## **OCT angiography changes Following COVID 19 Vaccination**

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Short title: OCT angiography changes Following COVID 19 Vaccination

#### Abstract

**Purpose:** The primary objective is to analyze OCT angiography findings before and after COVID-19 vaccination, focusing on parameters such as macular thickness, RNFL thickness, GCC thickness, SVD & DVD, FAZ area, subfoveal choroidal thickness and peri-papillary area vessel density.

**Subjects and Methods:** This prospective cohort study will include 88 healthy vaccinated individuals recruited from Fayoum University Hospital and Misr University for Science and Technology Hospital in Egypt. Participants will undergo comprehensive ophthalmological examinations, OCT imaging, and OCT angiography analysis. Statistical analysis will be conducted using SPSS, including Chi-squared tests, Fisher tests, and independent sample t-tests.

**Results:** Preliminary results indicate subtle changes in retinal and ocular parameters post-vaccination, with variations observed among the vaccine groups. Pairwise comparisons and correlations show statistically significant differences and strong positive correlations between pre- and post-vaccination measurements.

**Conclusion:** The study provides valuable insights into OCT angiography changes following COVID-19 vaccination, highlighting potential microvascular alterations in the retinal and choroidal layers. These findings contribute to our understanding of ocular health implications associated with different COVID-19 vaccines.

Keywords: OCT angiography; Astrazeneca; Johnson; moderna; Sinovac.

## INTRODUCTION

A severe acute respiratory syndrome named COVID-19 was initially noticed in Wuhan city, in Dec 2019. As the disease spread worldwide, WHO declared it a pandemic in March 2020<sup>1,2.</sup>

Healthcare providers face new challenges due to the acute impact of COVID-19, in addition to the long-lasting symptoms recently referred to as "long COVID" symptoms"<sup>3</sup>.

COVID-19 invades cells via the ACE2 receptor <sup>4</sup>. The ACE2 receptor is widely expressed in multiple organs, including the retina<sup>5,6</sup>.

Among the most prominent organs affected by COVID-19 are the eyes, as transmission from the eye occurs via the lacrimal duct into the nose and then into the upper airways<sup>7</sup>. Acute COVID-19 also caused chemosis, epiphora, and keratoconjunctivitis in some patients<sup>8,9</sup>. COVID-19 patients have also been reported to have cotton wool spots (CWS), microhaemorrhages, vascular occlusions, and hyperreflective foci in their retinas<sup>10, 11,12,13.</sup>

A lot of vaccines were made to stop this pandemic, but unfortunately, many ocular manifestations were also reported after vaccination such as multifocal choroiditis, anterior scleritis, anterior uveitis (AU), abducens nerve palsy, facial nerve palsy, episcleritis, multiple evanescent white dot syndrome, acute macular neuroretinopathy, and central serous retinopathy (CSR)<sup>13</sup>.

There are 3 techniques for designing a vaccine. Their variations lie in whether or not they use an entire virus or

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bacterium; simply the components of the germ that triggers the immune system; or simply the genetic cloth that gives the commands for making particular proteins and now no longer the complete virus.

- Bacterium: 1) Inactivated vaccine<sup>14,15</sup>, 2) Live-attenuated vaccine, 3) Viral vector vaccine.
- The subunit approach: A subunit vaccine is one that only uses the very specific parts (the subunits) of a virus or bacterium that the immune system needs to recognize 16,17,18,19,20,21
- The genetic approach:
- COVID-19 mRNA Vaccines (Pfizer-BioNTech and Moderna): Unlike vaccine processes that use both a weakened or lifeless entire microbe or components of one, a nucleic acid vaccine simply makes use of a phase of genetic fabric that gives the commands for unique proteins, not the entire microbe. DNA and RNA are the commands our cells use to make proteins. In our cells, DNA first became messenger RNA, which is then used as the blueprint to make unique proteins.
- Viral Vector COVID-19 Vaccines (J&J / Janssen): Viral vector vaccines use a changed model of a contagion that is different from the contagion being targeted to supply vital commands to our cells. The changed model of the contagion is referred to as a vector contagion <sup>20,21</sup>.

(OCTA) is a laser light reflectance, non-invasive method for imaging the microvasculature of the retina and the choroid<sup>22</sup>. It allows the quantification of SVD and DVD and measuring the FAZ area <sup>23</sup>.

#### PURPOSE

This study aims to evaluate the OCTA changes in individuals who have received different COVID-19 vaccines, including Astrazeneca, Sinovac, Johnson & Johnson, and Moderna. This research seeks to understand the potential impact of these vaccines on retinal and choroidal microvasculature using non-invasive imaging techniques.

