberroscope technique, whereas He, et al. (2000) used a ray-tracing technique for measuring aberrations on 8 subjects, whose refractive error ranged between Plano to -5.50D.

As it has been shown that aberrations increase with accommodation, studies measured aberrations during reading to see the effect of near work and accommodation on aberrations. Some studies measured aberrations following short term reading (15 minutes) (Shaw, et al., 2009; Ghosh, et al., 2011) and long term reading (2 hours) (Buehren, Collins and Carney, 2003;2005; Collins, et al., 2006). The studies mentioned above have reported changes in total higher order root mean square (HORMS) in the range of 0.4 to 0.7 μm with a trend towards negative spherical aberration, for both short term and long term near tasks. Apart from the change in shape, position and refractive index of the crystalline lens during accommodation, the changes in aberrations following near tasks were attributed to the shape and position of the eyelids, especially narrow palpebral fissures and the effect of these lid induced changes on corneal aberrations.

Collins, Buehren and Iskander, (2006) assessed retinal image quality before and after 2 hours of reading in a group of 20 myopes and 20 emmetropes using a Hartmann Shack sensor. They reported that the retinal image quality for near vision for myopes was substantially worse compared to emmetropes following two hours of reading. They further stated that it could be due to the near induced transient myopic shift (NITM) following near work and changes in higher order aberrations especially spherical aberration associated with accommodation and reading. As higher order aberration is dependent on pupil size, aberrations degrade retinal image quality to a greater extent if reading is performed in poor light.

Shaw, et al., (2009) assessed corneal changes with a videokeratoscope following 15 minutes of visual tasks (reading with gaze shifts and steady fixation without gaze shifts at 20^0 and 40^0) and reported changes in the magnitude of total root mean square (RMS) of aberrations and have attributed the change to shape and position of the eyelids. Buehren, Collins and Carney, (2003) investigated the effect of eyelid pressure on corneal shape and aberrations after 60 minutes of reading. They also found that there was an effect of eyelid pressure resulting in a change in vertical coma and trefoil along 30^0. Buehren, Collins and Carney, (2005) measured aberrations in 20 progressing myopes and 20 age matched emmetropes following 120 minutes of a reading task. After reading a book of choice at their habitual distance, myopes showed greater overall higher order wavefront changes (RMS) compared to emmetropes following prolonged reading. These differences were attributed to the narrower lid aperture during reading among myopes. Collins, et al. (2006) studied corneal optics using corneal topography and digital photography to capture the eyelid position before and after 60 minutes of reading a novel, performing a blood cell count on a microscope and internet searching. They found that reading at their habitual distance and microscopy caused more changes to corneal aberrations than computer work, where the working distance to the monitor was 50 - 80 cms. They stated that the reason could be due to the variations in the palpebral aperture and eye movements performed during these tasks. They further reported that while reading, the narrow palpebral aperture associated with downward gaze caused changes in corneal topography and optics. This could be one of the reasons for no significant change in aberrations with computer work. The other reason could be due to the higher accommodative demand in reading and microscopy compared to computer work. Evidence from the literature has shown that the trend towards negative spherical aberration increases with higher accommodative stimuli (Hazel, et al., 2003). Hazel, et al. (2003) measured wavefront aberrations at different accommodation levels using a Hartmann-Shack wavefront sensor on 30 subjects (20 myopic (-0.75 to -6.00D) and 10 emmetropic). Accommodation levels ranged from 0 to 4D in 1D steps. They reported that there was an increase in negative spherical aberration with increase in accommodative demand. This change in spherical aberration with accommodation has been mainly attributed to the change in central lens thickness.

In another study, Plainis, Ginis and Pallikaris, (2005) assessed the correlation between accommodative errors and change in aberrations and retinal image quality during accommodation. They found that spherical aberration was the main higher order aberration that contributes to changes in image quality during accommodation. Most of the above studies reported a change in spherical aberration, and increase in overall HORMS with accommodation (Buehren, Collins and Carney 2003; 2005; Shaw, et al., 2009). The results were less conclusive for other aberrations like coma and trefoil.

It is evident from the above that due to the effect of accommodation and also input from corneal changes, there is an increase in higher order aberrations especially spherical aberration and HORMS. Also in myopes, the asso ciation between near induced transient myopic shift and concurrent changes in aberrations have not been well understood. Aberrations were measured immediately following a near task among the cohort of myopes and emmetropes from study 1 and correlated with NITM magnitude, to explore if aberrations altered after near viewing in this cohort and also to identify any relationship between NITM and aberrations.

5.2 Apparatus

Ocular aberrations were measured by the Complete Ophthalmic Analysis System (COAS) (WaveFront Science, Inc., Albuquerque, NM) based on the Shack-Hartmann principle (for a detailed explanation of the instrument please refer to chapter-2 Methodology 2.3.5).

5.3 Methods

The subjects sat in the dark for 5 minutes to dissipate any residual accommodation (Ong and Ciuffreda, 1995). Following this, the subjects were asked to place their chin in the chin rest of the COAS and were instructed to look at the fixation target located inside the instrument that is optically projected to infinity. The myopic subjects wore their optimal CL refractive correction during the measurements to ensure an equivalent optical stimulus for all. Three measurements were taken for the right eye under subdued luminance (≈ 21.53 lux). After the pre-task measurements, the lights were turned on and subjects were asked to read a N12 target (Tennalirama story) with 90% contrast for 5 minutes at 0.2m. Immediately after the reading task, the lights were extinguished and subjects were asked to place the chin back on the chinrest of the COAS and the aberration measurements were obtained within approximately 2 seconds. The pupil diameter was set for 5mm in the COAS aberrometer. The instrument rescales the aberration data to 5 mm if the recorded pupil diameter was more or less than 5 mm at the time of measurement. The estimated ocular aberrations showed no statistical significance between natural pupil and rescaled pupil (Kalikivayi, Kannan and Ganesan, 2015).

5.4 Statistical analysis

The mean of the three measurements for a rescaled 5mm pupil were taken for analysis before and after reading. Repeated measures MANOVA was used to examine the change in spherical aberration (Z_4^0) and Higher order root mean square (HORMS) overtime and any subsequent interaction with the refractive error group. G* Power 3 was used to aid post hoc power calculations. A Pearson correlation co-efficient was used to assess the relationship between the NITM magnitude and HORMS (pre and post task).

5.5 Results

The study participants who underwent the NITM measurements (study 1) also underwent optical aberration measurements and therefore share the same demographic details (Table 3.1).

The age of study subjects ranged between 18 and 25 years of age with a mean (SD) of 20 ± 1.3 for emmetropes and 19.63 ± 2.1 for myopes. The mean spherical equivalent in the emmetropic group was 0.10D and in the myopic group was -3.32D. Please refer to study 1 (Table 3.1) for the demographic details.

The power using a two-tailed test with $\alpha = 0.05$ and N=24 is ≈ 5% for HORMS and spherical aberration. The required sample size for 80% power assuming a 5% significance level and a two-sided test is 285.

The mean and standard deviation (SD) of the aberrations (spherical aberration and HORMS) for emmetropes and myopes pre task and post task are shown in Table 5.1. Figures 5.1, 5.2 shows the pre and post task HORMS (microns) and SA (microns) for emmetropes and myopes following 5 minutes of reading.

Table – 5.1 Pre and post task optical aberrations (in microns) for emmetropes and myopes

Zernike Functions	Emmetropes pre-task	Emmetropes post-task	Myopes pre-task	Myopes post-task
Spherical Aberration (4,0)	0.039±0.06	0.040±0.06	-0.020±0.07	-0.022±0.07
Higher Order Root Mean Square	0.061±0.23	0.065±0.23	-0.137±0.14	-0.139±0.14

Figure 5.1: Pre and post task HORMS (microns) for emmetropes and myopes. Error bars indicate±1 SEM.

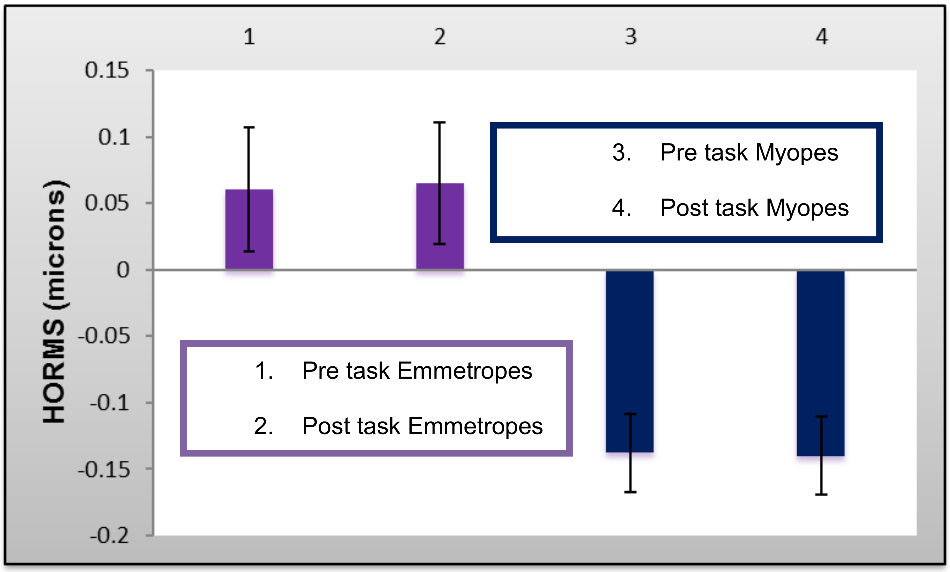
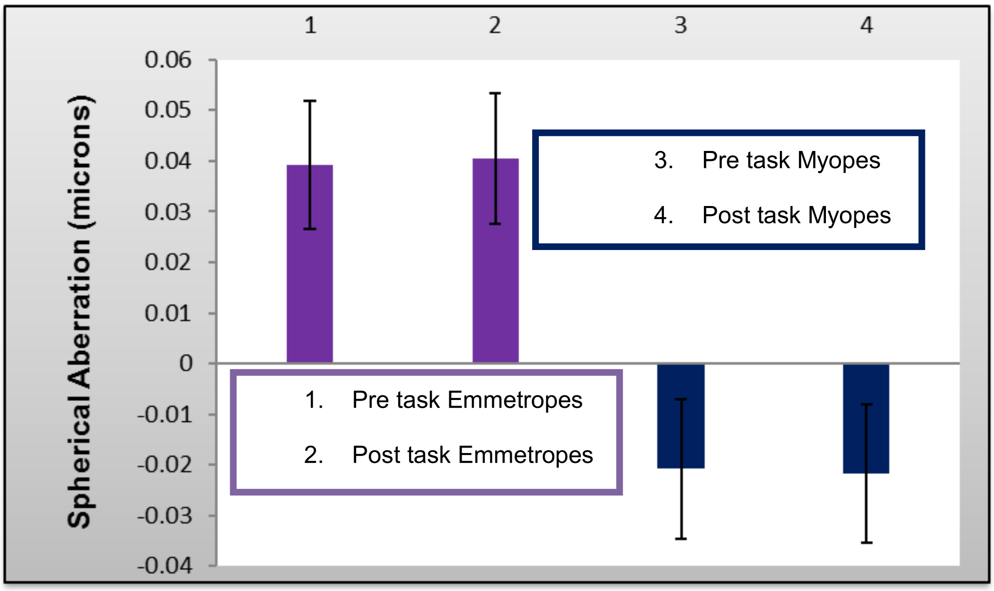


Figure 5.2: Pre and post task spherical aberration (microns) for emmetropes and myopes. Error bars indicate±1 SEM.



There was a significant main effect of refractive group at the multivariate level in the RM MANOVA, $F (6, 182) = 5.32$, $p<0.0005$; Wilk's $\Lambda = 0.724$, partial $\eta^2 = 0.15$. The Univariate F tests showed there was a significant difference in spherical aberration, ($F (3, 92) = 7.04$; $p<0.0005$; partial $\eta^2 = 0.19$) and HORMS, ($F (3, 92) = 8.98$; $p<0.0005$; partial $\eta^2 = 0.22$) between refractive groups.

Pre task

Post hoc Bonferroni pair-wise comparisons with a conservative (p value 0.05/6 = 0.008) showed a significant difference in pre task spherical aberration between emmetropes and myopes (p = 0.002, mean difference (SD): 0.06 (0.19); 95% CI: 0.02 to 0.09) and in pre task HORMS between emmetropes and myopes (p = 0.003, mean difference (SD): 0.19 (0.55); 95% CI: 0.05 to 0.34).