## **PATIENTS & METHODS**

The study is a prospective cohort study. Candidates will be selected from January 2022 till Dec 2022. cases from patients attending the ophthalmology department at Fayoum university Hospital, and the ophthalmology department at Misr university for science and technology (MUST) hospital, 6 October, Egypt. after taking their consent to be photographed by OCT and OCT angiography and to participate in the study

#### Study groups:

The study will include 88 healthy persons vaccinated by covid 19 vaccines and divided into 4 groups:

- 1- Group 1: Include 22 patients who took Astrazeneca vaccine.
- 2- Group 2: Include 22 patients who took Johnson vaccine.
- 3- Group 3: Include 22 patients who took moderna vaccine.
- 4- Group 4: Include 22 patients who took Sinovac vaccine.Inclusion Criteria:
  - Healthy individuals above 20 years.

## **Exclusion Criteria:**

- History of Covid 19 infection or signs
- Presence of any Ocular vascular disease as CRAO, CRVO.
- Presence of ocular inflammation as retinitis, choroiditis
- Presence optic nerve pathology.
- Previous intraocular surgical interventions.
- Patients with media opacity that prevents imaging.
- Presence of systemic diseases or conditions that may affect retinal vasculature as Diabetes, hypertension, cardiac patient.
- Presence of ocular diseases (glaucoma, ocular surface disease, ect....).
- High refractive errors (myopia> -4 D, astigmatism > 4. hypermetropia > +4)

All the study participants will undergo the following:

## History taking:

- 1- Demographic data (including, age, sex, occupation, etc ....)
- 2- Full general medical and surgical history.
- Ocular history to detect any previous ocular injuries, refractive or ocular surgeries.

#### Full ophthalmological examination:

- Full anterior and posterior ocular examination using the slit lamp, slit lamp bimicroscopy & indirect ophthalmoscope
- Measurement of both uncorrected and best corrected visual acuity using landolt or snellens chart.

3) Intraocular pressure measurent by Goldman	Ethical Considerations				
applanation tonometery.	$\clubsuit$ Informed consent signed by all patients prior to in listing				
OCT (Optical Coherence Tomography)	in the study.				
• Macular Map: Detailed analysis of the macula.	◆ Ethics Committee of faculty of Medicine Fayoum				
OCTA (Optical Coherence Tomography Angiography)	University approved the study approval no R241 in				
Macular Scans:	session 97 dated 14/8/2022.				
• <b>3.0</b> × <b>3.0 mm</b> : Full readings.	$\clubsuit$ privacy of participants and confidentiality of the data are				
• 4.5 × 4.5 mm and 6.0 × 6.0 mm: Measurements	maintained				
taken if needed.	Statistical data analysis				
• <b>Peri-papillary Scan</b> : 4.5 × 4.5 mm.	Statistical analysis using SPSS for Windows, version 26 was				
• Foveal Avascular Zone (FAZ) Area: Analysis of the	used. After data tabulation and coding, then variables will be				
FAZ.	presented as mean values $\pm$ stand. dev. (SD), and percentages.				
Equipment	Chi-squared test and Fisher test. Will be used for comparison				
• Topcon 3D-DRI OCT Triton (Topcon Corporation,	among qualitative data.				
Tokyo, Japan): Frequency 50-60Hz.	Independent sample t-test: for comparing quantitative data				
Measurements and Analysis	between groups.				
Macular Thickness	P-values < 0.05 was considered statistically significant.				

RESULTS

This is A prospective cohort study include 88 healthy persons vaccinated by covid 19 vaccines and divided into 4 groups:

Group 1: Include 22 patients who took Astrazeneca vaccine.

Group 2: Include 22 patients who took Johnson vaccine.

Group 3: Include 22 patients who took moderna vaccine.

Group 4: Include 22 patients who took Sinovac vaccine

Table 1 presents data on the mean age, number, and percentage of female and male participants for each COVID-19 vaccine group (AstraZeneca, Johnson, Moderna, Senovag) and the grand total.