Post task

Post hoc Bonferroni pair-wise comparisons with a conservative (p value 0.05/6 = 0.008) showed a significant difference in post task spherical aberration between emmetropes and myopes (p = 0.001, mean difference (SD): 0.062 (0.18); 95% CI: 0.02 to 0.09) and in post task HORMS between emmetropes and myopes (p = 0.002, mean difference (SD): 0.20 (0.54); 95% CI: 0.06 to 0.35).

Change in aberrations following the reading task

The difference between pre and post task amounts of OSA and HORMS were calculated.

Post hoc Bonferroni pair-wise comparisons did not reveal any difference between pre and post task spherical aberration among emmetropes (p = 0.95, mean difference (SD): -0.001 (0.18); 95% CI: -0.04 to 0.04) and myopes (p = 0.97, mean difference (SD): 0.0008 (0.19); 95% CI: -0.04 to 0.04).

Post hoc Bonferroni pair-wise comparisons did not reveal any difference between pre and post task HORMS among emmetropes (p = 0.94, mean difference (SD): -0.004 (0.05); 95% CI: -0.11 to 0.10) and myopes (p = 0.97, mean difference (SD): 0.002 (0.05); 95% CI: -0.11 to 0.11).

A Pearson product-moment correlation co-efficient was computed to assess the relationship between the NITM magnitude and post task HORMS among myopes. There was a moderate positive correlation between NITM magnitude and HORMS (pre and post task), (r=0.41, n=24, p=0.04). A scatter plot summarizes the results (Figures 5.3, 5.4). A positive value in the graph indicates more NITM and the trend shows an increase in HORMS with greater NITM.

Figure 5.3: Correlation between NITM and Pre task HORMS

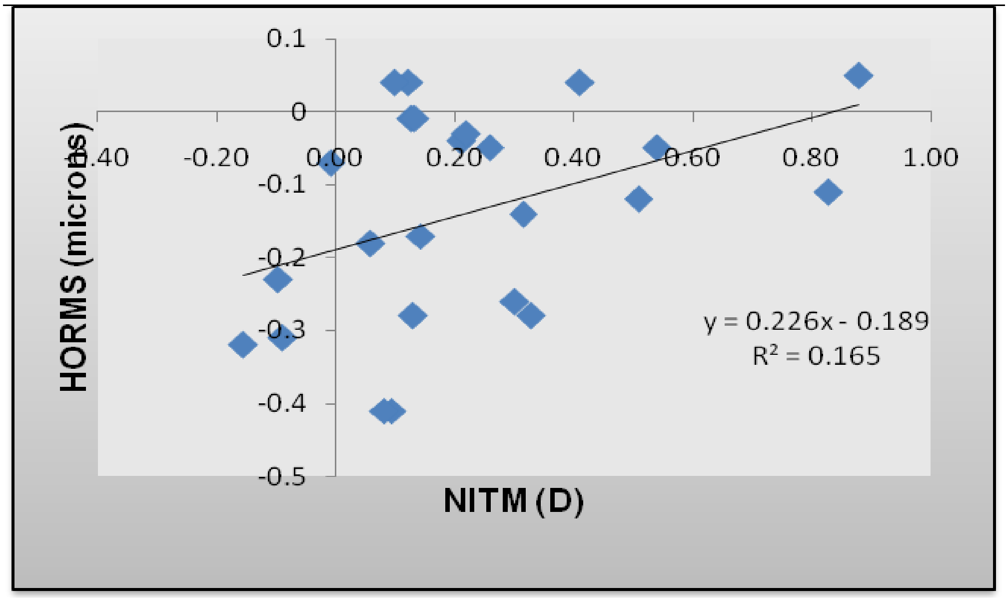
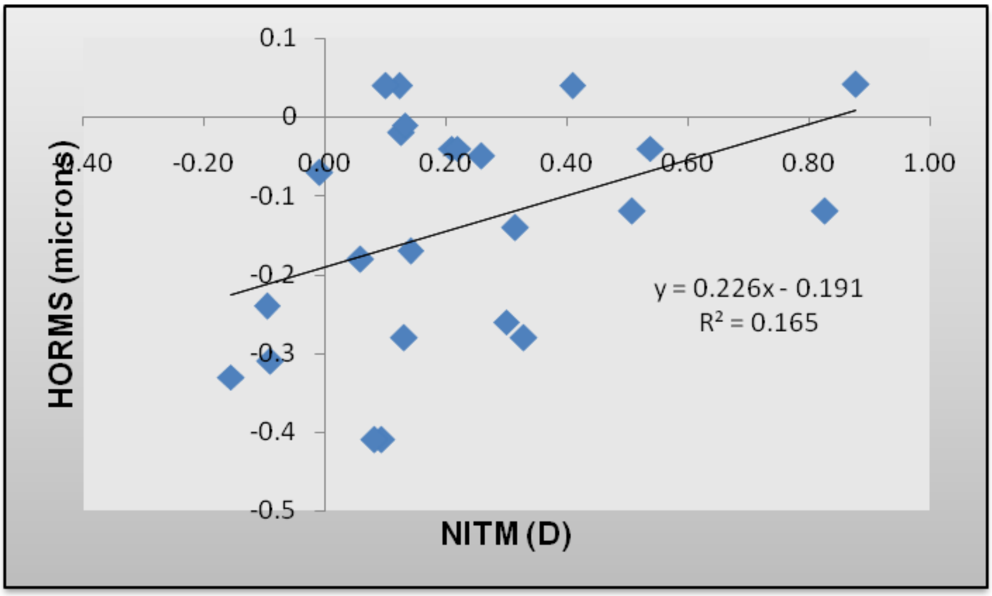


Figure 5.4: Correlation between NITM and Post task HORMS



5.6 Discussion

There was a difference in spherical aberration and HORMS between myopes and emmetropes at the pre task baseline, this difference between refractive groups did not change following 5 minutes of near task in this study subjects. There was no significant change in HORMS or SA after near viewing. Though a change in spherical aberration in the negative direction during accommodation is well documented in the literature (Atchison, et al., 1995; He, et al., 2000; Ninomiya, et al., 2002; Ghosh, et al., 2011), conclusive evidence on the mechanisms that contribute to this change still remains unclear. The eye accommodates to a stimulus until the retinal image clarity is maximum and the physiological change that occurs especially change in refractive power and position of the crystalline lens during accommodation could be the main factor for the negative shift in spherical aberration during accommodation (Lopez-Gil, et al., 2010).

Buehren, Collins and Carney, (2003) and (2005) found changes in HORMS and spherical aberration following 60 and 120 minutes of reading respectively. In the current study, there was no significant change. The main difference between the above study and the current study is the task duration. The current study measured aberrations following 5 minutes of near task whereas Buehren, Collins and Carney, (2005) measured aberrations following 60 and 120 minutes of near task and postulated that increase in near work had a cumulative effect on the aberrations. The current study tested the effect of near work on aberrations only once following near work in the Indian cohort, but did not test with prolonged reading and so the cumulative effect theory could not be verified in these study subjects.

Collins, Buehren and Iskander, (2006) while assessing retinal image quality before and after two hours of reading, reported NITM magnitude of 0.31D among myopes and 0.15D among emmetropes following reading, whereas the current study subjects had a NITM magnitude of 0.21D among myopes and 0.07D of hyperopic shift among emmetropes (Study-1). Collins, et al. (2006) reported that the higher initial NITM magnitude among myopes may play a role in degrading the retinal image quality of myopic eyes compared to emmetropes. We speculate that since NITM magnitude in this study is comparable to the above mentioned value, the aberrations would have increased atleast temporarily, as it has been postulated that NITM is lenticular in nature (Vasudevan and Ciuffreda, 2008). However, there was a moderate positive correlation between NITM magnitude and HORMS, (r=0.41, n=24, p=0.04).The interactions between accommodative response (lead and lag) and image quality metrics (visual strehl ratio based on modulation transfer function (VSMTF)) were studied by Collins, Buehren and Iskander, (2006) who found a significant correlation between accommodative response and VSMTF. They postulated that the reason for the retinal image degradation could be due to the combined effect of higher order aberrations and NITM. The NITM characteristics in this study population are unique (studies 1 and 2), and revealed faster decay duration even after 60 minutes of reading near task. So I postulate that there would be no significant difference in aberrations even after prolonged near task in this study population.

Another study by Collins, et al. (2005) found a link between higher order aberrations and accommodation accuracy, and speculated that higher order aberrations associated with a near task may degrade the retinal image quality and that could have caused the difference in the accommodation behaviour among myopes. It could be hypothesised that the swift NITM decay in our study subjects (studies 1 and 2) could be influential in reducing the aberrations back to baseline levels quickly, though this needs further testing.

Contact lens correction will have affected the aberration measurements. The contact lenses were all the same brand so it is likely that similar small amounts of induced aberration would have been imposed across the myopes. Contact lenses were consistently worn throughout the study so it is not likely that CL wear would have impacted the change in aberrations between pre and post task variable. No significant difference in aberration in this study supports the above statement. Measurement of spherical aberration with contact lenses was not significantly variable in a study by Rae and Price, (2009).

Although a longer task duration was not investigated we could speculate that there may not be any difference in aberration even after longer periods of reading as NITM characteristics did not change much following prolonged near work (study 2).The lack of correlation between aberration and NITM supports this hypothesis. However, there could be changes in aberrations due to the narrow palpebral aperture during reading (Collins, et al., 2006) and so future studies should focus on investigating the relationship between NITM recovery and recovery of aberrations, by taking aberration and NITM measurements simultaneously during and after reading, along with lid aperture position.

5.7 Conclusion

Though at the pre task level there was a difference in spherical aberration and HORMS between emmetropes and myopes, aberrations did not change significantly following 5 minutes of near reading task in either emmetropes or myopes. There was no correlation between NITM and pre and post task HORMS.

Chapter 6

Results of study 4: Biometry measurements before and after 5 minutes of reading

6.1 Introduction

A transient increase in axial length has been reported with accommodation (Shum, et al., 1993; Bayramlar, et al., 1999; Mallen, et al., 2006; Read, et al., 2010; Richdale, et al., 2016). Apart from an increase in the axial length, the above studies demonstrated a transient decrease in anterior chamber depth and an increase in lens thickness with accommodation. Shum, et al. (1993) measured ocular biometry parameters on 106 subjects at 6m, 0.33m and 0.12m. They reported that axial length increased significantly at higher accommodative demand (8D). Bayramlar et al. (1999) while measuring biometry components before and after cycloplegia in the eyes of 124 subjects at 6m (distance) and 0.20m (near), reported an increase in axial length with cycloplegia (0.18mm) and without cycloplegia (0.17mm) and attributed the change in axial length to the accommodative convergence rather than the accommodation itself. It has been suggested that these transient changes associated with accommodation may play a role in the development of refractive error and may lead to permanent myopia (Drexler, et al., 1998; Mallen, et al., 2006). Drexler, et al. (1998) assessed the effect of accommodation in a group of (21-30 years of age) 11 emmetropic and 12 myopic eyes during monocular fixation at far and near. The near measurement was determined by the subjects amplitude of accommodation by moving the target from far to near and was fixated where the target did not blur. They reported elongation of eyes during accommodation that was more pronounced for emmetropes (12.7 μm) than myopes (5.2 μm). Mallen, et al. (2006) measured the degree of transient increase in axial elongation (19.4-23.6 years of age) with shorter periods of fixating accommodative stimuli at 0, 2, 4 and 6 D. In contrast to Drexler, et al. (1998), Mallen, et al. (2006) reported a greater increase in axial length among myopes (early onset myopes) (0.058 mm) compared to emmetropes (0.037 mm), especially at higher accommodative demands (6-D Stimulus).