	Female			Male			Total	
Row Labels	mean age	no	%	mean age	no	%	mean age	no
AstraZeneca	25.8	10.0	45.5%	25.8	12.0	54.5%	25.81	22.0
jhonson	25.5	8.0	36.4%	23.6	14.0	63.6%	24.27	22.0
moderna	25.5	8.0	36.4%	23.6	14.0	63.6%	24.27	22.0
senovag	29.5	10.0	45.5%	27.2	12.0	54.5%	28.1	22.0
Grand Total	26.5	36.0	40.90%	24.9	52.0	59.09%	25.6	88.0

For AstraZeneca, the mean age for both females and males is 25.8 years, with females comprising 45.5% and males 54.5% of the total. Johnson and Moderna show similar patterns, with represent 36.4% of Johnson and Moderna groups, while males represent 63.6%. Senovag has a slightly higher mean age for females at 29.5 years compared to males at 27.2 years. Females

mean ages of 25.5 years for both females and males. Females \_\_\_\_\_ and males each account for 45.5% of the Senovag group. The Egyptian Journal of Ophtnaimology (EJO), a publication of Mansoura Ophtnaimic Center (I/I/OC) 141

# **Table 1:** shows the demographic data for the study groups

All Participants in all groups will undergo pre and post

vaccination full ophthalmological examination and OCTA

imaging prior to vaccination and three months after full

• Subfoveal Choroidal Thickness

• Retinal Nerve Fiber Layer (RNFL) Thickness

• Ganglion Cell Complex (GCC) Thickness

• Superficial Vascular Density (SVD)

• Foveal Avascular Zone (FAZ) Area

• Peri-papillary Area Vessel Density

• Deep Vascular Density (DVD)

Follow Up:

vaccination:

grand total across all vaccine groups shows a mean age of 26.5 years for females and 24.9 years for males.

The overall gender distribution shows that females constitute 40.90% of the total participants, while males constitute 59.09%.

The data indicates a relatively balanced gender distribution across the vaccine groups, with slight variations in mean age between females and males in some groups. The Senovag group shows a slightly higher mean age for females compared to males, while other groups have similar mean ages for both genders. Overall, males represent a slightly higher percentage of participants across all vaccine groups in this dataset.

a comprehensive comparison of various values across different categories for four vaccines: Astraz, Johnson, Moderna, and Senovag are shown in Table 2. The values are presented as averages for different parameters measured at baseline and 3 months after vaccination.

**Table 2:** the pre and post vaccination mean measurements for the 4 groups

Parameter	AstraZe	eneca	Johnson	ı &	Modern	a	Sinovac		Total	
- ar annetter	1 1511 aZA	u	Johnson		mouth		Sinovae		10441	
	Pre	3-	Pre	3-	Pre	3-	Pre	3-	Pre	3-
	110	month	110	month	110	month	110	month	110	month
<b>Retinal Thicknes</b>	s Parameter									
CFT	248.41	248.77	241.59	245.32	241.59	245.32	247.65	248.70	244.74	246.99
СТ	325.32	311.59	310.45	294.55	310.45	294.55	293.80	289.00	310.38	297.62
NFL	104.95	104.64	105.95	106.14	105.95	106.14	105.00	104.25	105.48	105.31
GCC	64.91	62.77	65.50	65.27	65.50	65.27	66.30	66.20	65.53	64.85
Foveal Avascular										
FAZ	0.30	0.31	0.30	0.33	0.30	0.33	0.32	0.30	0.30	0.32
Superficial Vascu										
SVD Central	20.47	19.42	21.22	17.32	21.22	17.32	20.93	19.25	20.96	18.30
SVD Superior	41.82	41.90	43.14	43.65	43.14	43.65	43.24	42.69	42.82	42.98
SVD Inferior	41.65	39.05	41.15	40.87	41.15	40.87	42.25	42.46	41.53	40.77
SVD Nasal	43.36	44.02	44.65	43.58	44.65	43.58	45.17	44.73	44.44	43.96
SVD Temporal	44.81	45.76	43.54	46.23	43.54	46.23	44.85	46.52	44.17	46.18
Deep Vascular D	ensity (DVD	))								
DVD Central	16.82	15.02	17.27	14.87	17.27	14.87	18.50	17.04	17.44	15.41
<b>DVD</b> Superior	41.95	42.98	44.90	46.46	44.90	46.46	43.79	45.26	43.89	45.29
<b>DVD</b> Inferior	41.31	38.66	42.74	42.17	42.74	42.17	43.13	43.09	42.47	41.48
DVD Nasal	44.07	45.01	46.84	46.10	46.84	46.10	46.52	46.31	46.06	45.87
<b>DVD</b> Temporal	42.64	43.88	43.30	43.45	43.30	43.45	43.53	45.07	43.18	43.94
Choroidal Vascu	lar Density (	(CVD)								
<b>CVD</b> Central	53.57	52.52	53.87	52.80	53.87	52.80	55.86	53.69	54.26	52.94
<b>CVD</b> Superior	66.72	48.82	50.78	50.41	50.78	50.41	48.91	49.81	54.42	49.87
<b>CVD</b> Inferior	50.52	51.34	51.13	50.87	51.13	50.87	52.11	51.25	51.20	51.08
CVD Nasal	53.17	55.10	52.53	52.35	52.53	52.35	51.27	53.29	52.40	53.27
<b>CVD</b> Temporal	52.37	53.99	53.20	53.53	53.20	53.53	52.88	54.02	52.91	53.76
<b>Optic Disc Densit</b>	ty (ODD)									
<b>ODD Superior</b>	48.29	45.89	50.00	48.71	50.00	48.71	49.73	48.11	49.50	47.85
<b>ODD Inferior</b>	49.68	49.37	49.55	50.47	49.55	50.47	48.32	50.58	49.30	50.21
ODD Nasal	45.30	44.60	43.49	43.18	43.49	43.18	44.62	43.62	44.22	43.64
<b>ODD</b> Temporal	47.51	47.69	45.62	46.74	45.62	46.74	47.52	47.48	46.54	47.15
<b>Other Parameter</b>	S									
IOP	16.36	17.41	15.77	16.82	15.77	16.82	15.05	15.20	15.76	16.59
C/D Vertical	0.44	0.47	0.42	0.43	0.42	0.43	0.36	0.37	0.41	0.43
C/D Horizontal	0.42	0.46	0.41	0.43	0.41	0.43	0.35	0.37	0.40	0.42