Read, et al. (2010) investigated the influence of accommodation on axial length in 21 myopes and 19 emmetropes under 3 different accommodation demands (0 D, 3D and 6D) and reported that there was no difference in the magnitude of eye elongation in myopic and emmetropic subjects. The difference could be that Mallen, et al. (2006) used early onset myopes whereas Read, et al. (2010) used both late onset and early onset myopes. Also, the Mallen, et al. (2006) participants had a greater amount of myopia (-3.59 (±0.75) D) compared to Read, et al. (2010) (-1.8 (±0.8) D), suggesting that higher amounts of myopia are associated with greater accommodation induced axial elongation. Read, et al. (2010) further suggested that early onset myopes could be more prone to these changes during accommodation due to changes in scleral biomechanical properties. Richdale, et al. (2016) quantified changes in ocular dimensions associated with age, refractive error, and accommodative response in participants of 30-50 years and reported an increase in lens thickness (0.03 mm/yr) (using optical coherence tomography, magnetic resonance imaging and ultrasonography), steepening of anterior lens curvature (0.11 mm/year) (using phakometry) and decrease in anterior chamber depth (0.02 mm/year)(using ultrasonography) with age. They also reported that, for each dioptre of myopic refractive error, the vitreous chamber depth (0.34 mm/D) and height (0.09 mm/D) increased (using magnetic resonance imaging), demonstrating that myopia is associated with axial elongation rather than overall expansion. These changes in ocular dimensions with age and refractive error are of value to the field of refractive error development.

While the above studies measured biometry parameters during accommodation, the following studies measured it immediately after reading (Woodman, et al., 2010) and during and following reading (Alderson, et al., 2012). Woodman, et al. (2010) investigated the influence of prolonged near work upon axial length in a group of 20 myopes and 20 emmetropes. Axial length was measured before, immediately after and then again 10 minutes after 30 minutes of continuous near task at 5D accommodation demand. The change in axial length was greater in myopes (EOM (0.027±0.021mm) and progressing myopes (a change in spherical equivalent of -0.50D or more over the previous two years) (0.031±0.022mm)) compared to emmetropes (0.010±0.015mm) immediately following the near task, but not after 10 minutes of cessation of near task. Alderson, et al. (2012) studied the biometric changes in 10 adult participants during disaccommodation (after cessation of near task). Ocular biometric parameters of crystalline lens thickness and anterior chamber depth were measured with the LenStar device during the 1 minute task at 5D demand. Immediately after the cessation of the near task, post task biometry measurements were taken for 90 seconds. They reported an increase in lens thickness of 0.077 mm and decrease in anterior chamber depth of 0.049 mm during reading, with a decay time course of 7.7 seconds and 7.3 seconds for anterior chamber depth and lens thickness respectively to return to the baseline values, for participants who reported significant blurred distance vision (NITM). It is interesting to note that the increase in lens thickness (0.077 mm) was greater (Alderson, et al., 2012) than the increase in axial length among myopes (Woodman, et al., 2010). Though similar changes were reported for lens thickness and anterior chamber depth for participants who did not report significant blurred distance, rapid regression of accommodation (3.1 seconds and 3.4 seconds for anterior chamber depth and lens thickness respectively) back to baseline after cessation of the near task were reported compared to participants who reported blurred vision for distance.

Ostrin, et al. (2006) measured crystalline lens thickness in a cohort of 22 young adults and reported a linear relation between degree of myopia and an increase in lens thickness during accommodation where they demonstrated an anterior movement of the anterior lens surface and posterior movement of the posterior lens surface as refraction became more myopic using A-scan ultrasonography technique.

It is evident from the above studies that structural changes occur in the eye with accommodation and also there is a lack of information relating biometry changes and near induced transient myopia (NITM). Physiologically all the individuals would be myopic (NITM) immediately after performing near work (accommodation) and it is the recovery to the baseline (disaccommodation) that varies among refractive errors. From our results (studies 1 and 2), it was shown that NITM magnitude were comparable to other studies, however, the recovery time (decay duration) among Indian myopes was faster compared to other ethnicities both for shorter (study-1) and longer (study-2) near tasks. The purpose of this study was to investigate the changes in biometry parameters: axial length, corneal thickness, anterior chamber depth and lens thickness occurring immediately following a short term near task (5 minutes) among the cohort of myopes and emmetropes from study 1.

6.2 Apparatus

Ocular biometry measurements were collected with a Allegro Biograph (Wave-light AG, Erlangen, Germany) based on partial coherence interferometry.

6.3 Methods

The subjects (study-1) sat in the dark for 5 minutes to dissipate any residual accommodation (Ong and Ciuffreda, 1995). Following this, lights were turned on and the subjects were asked to place the chin in the chin rest of the Biograph and aligned in such a way that the biometry measurements (axial length, anterior chamber depth, lens thickness and corneal thickness) were taken at the centre of the pupil. Three measurements were taken for the right eye. All the subjects were tested for change in biometry parameters pre and post task under the same testing conditions (myopes wearing contact lens and emmetropes without – pre and post). The myopic subjects wore their optimal CL refractive correction during the measurements to ensure an equivalent optical stimulus. After the pre-task measurements, subjects were asked to read N12 target (Tennalirama story) with 90% contrast for 5 minutes at 5D. Immediately (approximately 2 seconds) after the reading task, the biometry measurements were taken again.

6.4 Statistical analysis

The mean of the three measurements were taken for analysis before and after reading. Repeated measures MANOVA was used to compare the biometry measurements pre and post reading task. Axial length, anterior chamber depth, lens thickness and corneal thickness were the parameters of interest. A Pearson product-moment correlation co-efficient was computed to assess the relationship between the NITM magnitude and Axial Length (AL) and the NITM magnitude and Lens Thickness (LT) among myopes. A posthoc power analysis was conducted using the software package, GPower (Faul and Erdfelder, 1992).

6.5 Results

The study participants who underwent the NITM measurements (study 1) also underwent measurements of biometry parameters and therefore share the same demographic details (Table 3.1).

The age of study subjects ranged between 18and 25 years with a mean (SD) of 20 ± 1.3 years for emmetropes and 19.63 ± 2.1 years for myopes. Mean spherical equivalent in the emmetropic group was 0.10D and in the myopic group was -3.32D. Please refer to Table 3.1 for the demographic details.

The power using a two-tailed test with α = 0.05 and N=24 is ≈ 95% for axial length (0.02 mm), corneal thickness (15.6 µm) , aqueous depth (0.01mm) and lens thickness (0.01mm).

Mean and standard deviation (SD) of biometry measurements for emmetropes and myopes pre and post task are shown in Table – 6.1. Figures 6.1, 6.2, 6.3 and 6.4 show the pre and post task axial length (mm), corneal thickness (µm), anterior chamber depth (mm) and lens thickness (mm) for emmetropes and myopes following 5 minutes of reading.

Table – 6.1 Pre and post task biometry measurements for emmetropes and myopes

Biometry Parameters	Emmetropes pre-task	Emmetropes post-task	Myopes pre-task	Myopes post-task
Axial Length (mm)	22.69±0.85	22.68±0.85	24.31±0.74	24.35±0.74
Corneal Thickness (μm)	531.79±42.36	526.21±38.04	605.63±39.92	601.88±40.87
AC Depth (mm)	2.92±0.19	2.90±0.19	3.19±0.23	3.17±0.22
Lens Thickness (mm)	3.62±0.25	3.63±0.25	3.57±0.46	3.58±0.46

Figure 6.1: Pre and post task axial length for emmetropes and myopes. Error bars indicate ±1 SEM.

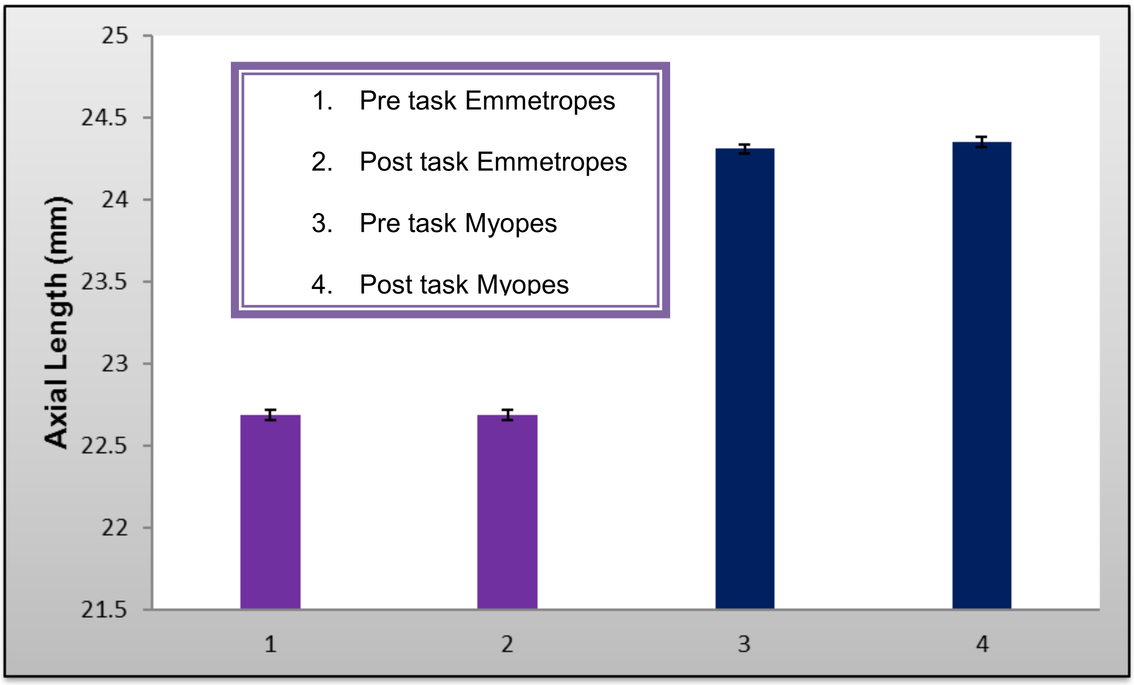


Figure 6.2: Pre and post task corneal thickness for emmetropes and myopes. Error bars indicate ±1 SEM.

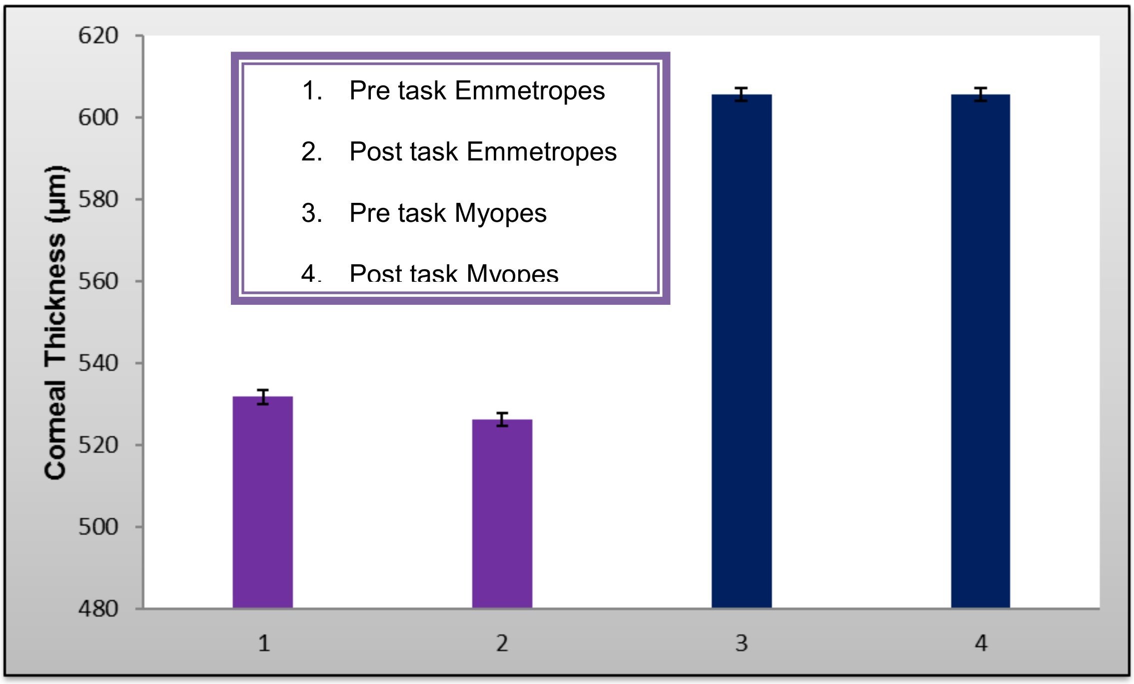


Figure 6.3: Pre and post task anterior chamber depth for emmetropes and myopes. Error bars indicate ±1 SEM.

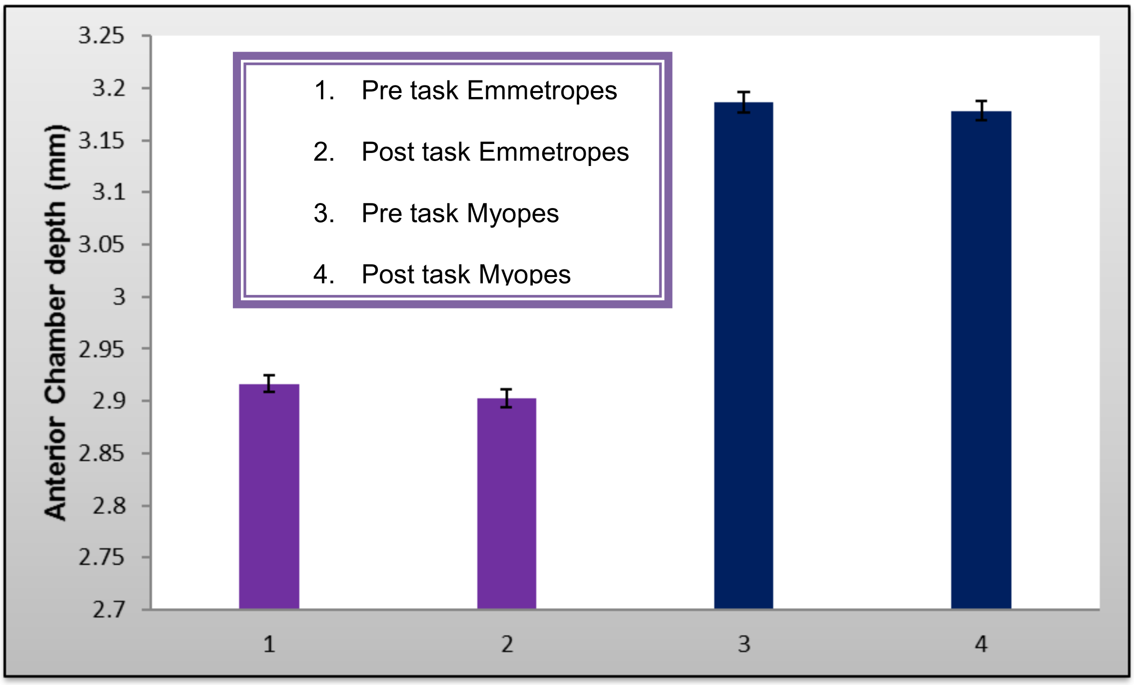
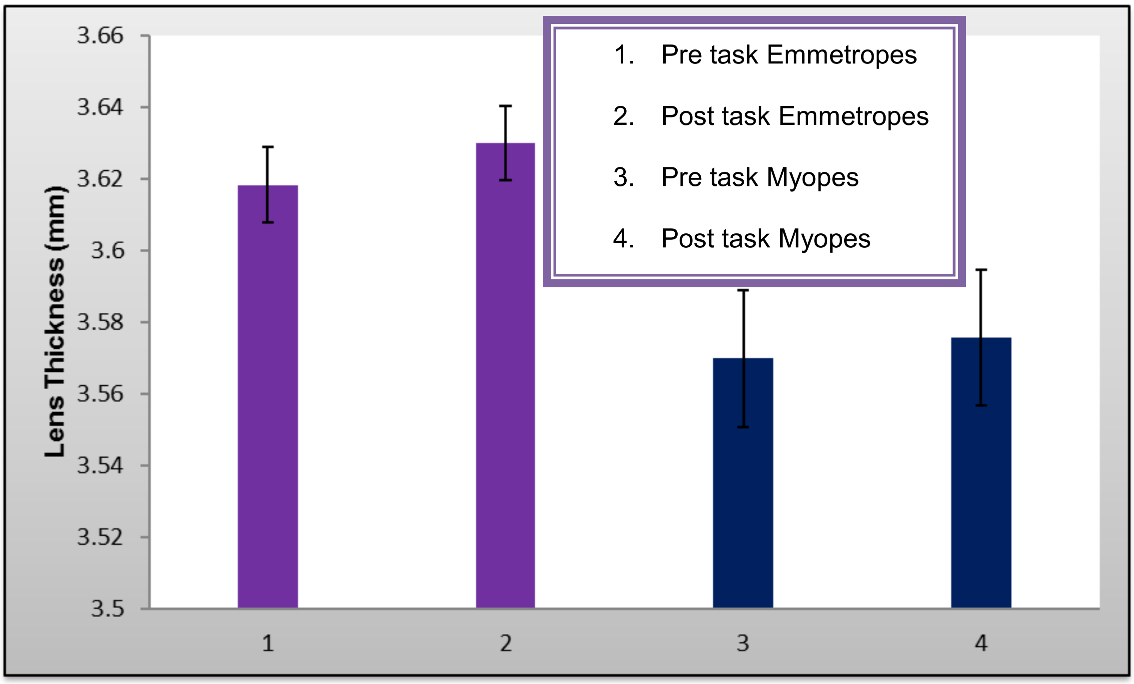


Figure 6.4: Pre and post task lens thickness for emmetropes and myopes. Error bars indicate ±1 SEM.



Pre task

There was a significant main effect of refractive group at the multivariate level in the RM MANOVA, F (12, 235.76) = 10.30, p<0.0005; Wilk's Λ = 0.328, partial η^2 = 0.31. The Univariate F tests showed there was a significant difference between refractive groups in axial length, (F (3, 92) = 33.72; p<0.0005; partial η^2 = 0.52), corneal thickness, (F (3, 92) = 45.44; p<0.0005; partial η^2 = 0.47) and anterior chamber depth, (F (3, 92) = 0.59; p<0.0005; partial η^2 = 0.30) but not for crystalline lens thickness, (F (3, 92) = 0.16; p=0.92; partial η^2 = 0.005).

Post hoc Bonferroni pair-wise comparisons with a conservative (p value 0.05/16 = 0.003) showed a significant difference in pre task axial length between emmetropes and myopes (p <0.0005, mean difference (SD): -1.62 (0.23); 95% CI: -2.22 to -1.01), in pre task corneal thickness between emmetropes and myopes (p<0.0005, mean difference (SD): -73.83 (11.64); 95% CI: -104.29 to -43.37) and in pre task anterior chamber depth between emmetropes and myopes (p< 0.0005, mean difference (SD): -0.27 (0.06); 95% CI: -0.43 to -0.10).

Post task

Post hoc Bonferroni pair-wise comparisons with a conservative (p value 0.05/16 = 0.003) showed a significant difference in post task axial length between emmetropes and myopes (p <0.0005, mean difference (SD): -1.66 (0.23); 95% CI: -2.26 to -1.06), in post task corneal thickness between emmetropes and myopes (p<0.0005, mean difference (SD): -75.66 (11.64); 95% CI: -106.12 to -45.20) and in post task anterior chamber depth between emmetropes and myopes (p< 0.0005, mean difference (SD): -0.28 (0.06); 95% CI: -0.44 to -0.11).

Change in biometry parameters following the reading task

The difference between pre and post task amounts of AL, CT, ACD and LT were calculated.

Post hoc Bonferroni pair-wise comparisons did not reveal any difference between pre and post task axial length, corneal thickness, anterior chamber depth and crystalline lens thickness among emmetropes (p = 0.98, mean difference (SD): 0.005 (0.23); 95% CI: -0.45 to 0.46), (p = 0.96, mean difference (SD): 5.58 (11.64); 95% CI: -24.87 to 36.04), (p = 0.83, mean difference (SD): 0.01 (0.06); 95% CI: -0.11 to 0.13), (p = 0.91, mean difference (SD): -0.01 (0.11); 95% CI: -0.22 to 0.19) and myopes (p = 0.86, mean difference (SD): -0.41 (0.23); 95% CI: -0.49 to 0.42), (p = 0.98, mean difference (SD): 3.75 (11.64); 95% CI: -26.71 to 34.21), (p = 0.89, mean difference (SD): 0.008 (0.06); 95% CI: -0.11 to 0.13), (p = 0.95, mean difference (SD): -0.005 (0.10); 95% CI: -0.21 to 0.20) respectively.

A Pearson product-moment correlation co-efficient was computed to assess the relationship between the NITM magnitude and axial length among myopes. There was no correlation between NITM magnitude and change in axial length, (r=-0.14, n=22, p=0.53) and NITM magnitude and change in lens thickness, (r=-0.38, n=22, p=0.08). A scatter plot summarizes the results (Figures 6.5 and 6.6).

Figure 6.5: Correlation between NITM and Axial Length

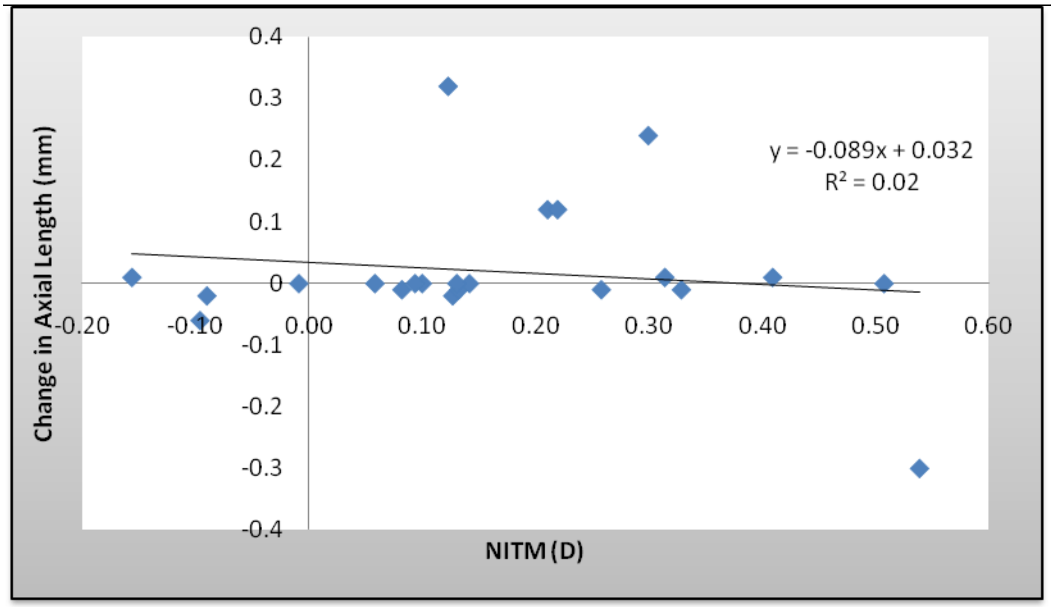
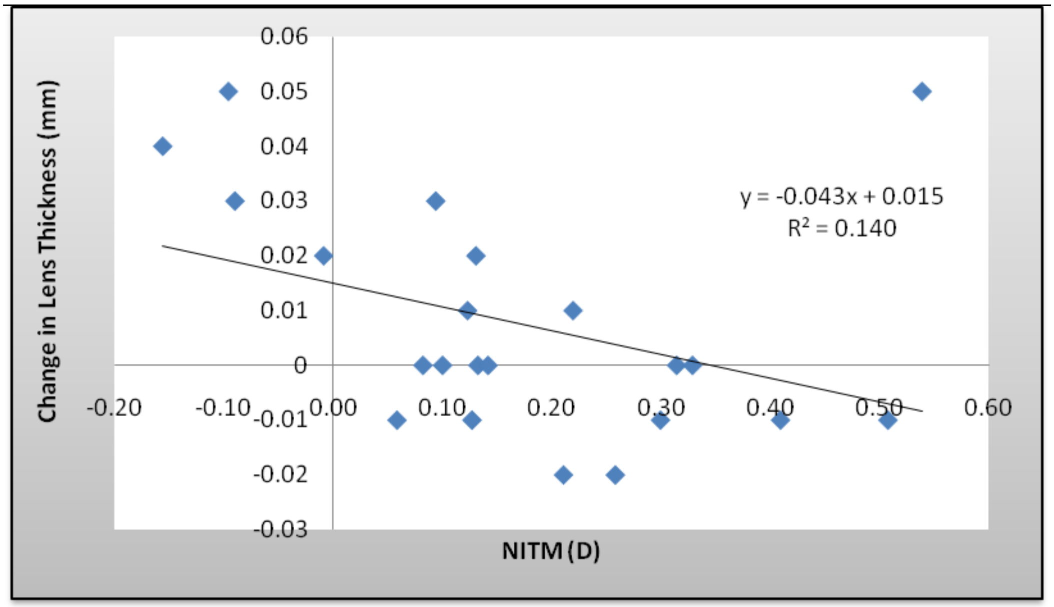


Figure 6.6: Correlation between NITM and Lens Thickness



6.6 Discussion

As expected, there was a difference in axial length, corneal thickness and anterior chamber depth between myopes and emmetropes at the pretask baseline, and this difference did not change following 5 minutes of near task in this study's subjects. There was no significant change in axial length, corneal thickness and anterior chamber depth after near viewing. Though a transient change in axial length during accommodation has been reported previously (Drexler, et al., 1998; Mallen, et al., 2006; Ostrin, et al., 2006; Bolz, et al., 2007; Read, et al., 2010; Woodman, et al., 2010), the mechanism that contributes to this change still remains unclear.