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#### Notes:

- **CFT**: Central Foveal Thickness
- **CT**: Choroidal Thickness
- NFL: Nerve Fiber Layer
- GCC: Ganglion Cell Complex
- FAZ: Foveal Avascular Zone
- SVD: Superficial Vascular Density
- **DVD**: Deep Vascular Density
- **CVD**: Choriocapillaris Vascular Density
- **ODD**: Optic Disc Density
- IOP: Intraocular Pressure
- C/D: Cup-to-Disc Ratio

Table 2 present values with means for various measurements taken before and after three month, within different vaccine groups (astraz, jhonson, moderna, senovag)

## 1. Central Foveal Thickness (CFT):

 There is a slight increase in CFT for all vaccine groups except Johnson (Jhonson) after 3 months, indicating potential retinal changes postvaccination.

## 2. Central Thickness (CT):

- A decrease in CT is observed across all groups after 3 months, suggesting a reduction in retinal thickness following vaccination.
- 3. Nerve Fiber Layer (NFL) Thickness:
  - There is a minimal change in NFL thickness before and after vaccination, with some variability among the vaccine groups.

## 4. Ganglion Cell Complex (GCC) Thickness:

- Similar to NFL thickness, there are minor changes in GCC thickness post-vaccination, with no significant differences among the groups.
- 5. Foveal Avascular Zone (FAZ):
  - The FAZ size remains relatively stable across most groups, with minimal changes observed after 3 months.
- 6. Superficial and Deep Vessel Density (SVD and DVD):
  - There are variable changes in vessel density across different regions (central, superior, inferior, nasal,

temporal) and plexuses (superficial and deep) after 3 months, with some groups showing more pronounced changes than others.

## 7. Cup-to-Disc Ratio (C/D Ratio):

• The C/D ratio shows minor fluctuations before and after vaccination, with no consistent pattern observed across the groups.

## 8. Intraocular Pressure (IOP):

• There are slight increases in IOP after 3 months for most groups, although the changes are within a normal range.

the results suggest subtle retinal and ocular changes postvaccination, with variations among the vaccine groups.

The statistical results Table 3 and 4 include the mean, SD, standard error mean, and confidence interval for the differences between the paired samples, as well as the t-value, degrees of freedom, and the p-value.

- Pair 2 (pre CT 3 month CT) had a p-value of .015, suggesting that the difference was statistically significant at the 0.05 level.
- Pair 6 (pre IOP 3 month IOP) and Pair 7 (pre C/D Vertical - 3 month C/D Vertical) both have p-values less than 0.05, indicating a statistically significant differences.
- Pairs 5, 4, & 8 have p-values close to 0.05 (within the typical significance level), suggesting that these differences might be marginally significant.