Mallen, et al. (2006) reported a transient increase in axial length during accommodation in both emmetropic and myopic subjects. Greater transient increase in axial length was reported in myopic subjects compared to emmetropes for a higher accommodative stimulus of 6D.The change in axial length between pre and post task in our myopic study subjects was smaller than Mallen, et al. (2006) and we speculate that this could be due to the faster decay in our study subjects (study 1). Also, this study did not further classify myopes as early and late onset and also the accommodative stimulus used was 5D.

One study measured biometry following 30 minutes of near task at 5D (Woodman, et al., 2010) and reported that with accommodation, there was an increase in axial length and lens thickness and a decrease in anterior chamber depth. They have reported that myopes, especially progressing myopes are more likely to exhibit this transient ocular elongation. They also reported that the choroidal thickness decreased with accommodation especially for myopes. They attributed the temporary change in axial length immediately after the near task to the near induced transient myopic effect due to the near task (NITM). The NITM could be lenticular and or axial. The percentage change relative to pre-test value of lens thickness was marginally high (0.28%) compared to axial length (0.16%) in this study, but this change in lens thickness was not statistically significant. The main difference between the Woodman, et al. (2010) study and the current study is the task duration. Woodman, et al. (2010) measured biometry parameters following 30 minutes of near work whereas the current study measured biometry parameters following 5 minutes of near work.

Reported NITM studies including our previous studies (1 and 2) have found that myopes have different NITM effects compared to non-myopes. Though this study did not measure biometry parameters during reading, I hypothesize that the biometry parameters changed during accommodation and then recovered quickly, aligning with faster NITM recovery in the same subjects (study – 1). When Woodman, et al. (2010), measured axial length immediately after the near task, they found changes in axial length compared to the baseline. But when measured 10 minutes after the cessation of the near task, the axial length had returned to the baseline levels. This suggests that the structural changes with accommodation may be associated with the temporary myopic effect immediately following a near task (NITM). Since the mean NITM magnitude in Woodman, et al. (2010) study following 30 minutes of near task was 0.19D and the mean NITM magnitude in this study following 5 minutes of near task (study-1) was 0.21 D, and since the above values were comparable, a similar ocular change could have occurred. This transient elongation may be due to the effect of contraction of smooth ciliary muscle into the choroid and sclera.

The decay duration for myopes and emmetropes in (study-1 and 2) was faster than found in Caucasian population (Ehrlich, 1987; Owens and Kelly, 1987; Arunthavaraja, 2010). The faster decay dynamics in this population may possibly explain the presenting axial length recovery. This needs further work to establish the relationship between the decay time constant and axial length recovery following accommodation by measuring axial length and accommodative response continuously during and following a short and prolonged near task.

6.7 Conclusion

Unsurprisingly there were differences in the current study in ocular biometry parameters especially in axial length, anterior chamber depth and corneal thickness between myopes and emmetropes at the pre and post task level. There was a very small increase in axial length among myopes following reading, but not for emmetropes, although this difference was not statistically significant. Further studies should be performed with longer task duration with biometry parameters measured continuously during and after the cessation of near work, to confirm the relationship of NITM recovery and biometry parameter.

Chapter 7

Results of study 5: NITM parameters in pre and post LASIK refractive surgery

7.1 Introduction

LASIK (Laser-assisted in situ keratomileusis), is a type of refractive surgery for the correction of myopia, hypermetropia and astigmatism. The corneal surgeon uses a surgical tool called a microkeratome (instrument which contains a disposable blade to cut the cornea) to create a thin, circular "flap" in the cornea. The surgeon then folds back the flap to access the underlying cornea (stroma) and removes some corneal tissue using an excimer laser. An excimer laser is an instrument which uses ultraviolet light to remove (ablate) tissue from the cornea to reshape it, as the goal of the surgery is to flatten the cornea for myopes. Following removal of the tissue the flap is replaced back and the cornea is allowed to heal naturally. Currently, bladeless femtosecond lasers are being used in corneal and refractive surgery for accuracy, safety and repeatability. Femtosecond lasers emit radiation at 1053 nm wavelength to remove the tissue with minimal damage. Advantages of femtosecond assisted laser over conventional microkeratome include reduced dry eye symptoms, reduced risk of flap complications and a substantial improvement in the patient's quality of life (Aristeidou, et al., 2015).

LASIK is considered to be safe for the correction of myopia, although complications may occur in approximately 5% of cases, but it rarely leads to more than a 2 line loss of VA postoperatively below 6/12 (Reinstein, et al., 2011). Compared to the older techniques of radial keratotomy (RK) and photorefractive keratectomy (PRK), the complications (dry eyes, glare, and halos) are less and the pain recovery is faster with LASIK surgery (Shortt, Allan and Evans, 2013). With 16.3 million LASIK procedures performed worldwide (2009), 95.4% of the patients were satisfied with their outcome following LASIK surgery (Taner, et al., 2013).

Studies (McBrien and Millodot, 1986b; Bullimore and Gilmartin, 1987a; Gilmartin and Bullimore, 1991; Gwaizda, et al., 1993; Strang, et al., 1994; Allen and O'Leary, 2006) have shown that the accommodation responses are different for myopes compared to non-myopes. Myopes exhibit more NITM magnitude compared to hypermetropes and emmetropes (Ong and Ciuffreda, 1995; Ciuffreda and Wallis, 1998; Schmidt, et al. 2005; Lin, et al. 2012). Though the NITM magnitude in Indian subjects (studies 1 and 2) is relatively low it is comparable to other ethnicities.

Lin, et al. (2013) measured NITM in a group of 43 anisometropic (SE ≥ 1.00D difference between eyes) subjects who had visual acuity of 6/6 in each eye with normal binocular vision. Though the subjects were asked to look at the complex pictures binocularly, measurements were taken for one eye at a time for 5 minutes at a 5D viewing distance. The authors were comparing the less myopic and more myopic eye among anisometropes and repeated the experiment for the other eye with a gap of 25 minutes in-between each eye's measurements. Refraction was assessed for each eye immediately after completion of the near task. The refractive error (SE) in the more myopic eye was -3.37 ± 1.57D and the less myopic eye was -1.33 ± 1.66D. The authors reported that the more myopic eye exhibited a greater mean initial NITM magnitude and extended decay (0.21 D and 108.4s) compared to the less myopic eye (0.15D and 87s). They suggested that there could be peripheral accommodative apparatus differences between each eye of the anisometrope, rather than the NITM response being mediated at a central neurological area, which is unlikely to have caused the accommodative system to drive differently in each eye, resulting in an increased NITM response in one eye compared to the other eye. They reported that the ciliary muscle was longer and thicker in more myopic eyes and axial length was positively correlated with ciliary body thickness. They stated that all or any of the above might be a factor in this inter-ocular peripheral NITM phenomenon. The change of retinal image quality with accommodation, secondary to the differences in retinal image size (aniseikonia) and clarity (anisometropia) are known to affect accommodation and vergence performance (Bharadwaj and Candy, 2011) and this could also have affected the NITM.

Guo-Tao and Ya-Jie, (2012) investigated the changes in accommodative status following LASIK in a group of 60 myopes, aged 18 to 35 years. The objective of this study was to investigate the relationship between accommodation status and asthenopia following LASIK surgery. They measured the accommodative amplitude with optical correction prior to Lasik surgery. The baseline accommodative amplitude was 9.25±0.35D and 9.60±0.37D monocularly and binocularly respectively prior to the surgery. After LASIK, the accommodative amplitude decreased (7.82±0.58D and 8.10±0.54D monocularly and binocularly respectively) in the first week and then recovered gradually (9.14±0.37D and 9.43±0.38D monocularly and binocularly respectively), due to the new accommodative status (as there is a shift in the focal plane) and an increase in accommodative response of the newly adapted emmetropic status. The study reported that the asthenopic symptoms following surgery could be related to the change in accommodative amplitude.

Prakash, et al. (2007) assessed the effect of LASIK eye surgery on the AC/A ratio in a cohort of 61 myopic subjects. As AC/A ratio is an established method to assess the relationship of accommodation and convergence, they analysed the effect of bilateral LASIK on the AC/A ratio. They reported that AC/A ratio decreased initially (first week) and recovered to near pre-operative values between 3 months and 9 months following the surgery.They further stated that the initial decrease could be due to the additional accommodative effort to produce the same amount of convergence in the newly adapted emmetropic eye, with a subsequent increase as there was improvement in the quality of accommodative effort increasing the amount of convergence produce per unit of accommodation.

It has been well documented that the accommodative responses vary among myopes compared to emmetropes. Myopes, in particular progressing myopes, tend to accommodate less especially for near targets compared to emmetropes (Gwiazda, et al., 1993; 2005). The differences in accommodation pre and post Lasik, suggests that NITM among subjects undergoing LASIK surgery may have different accommodative characteristics (lens) before and after surgery. To test if this hypothesis is true, accommodation measurements were carried out prior to (myopic) and following (emmetropic) LASIK refractive surgery in young Indian myopic adults.

Few studies (Fledelius, 1981; Maddock, et al. 1981; McBrien and Millodot, 1986a; Lekha, et al., 2005; Maheshwari, et al., 2011) have reported that myopes have relatively high amplitudes of accommodation. Some others (Zhai and Guan 1988; Fong, 1997; Allen and O'Leary, 2006) have reported that myopes have relatively low amplitudes of accommodation. Other studies have shown no difference in amplitude of accommodation among refractive groups (Gawron, 1980; Fisher, Ciuffreda and Levine, 1987; Mantyjarvi, 1987). Emmetropic children who became myopic were found to be more esophoric at near with elevated AC/A ratios compared to those who remained emmetropic (Jiang, 1995). Studies have shown reduced distance accommodative facility in myopes when compared to emmetropes (O'Leary and Allen, 2001; Allen and O' Leary, 2006; Pandian, Sankaridurg, Naduvilath, et al., 2006; Radhakrishnan, Allen and Charman, et al., 2007; Allen, et al., 2013), but not for near accommodative facility. Myopic subjects have been reported to exhibit a larger lag of accommodation, especially at a higher stimulus, compared to emmetropes (Gwiazda, et al., 1985; 1998). Larger lags in accommodation could lead to degradation in the quality of retinal image by producing hypermetropic defocus and may result in elongation of axial length of the eye and myopia. This peripheral hypermetropic defocus which lies behind the prolate retina may stimulate axial growth of the eye towards the defocus (Gwiazda, et al., 1993; Gwiazda, et al., 1995; Jiang, 1997; Abbott, et al., 1998). It is not clear if lag of accommodation occurs as an accompaniment (Gwiazda, et al., 1985; 1998), prior (Goss, 1991, Portello, Rosenfield and O' Dwyer, 1997) or after (Rosenfield, Desai and Portello, 2002; Mutti, et al., 2006) the onset of myopia.

Currently there is paucity of literature on other accommodative parameters following LASIK refractive surgery. So a range of accommodative and vergence parameters including NITM were compared pre and post Lasik surgery. To the best of my knowledge, this is the first study to report a range of accommodative measures in LASIK subjects pre and post procedure.

7.2 Methods

Subjects who visited Sankara Nethralaya tertiary eye hospital, Chennai, India, for refractive surgery were recruited. All the subjects gave written informed consent for taking part in the study, which followed the tenets of the Declaration of Helsinki. This study was approved by a separate institutional review board (Vision Research Foundation, Chennai, India) and ethics committee. Pre-Lasik, all the subjects underwent a detailed ocular examination including objective and subjective refraction, slit lamp examination, dry eye testing, pupillary evaluation, pachymetry, keratometry, corneal topography and wavefront analysis.

Also the following accommodation and vergence functions were measured,

- Near point of convergence (NPC),
- Amplitude of accommodation ,
- Accommodative facility and
- Accommodative lag

(All the subjects were given training prior to each test to ensure that they understood the test and the details of these procedures are described in chapter-2).

Pre Lasik NITM measurement (NITM paradigm – study 1)

The subjects sat in the dark for 5 minutes to dissipate any pre-existing transient accommodative effects (Ong and Ciuffreda, 1995). Following this, they were asked to look at a logMAR chart at 3m and distance refraction readings were recorded continuously using a

WAM-5500, open field auto-refractor for 1 minute for the right eye and averaged. The subjects read a N12 target (Tennalirama story) with 90% contrast for 5 minutes at 0.2m. Immediately after the task, NITM measurements were taken for 120 seconds. Though the decay duration was faster in study-1 & 2, this study maintained 120 seconds of post-task measurements to confirm the same in a separate myopic cohort.

LASIK

LASIK was performed under topical anaesthesia (proparacaine 0.5%). A flap with a diameter of 9.0 mm and a thickness of 130 ± 20 μm was created with a superior hinge by means of the Supratome (Schwind, Kleinostheim, Germany). For the photo ablation, a medical scanning spot eximer laser system (Allegretto, Wavelight, Erlangen, Germany) was used. This device includes a fast eye tracking system (reaction time delay 6 ms), and a laser with a repetition frequency of 500 Hz and Gaussian spot profile with an ablation diameter of 0.1 mm. The ablation pattern calculated from the wavefront deviation map had a circular full correction area with a diameter of 7.0 mm (ablation optical zone), surrounded by a transition zone of 1.0 mm. After photo ablation, the flap was repositioned and the interface was rinsed with balanced salt solution; Vigamox, Lotepred and refresh tears were used post operatively.

The LASIK procedure was performed by specialized Corneal Refractive surgeons (Dr.Prema Padmanabhan and Dr.R. R. Sudhir) who had 5 years or more experience in performing the procedure.

Figure 7.1 Corneal refractive surgery being performed using the eximer laser system (Allegretto, Wavelight, Erlangen, Germany)

Post LASIK

All the subjects underwent a detailed ocular examination after one month. The assessments included subjective refraction, corneal topography and slit lamp examination. The pre-operative procedures were performed by two Optometrists who had 5 or more years of experience in a LASIK clinic and the other outcome parameters were performed by me only.

The NITM measurements and binocular vision assessment were repeated by myself, at least one month after refractive surgery (30 to 65 days). Out of the total 29 subjects, the measurements for 26 subjects were taken between 31 to 43 days and for the remaining 3 subjects between 51 to 64 days and the same (study-1) NITM protocol was followed for all.

Paired t-tests were used to evaluate changes in NITM magnitude, and accommodative parameters pre and post LASIK refractive surgery. Near point of convergence (NPC- cm), Amplitude of accommodation (D), Accommodative facility (AF – cycles/minute) and Lag of accommodation (dioptres) were evaluated.

7.3 Results

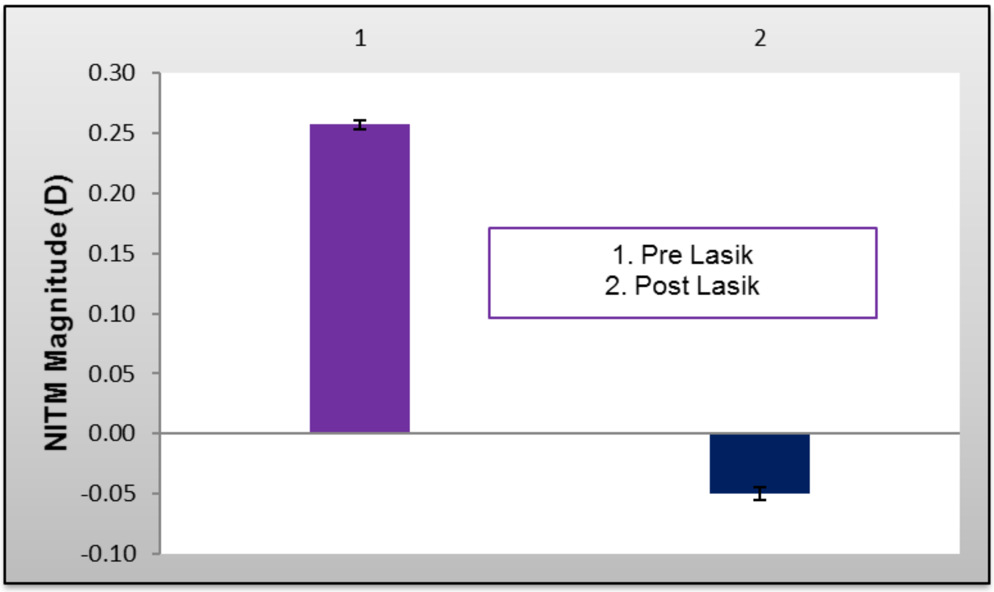
The subjects were 21 to 35 years with an average of 26.1±3.5 years. The spherical equivalent range was -2.00D to-7.75D with a mean spherical equivalent of -3.86D ± 1.57D with a corneal astigmatism of ≤ 1.00D.The mean NITM magnitude and decay time constants for myopic subject's pre and post LASIK refractive surgery are shown in Table 7.1

Table - 7.1: Mean and standard deviation of NITM magnitude (dioptres) for myopic subject's pre and post LASIK refractive surgery. A positive magnitude value indicates a myopic shift in refractive error.

	Magnitude (D)
Pre LASIK	0.26 ± 0.12
Post LASIK	-0.05 ± 0.15
p-value	p<0.001

A paired samples t test revealed that NITM magnitude was significantly more before (M=0.26D, SD=0.12) than after the LASIK surgery (M=-0.05D, SD=0.15), t (28) =-9.50, $p<0.001$). The decay time constant was 2.98 ± 2.1 seconds for myopes before the surgery. As there was a hypermetropic shift following surgery, the decay time was not calculated.

Figure 7.2: Pre and post Lasik: NITM magnitude (D). Error bars indicate ±1 SEM.



The mean binocular vision parameters pre and post LASIK refractive surgery are shown in Table – 7.2. A positive value indicates a myopic shift and a negative value indicates a hyperopic shift in refractive error.

Table – 7.2: Mean and standard deviation of binocular vision parameters for myopes pre and post LASIK refractive surgery.

	NPC (cm)	AA (D)	AF (Cycles/sec)	Lag(D)
PreLASIK	5.62 ± 1.71	12.18 ± 2.02	8.65 ± 2.74	0.77 ± 0.51
PostLASIK	7.96 ± 1.63	10.27 ± 2.24	10.70 ± 2.29	0.38 ± 0.38
p-value	p<0.001	p<0.001	p<0.001	p<0.001

Statistically significant differences were obtained for binocular vision parameters. NPC significantly increased post LASIK (t (28) = -5.55, p<0.001), AA significantly decreased post Lasik (t (28) = -4.18, p<0.001), AF significantly increased post Lasik (t (28) = -3.6, p=0.001) and Lag of accommodation significantly decreased post Lasik (t (28) = 3.73, p=0.001). These changes are graphically represented in Figures 7.3, 7.4 , 7.5 and 7.6.

Figure 7.3: Pre and post Lasik: Near Point of Convergence (cm). Error bars indicate ±1 SEM.

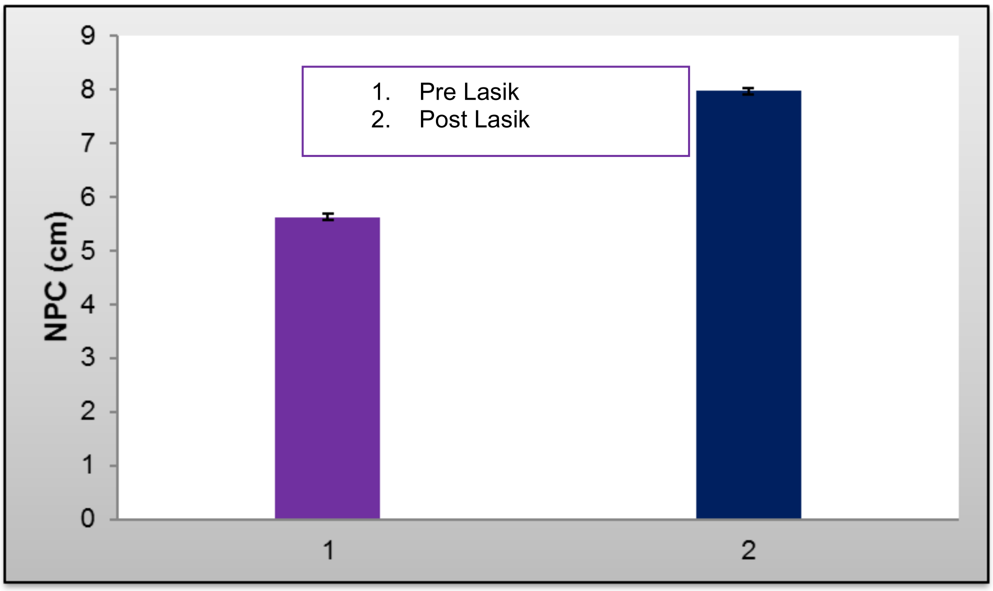


Figure 7.4: Pre and post Lasik: Amplitude of Accommodation (D). Error bars indicate ±1 SEM.

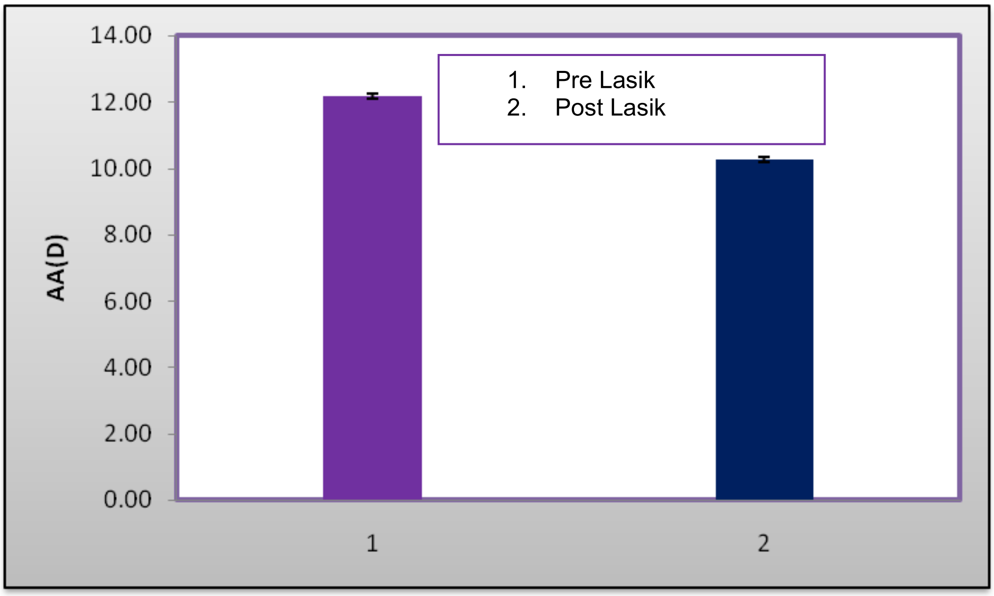


Figure 7.5: Pre and post Lasik: Accommodative Facility (cycles/sec). Error bars indicate ±1 SEM.

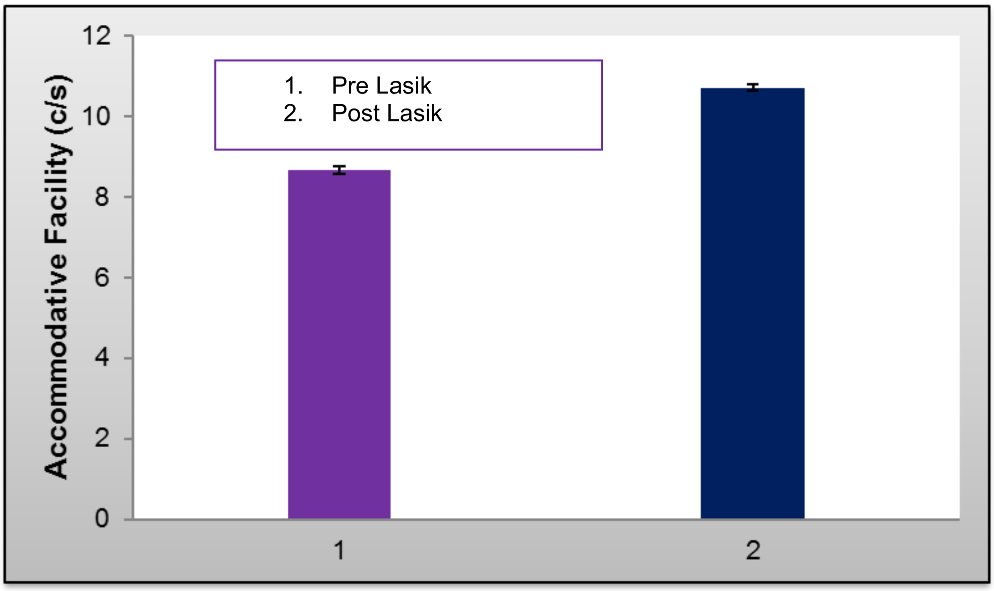
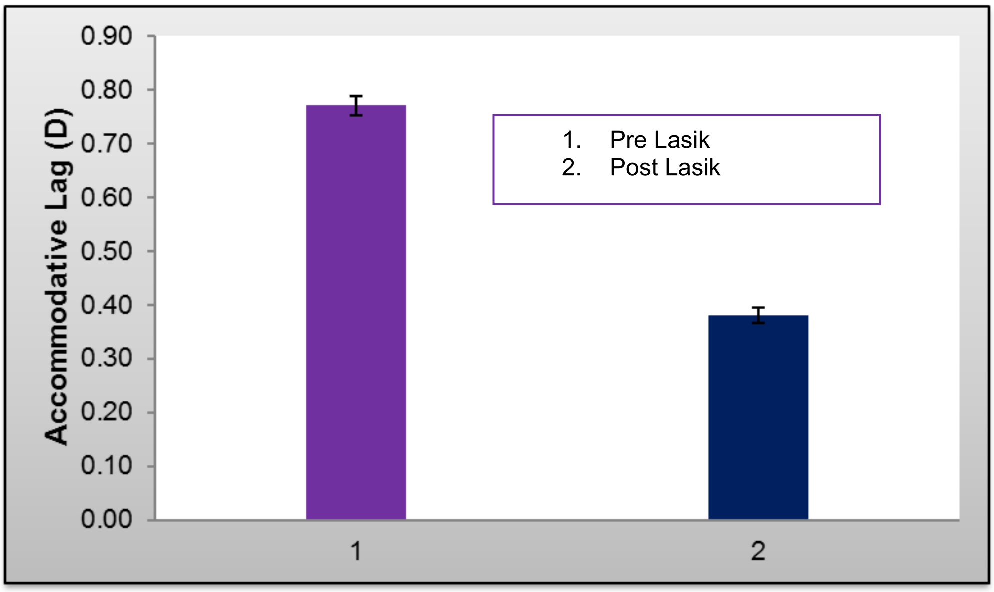


Figure 7.6: Pre and post Lasik: Lag (D). Error bars indicate ±1 SEM.



7.4 Discussion

7.4.1 NITM pre and post Lasik surgery

NITM magnitude was significantly higher before LASIK surgery than following the surgery. The decay time constant was found to be 2.98 seconds for myopes before the surgery. Since there was a hypermetropic shift the decay time constant was not calculated following the surgery. Ciuffreda and Wallis, (1998) reported 0.35D of NITM magnitude after 10 minutes of reading at 0.2m, Arunthavaraja, (2010) reported 0.32D of NITM magnitude after 10 minutes of reading at 0.12m, and Lin, et al. (2013) reported 0.21D of NITM magnitude after 5 minutes of reading at 0.2m. In study1, after 5 minutes of reading, NITM magnitude was 0.21D and in study-2, after 60 minutes of reading, NITM magnitude was 0.31D among myopes. From the above studies, it is clear that although NITM magnitude in this study is relatively low, it is comparable with other populations and Indian subjects, prior to the LASIK surgery when the subjects were in myopic state. After the surgery the LASIK induced a state of emmetropia (0.01 ± 0.5 DS) in patients who were previously myopic. Also, concurrent changes in binocular vision parameters could have influenced the decrease in NITM magnitude which is discussed in detail below.

This study confirmed in a separate cohort that the decay time constant in myopic Indian subjects was faster than other ethnicities (Table 7.3). In a Chinese population, the decay time constant was 108.4 seconds after 5 minutes of near task performed at 0.2m (Lin, et al. 2013). In a US population it was 63 seconds after 10 minutes of near task performed at 0.2m and 68.2 seconds after 10 minutes of near task performed at 0.12m. However, in study 1, the decay constant was 6.07 seconds after 5 minutes of near task performed at 0.2m and 8.16 seconds after 60 minutes of near task performed at 0.25 to 0.3m. In the current study, the decay constant was 2.98 seconds after 5 minutes of near task performed at 0.2m. A decay time constant was not calculated following surgery as there was hypermetropic shift. From the above, it is evident that the decay time constant is faster in this study subjects like in study-1 and 2 compared with other published studies. These subjects may have a faster sympathetic response compared to other ethnic groups (Ciuffreda and Wallis, 1998). The faster decay time constant among these subjects may indicate a reduced susceptibility to myopia development in this population. As the underlying reason for a lower prevalence of myopia in India is yet to be determined, further research should be carried out to investigate the relationship between NITM characteristics and myopia progression, and also NITM characteristics and onset of myopia which may possibly explain the protective mechanism in this population.

Table 7.3: Studies showing decay in myopes with differing task duration

Studies	Decay (secs)	Task duration - task distance
Ciuffreda and Wallis (1998)	63	10 minutes - 20 cms
Arunthavaraja (2010)	68.2±9.1	10 minutes - 12 cms
Lin et al. (2013)	108.4±64.3	5 minutes - 20 cms
Study I	6.07±7.11	5 minutes - 20 cms
Study II	8.16±10.83	60 minutes - 25-30 cms
Current study	2.98±2.18	5 minutes - 20 cms

7.4.2 Binocular vision parameters pre and post LASIK surgery

7.4.2.1 Accommodation parameters

7.4.2.1.1 Lag of accommodation

This study measured lag of accommodation prior to and after the surgery, and found that the lag of accommodation was significantly higher prior to (myopic state) compared to following the surgery (emmetropic state).

When a target is presented, most individuals accommodate less than is actually needed to bring the target into focus. This under-accommodation is termed as lag of accommodation and is calculated by the difference between the accommodative stimulus and the measured accommodative response. Lag of accommodation for near has been reported to be higher among myopes than emmetropes (Gwiazda, et al., 1993). However, there are discrepancies in the literature on the relationship between accommodative lag and the onset of myopia. Gwiazda, et al. (2005) reported that emmetropes who became myopes had elevated AC/A ratios and increased lag of accommodation before the onset of myopia than those who remained emmetropic. In contrast, Mutti, et al. (2006) measured accommodative lag before and after onset of myopia and accommodative lag was not elevated during the year of onset, but higher lag was found after their onset and it was highest among Asians.

A larger lag of accommodation in association with near work has been shown to be a risk factor in the development and progression of myopia. A possible consequence of the reduced accommodation to near targets especially during prolonged reading is that it may lead to increased axial eye growth due to extended periods of retinal defocus (Gwiazda, et al., 2004).

NITM magnitude was also higher prior to the surgery but not following the surgery. A Pearson product-moment correlation was calculated to assess the relationship between the NITM magnitude and lag of accommodation. There was a weak non-significant correlation between NITM magnitude and lag of accommodation ($r=-0.11$, $n=29$, $p=0.54$). As stated above, myopes tend to have more lag of accommodation for near compared to non-myopes, where the plane of best focus is behind the retina (hyperopic defocus), which is a stimulant to eye growth that moves the retina towards the point of best focus. When myopes look at far immediately after reading, depending on the magnitude of the lag of accommodation, the response time to focus the distance objects clearly could vary. Also the fact that myopes accommodate less accurately compared to emmetropes suggests that there could be a link between hypermetropic defocus and accelerated growth (Gwiazda, et al., 1993). Another possibility for increased lag prior to the surgery could be that the myopes do not appreciate the blur fully due to sensory deficit and by increasing the depth of field (Ong and Ciuffreda, 1995). In this study all were stable myopes prior to the surgery and with the increase in lag of accommodation for near following the surgery, I speculate that the above mechanisms may not be applicable to these study subjects.

Blur is the main stimulus driving the accommodative system. As myopes tend to have increased blur tolerance, the response time to focus any target clearly may be more when looking from near to far compared to non-myopes. This could be the reason for the increased NITM magnitude for myopes before the surgery. Also, increased accommodation and convergence effort are required when wearing contact lenses in the myopic state (Jimenez, et al., 2011). In contrast, as LASIK induces a state of emmetropia in a patient with previous myopia, the blur which was the main stimulus prior to the surgery in myopic state has been eliminated and could be the reason for the disappearance of NITM following the surgery.

7.4.2.1.2 Amplitude of accommodation

In this study, the accommodative amplitude decreased from 12.18 ± 2.02 to 10.27 ± 2.24 (D) after one month. However, there is discordance in the literature on accommodative parameters following LASIK surgery compared to the baseline values before surgery. Guo-Tao and Ya-Jie, (2012) reported that accommodative amplitude decreased binocularly from 9.60±0.37D to 8.10±0.54D in the first week, and returned to 9.43±0.38D after one month.

Following surgery, the near point has receded and that could be the reason for the decrease in amplitude of accommodation in this study. There was a weak non-significant correlation between NITM magnitude and amplitude of accommodation (r=-0.11, n=29, p=0.54).

7.4.2.1.3 Facility of accommodation

The accommodative facility rate increased by approximately 2-3 cycles/minutes at the one month post-operative visit compared to the baseline values prior to the surgery in this study.

Studies have shown reduced distance accommodative facility in myopes when compared to emmetropes (O'Leary and Allen, 2001; Allen and O' Leary, 2006; Pandian, Sankaridurg, Naduvilath, et al., 2006; Radhakrishnan, Allen and Charman, et al., 2007). Zellers, Alpert and Rouse, (1984) measured accommodative facility for near (0.4 m) on 100 non presbyopic subjects and reported normative values as 11.59 (right eye), 11.09 (left eye) and 7.72 cycles/minute for both eyes. In the current study the accommodative facility for near prior to the surgery was 8.65±2.74 cycles/minute and 10.70±2.29 cycles/minute following the surgery, and cannot be directly compared to Zellers, Alpert and Rouse, (1984) study as they did not classify their subjects based on refractive error. However, the current study can be compared with Allen and O' Leary, (2006) as they classified their subjects based on refractive error. They reported 13.69±5.93cpm for emmetropes and 12.62±5.07cpm for myopes monocularly and 10.03±6.19cpm for emmetropes and 9.00±5.76cpm for myopes binocularly. The accommodative facility rate in this study was relatively low prior to the surgery compared to the above study, but increased by approximately 2-3 cycles/minute at the one month post-operative visit.

Radhakrishnan, Allen and Charman, (2007) reported that subjective and objective facility measurements were lower in myopes when compared with emmetropes. Velocity of disaccommodation was lower in myopes than in emmetropes at both distance and near. The lower accommodative facility shown by myopes could be due to the reliance on disparity cues compared to emmetropes as individuals use a variety of monocular and binocular cues to guide their dynamic accommodative response. As stated in the literature, this study also showed that the dynamics of accommodation improved in the emmetropic state (following the surgery) compared to myopic state (prior to the surgery).Though the exact reason for the sluggish accommodative response among myopes is not clear, it could be due to deficit in autonomic innervations (both sympathetic and parasympathetic) (Chen, Schmid and Brown, 2003).

7.4.2.2 Near point of convergence

The near point of convergence increased from 5.62 ± 1.71 to 7.96 ± 1.63 (cm) after one month in this study. Prakash, et al. (2007) reported a decrease in AC/A ratio (deg/D) from 3.63±1.79 preoperatively to 4.57±1.12 in the first week and 6.54±1.05 in the first month. After three months, it stabilised to 4.05±1.16, near pre-operative value. They stated that this change in AC/A ratio was due to the increased accommodative effort of the eye in emmetropic state. The reason for the decrease in near point of convergence in this study could be due to the increased convergence effort required while wearing contact lenses in myopic state (pre-surgery) (Jimenez, et al., 2011). Also, as the amplitude of accommodation was reduced following the surgery, due to the change in far point, similar change in vergence was also noticed.

Most of the accommodative parameters especially the lag of accommodation, facility of accommodation improved following the surgery.

Some Lasik patients report asthenopic symptoms and visual disturbances following refractive surgery due to some of the accommodative parameters especially accommodative spasm (Shetty, et. al., 2015). This finding supports the importance of evaluation of accommodative parameters prior to and following the surgery. Those who have symptoms associated with accommodative/vergence anomaly vision therapy can be tried to reduce the symptoms (Cooper and Feldman, 2009).

The above changes in accommodative parameters could be due to the sudden change in refractive error and may revert back to normal levels over time. It would be sensible to re-examine the cohort in the future to identify if findings return to preoperative levels.

7.5 Conclusion

NITM magnitude was significantly higher and comparable to other ethnicities pre surgery, but not following the surgery. This once again suggests that NITM is affected by the refractive status of the eye where myopes are more susceptible than emmetropes. The decay time constant was faster compared to other study populations. To the best of my knowledge this is the first study to report NITM characteristics and accommodative parameters pre and post LASIK.

Chapter-8

Conclusions and future research

Conclusions

This work has come to number of conclusions that in some cases point to further work.

NITM magnitude and decay.

My results demonstrate that the initial magnitude of NITM is higher in Indian myopes compared to Indian emmetropes. The emmetropic group demonstrated a hypermetropic shift. This is in agreement with the findings of Ciuffreda and Wallis, (1998). Previous research has shown a mean initial NITM magnitude of about 0.40D with the myopic shift decaying to baseline levels after 60 seconds. Myopes are more susceptible than emmetropes. The prime finding in this thesis is the decay duration in Indian myopes was faster (6.07 seconds) compared to other ethnicities.

There was no significant effect of target size and contrast on NITM for both myopes and emmetropes. Interestingly, Schmid et al. (2005) also found that target contrast had no effect on NITM and that target size produced only a small change in NITM that was not clinically significant. The effects of letter size and contrast on NITM were tested using printed text in study1. This can be extended to other types of near target used frequently, such as mobile phone and tablets at various distances especially at a higher stimulus level as many children are exposed to these devices early in life. NITM appears to be greater when the near vision task is of high accommodative demand (Ong and Ciuffreda, 1995). Myopic subjects have been reported to exhibit a larger lag of accommodation, especially at a higher stimulus, compared to emmetropes (Gwiazda, et al., 1985; 1998). A larger lag of accommodation could lead to degradation in the quality of the retinal image by producing hypermetropic defocus. This hypermetropic defocus which lies behind the prolate retina may stimulate axial growth of the eye towards the defocus (Gwiazda, et al., 1993; Gwiazda, et al., 1995; Jiang, 1997; Abbott, et al., 1998).

With an increase in task duration, there was no significant increase in NITM magnitude. The decay duration was faster among myopes compared to previous work even with increased task duration. The difference in the values of decay between the present study and those of other studies suggests a faster relaxation to the baseline in the Indian subjects and this requires some consideration. It may be due to a genetically-driven difference in lens structure that may allow some subjects to relax their accommodation more quickly after near work (Ong and Ciuffreda, 1995). Alternatively, Indian subjects may have a faster sympathetic response compared to other ethnic groups.

It has been well documented that the accommodative system receives dual innervations, consisting primarily of a parasympathetic (cholinergic) and secondarily a sympathetic (adrenergic) component. An increase in parasympathetic stimulation results in an increase in accommodation. Prior investigation has demonstrated that the sympathetic system is slower in onset (40 secs) and smaller in effect than the parasympathetic system (Ciuffreda, 1991). Ong and Ciuffreda, (1995) suggest that a deficit in this system may slow the decay of NITM. The longer decay time found in previous studies compared to the present study could be attributed to differences in parasympathetic stimulation between our subjects and those of different ethnicity. Therefore, the sympathetic response efficiency in Indian subjects compared to other ethnicities especially those with a higher prevalence of myopia should be investigated further, particularly as the prevalence of myopia (4-7%) in Indian populations is low compared to other populations where decay duration is longer. The difference in NITM decay time may indicate a reduced susceptibility to myopia development in this population. Unfortunately, our study did not attempt to measure the progression of myopia among our subjects, so we are not able to investigate the relationship between their NITM characteristics and myopia progression.

The underlying reason for a lower prevalence of myopia in India is yet to be determined. While both the countries have a large population of young children and adults who perform significant magnitudes of near work during the day, the prevalence of myopia in the Chinese population is much higher than that of Indian (He, et al., 2004; 2007, Dandona, et al., 1999; 2002, Murthy, et al., 2002). Aside from the genetic predisposition, Indian children and adults living within the cities study using both English and native Indian language characters, which might have a different spatial content in the text compared to that of the Chinese language characters. More research would help us understand the apparent protective mechanism present in the Indian population that enables a lower prevalence of myopia, and could possibly serve as a potential treatment option for countries with high myopia. Our data shows faster decay dynamics which may possibly explain why the presenting NITM does not persist, which may in turn lead to lower myopia prevalence. Further research is needed to better understand the effect of sympathetic and parasympathetic influence on accommodative response and NITM in different ethnicities.

To confirm the above hypothesis, Vasudevan, Ciuffreda and Gilmartin, (2009), assessed the effect of near work in young Caucasian adults following one hour of reading. All the subjects received timolol maleate to block the sympathetic nervous system and betaxolol as a control agent. NITM magnitude and decay duration was increased in subjects who received timolol. They further stated that the decay duration among myopes was more prolonged than emmetropes suggesting a possible role of impaired sympathetic system to myopia. This reduced NITM decay time in this thesis cohort may indicate a reduced susceptibility to myopia development in this population.

Aberrations

There was no significant change in higher order aberrations especially spherical aberration and HORMS in either myopes or emmetropes following a task of short duration. Though a change in spherical aberration in the negative direction during accommodation is well documented in the literature (Atchison, et al., 1995; He, et al., 2000; Ninomiya, et al., 2002; Ghosh, et al., 2011), conclusive evidence on the mechanisms that contribute to this change still remains unclear. Buehren, Collins and Carney, (2003, 2005) found changes in HORMS and spherical aberration following 60 and 120 minutes of reading respectively. In the current study, there was no significant change. The main difference between the Buehren et al. study and the current study is the task duration. The current study measured aberrations following 5 minutes of near task whereas Buehren, Collins and Carney, (2005) measured aberrations following 60 and 120 minutes of near task and postulated that an increase in near work had a cumulative effect on the aberrations. The current study tested the effect of near work on aberrations only once following near work in the Indian cohort, but did not test with prolonged reading and so the cumulative effect theory could not be verified in these study subjects.

Although a longer task duration was not investigated we could speculate that there may not be any difference in aberration even after longer periods of reading as NITM characteristics did not change much following prolonged near work (study 2). The swift NITM decay in our (studies 1 and 2) could be influential in reducing the aberrations. Also there was lack of correlation between aberration and NITM and this supports the above hypothesis. However, there could be changes in aberrations due to the narrow palpebral aperture during reading (Collins, et al., 2006) and so future studies should investigate the relationship between NITM recovery and change of aberrations, by taking aberration and NITM measurements simultaneously during and after reading, alongside lid aperture position.

Biometry

Similarly, there was no significant difference in ocular biometry parameters namely axial length, corneal thickness, aqueous chamber depth and lens thickness within myopes and emmetropes following the shorter task. Mallen, et al. (2006) reported a transient increase in axial length during accommodation in both emmetropic and myopic subjects. A greater transient increase in axial length was reported in myopic subjects compared to emmetropes for the higher accommodative stimulus of 6D.

The change in axial length between pre and post task in our Indian myopes was smaller than Mallen, et al. (2006), which could be due to the faster decay in our study subjects (study 1). A Pearson product-moment correlation co-efficient did not reveal any correlation between the decay of NITM and change in axial length (r=0.31, n=24, p=0.15). Further studies should be conducted with longer task durations with biometry parameters measured continuously during and after the cessation of near work, to confirm the association of NITM recovery and biometry parameters.

NITM in Lasik subjects

This thesis demonstrates a number of new findings in this area. NITM magnitude was significantly higher before LASIK surgery than following the surgery. Studies (1 and 2) also confirmed in a separate cohort that the decay time constant in myopic Indian subjects is faster than other ethnicities. This study also found that the lag of accommodation was significantly higher prior to (myopic state) compared to following the surgery (emmetropic state). Lag of accommodation and facility of accommodation improved following the surgery, although the latter may be due to a training effect inherent in the measurement (Allen, et al., 2009). The above changes in accommodative parameters could be due to the sudden change in refractive error (but the exact mechanism is unknown) and may revert back to pre-operative levels over time. It would be sensible to re-examine the cohort in the future to identify if accommodative variables return to preoperative levels.

Clinical considerations

Some of the (NITM) symptomatic patients visit our tertiary eye care with diverse symptoms. These include headache, fluctuation of vision, frequent change of glasses and blurred vision. Vasudevan, Ciuffreda and Gilmartin, (2009) assessed the effect of a sympathetic inhibitory pharmacological agent, timolol maleate in a group of ten myopes and ten emmetropes. They demonstrated that only 15% of the myopic subjects had access to sympathetic facility.

Some of these symptomatic individuals may have access to sympathetic innervation of the ciliary muscle, and could be profiled by a previously published method (Mallen, Gilmartin and Wolffsohn, 2005).

It is important to assess these individuals in order to target populations with NITM. When patients have symptoms they are asked to report when they notice blurred distance vision following prolonged near work and it would also be useful to know the activity they had been undertaking and if they were wearing their correction during the near task. Though the faster decay duration among myopes in an Indian population could be protective in nature, other factors like cognitive demand (Wolffsohn, et al., 2003), and other environmental factors like close reading distance (< 30 cm), continuous reading (> 30 minutes), and less time spent outdoors are considered to influence myopia development (Rose, et al., 2008; Dirani, et al., 2009; Guo, et al., 2013). Good visual habits, including taking short breaks during reading, and maintaining a good distance during reading may prevent or reduce the progression of myopia (Rose, et al., 2008). Also different optical modalities like bifocals and progressive lenses to help reduce ‘visual stress’ from near activities to prevent or slow the progression of myopia are recommended in young progressing myopes with esophoria (Gwiazda, et al., 2003). Vision therapy can be used as a conservative mode of treatment along with optimal optical correction (Li, et al., 2015; Chia, Lu and Tan, 2016).

Conclusion

The overarching conclusions of this thesis are:

- NITM magnitude in myopes in Indian subjects was comparable to other populations whereas the decay was faster. The finding of reduced decay was repeated in a second Indian myopic cohort.
- Though at the pre task level there was a difference in spherical aberration and HORMS between emmetropes and myopes, aberrations did not change significantly following 5 minutes of near reading task in either emmetropes or myopes.
- Similarly biometry parameters did not change significantly following 5 minutes of near task in both emmetropes and myopes.
- NITM magnitude was evident and comparable to other ethnicities pre surgery, but not following the LASIK surgery. This once again suggests that NITM is affected by the refractive status of the eye where myopes are more susceptible than emmetropes.

Appendix

INFORMED CONSENT FORM

TITLE: NITM in myopic and non myopic Indian subjects

INVESTIGATORS: S.Viswanathan, Dr.Krishna kumar, Ms.Jameel Rizwana

AIM: Aim of the research is to find out the effect of the target size and contrast on NITM magnitude and decay time and to quantify the concurrent changes in optical and biometric parameters during NITM.

INSTRUMENT: Shin Nippon Open-view auto-refractor (WAM 5500)

COAS-HD wavefront analyzer

BIO-GRAPH

PROCEDURE:

First you will undergo Comprehensive eye examination and cycloplegic refraction. These are regular procedures done in the Out patient department. In addition the cycloplegic refraction would be done using an instrument called Open field autorefractometer. This will non invasively document the power of your eyes in the dilated state. After three days, a post mydriatic test would be done to confirm the power after which you will be given a near task which you have to read for 10 minutes. The open field measurements would be taken before and after the task. Similar measurements would also be obtained using two other instruments namely Biograph and Aberrometer. Biograph will give the dimensions of your eyes and Aberrometer will give the aberration status of your eyes.

STATEMENT OF RISK AND BENEFIT: All the procedures are non-invasive and no risk involved.

INVESTIGATOR GUARANTEE:

The above mentioned statements are true to the best of my knowledge.

Date:

Investigator's Signature

Place:

SUBJECT'S CONSENT

I have read all the details mentioned above and understood the risks and benefits of the experiment. The investigators have orally clarified all the doubts I had about my participation. I voluntarily accept to participate in the experiment. I understand that there will not be monetary or any other compensation given to me for participating in the study.

Date:

Place: Signature

SUBJECT INFORMATION

Name: Subject ID:

Gender:

Age:

Date of birth:

Residential address:

Phone No: Email:

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