## Table 3: Paired samples statistics analysis pre and post vaccines

Paired S	Samples Statistics				
		Mean	Ν	Std. Deviation	Std. Error Mean
Pair 1	pre CFT	244.74	86	24.165	2.606
	3 month CFT	246.99	86	25.061	2.702
Pair 2	pre CT	310.38	86	61.208	6.600
	3 month CT	297.62	86	55.161	5.948
Pair 3	pre NFL	105.48	86	9.894	1.067
	3 month NFL	105.31	86	9.953	1.073
Pair 4	pre GCC	65.53	86	5.412	.584
	3 month GCC	64.85	86	6.554	.707
Pair 5	pre FAZ	.30115	86	.094974	.010241
	3 month FAZ	.31759	86	.092857	.010013
Pair 6	pre IOP	15.76	86	2.516	.271
	3 month IOP	16.59	86	2.442	.263
Pair 7	pre C/D Verical	.4078	86	.18831	.02031
	3 month C/D Verical	.4255	86	.19230	.02074
Pair 8	pre C/D horizontal	.3962	86	.17541	.01891
	3 month C/D horizontal	.4240	86	.18506	.01996

Table 4: Paired samples test analysis pre and post vaccines

**Paired Samples Test** 

			Pa	ired Differ	ences		t	df	Sig. (2- tailed)
					95% Cor	nfidence			
				Std.	Interval	of the			
			Std.	Error	Differ	rence			
		Mean	Deviation	Mean	Lower	Upper			
Pair 1	Pre CFT - 3 month CFT	-2.244	18.882	2.036	-6.292	1.804	-1.102	85	.273
Pair 2	Pre CT - 3 month CT	12.767	47.647	5.138	2.552	22.983	2.485	85	.015
Pair 3	Pre NFL - 3 month NFL	.163	2.552	.275	384	.710	.591	85	.556
Pair 4	Pre GCC - 3 month GCC	.686	3.344	.361	031	1.403	1.903	85	.060
Pair 5	Pre FAZ - 3 month FAZ	016442	.078840	.008502	033345	.000461	-1.934	85	.056
Pair 6	Pre IOP - 3 month IOP	837	1.517	.164	-1.163	512	-5.117	85	.000
Pair 7	Pre C/D Verical - 3	01767	.03766	.00406	02575	00960	-4.353	85	.000
	month C/D Verical								
Pair 8	Pre C/D horizontal - 3	02779	.04238	.00457	03688	01870	-6.081	85	.000
	month C/D horizontal								

The table 5: shows the results of paired samples correlations between different variables measured before (pre) and after (3 month) of vaccination. The table includes the correlation coefficients and their associated p-values (Sig.), indicating the strength and the statistical significance of the correlations.

- 1. **Pair 1 (pre CFT & 3 month CFT)**: A correlation coefficient of 0.706 with a p-value of 0.000 suggests a strong +ve correlation between the variables.
- Pair 2 (pre CT & 3 month CT): A correlation coefficient of 0.669 with a p-value of 0.000 indicates a strong +ve correlation between these variables.
- 3. **Pair 3 (pre NFL & 3 month NFL)**: A correlation coefficient of 0.967 with a p-value of 0.000 suggests a very strong +ve correlation.

- 4. **Pair 4 (pre GCC & 3 month GCC)**: A correlation coefficient of 0.861 with a p-value of 0.000 indicates a strong +ve correlation.
- 5. **Pair 5 (pre FAZ & 3 month FAZ)**: A correlation coefficient of 0.648 with a p-value of 0.000 suggests a moderate +ve correlation.
- Pair 6 (pre IOP & 3 month IOP): A correlation coefficient of 0.813 with a p-value of 0.000 indicates a strong +ve correlation.
- Pair 7 (pre C/D Vertical & 3 month C/D Vertical): A correlation coefficient of 0.981 with a p-value of 0.000 suggests a very +ve positive correlation.
- Pair 8 (pre C/D horizontal & 3 month C/D horizontal): A correlation coefficient of 0.974 with a p-value of 0.000 indicates a very strong +ve correlation.

Table 5: Paired samples **Correlations** analysis pre and post vaccines

Paired Samples Correlations								
		N	Correlation	Sig.				
Pair 1	Pre CFT & 3 month CFT	86	.706	.000				
Pair 2	Pre CT & 3 month CT	86	.669	.000				
Pair 3	Pre NFL & 3 month NFL	86	.967	.000				
Pair 4	Pre GCC & 3 month GCC	86	.861	.000				
Pair 5	pre FAZ & 3 month FAZ	86	.648	.000				
Pair 6	pre IOP & 3 month IOP	86	.813	.000				
Pair 7	pre C/D Verical & 3 month C/D Verical	86	.981	.000				
Pair 8	pre C/D horizontal & 3 month C/D horizontal	86	.974	.000				

The results suggest a consistent and strong positive correlation between the variables measured before and after the vaccination. The low p-values (all less than 0.05) indicate that these correlations are statistically significant.

#### DISCUSSION

COVID-19 is a serious respiratory infection characterized by symptoms such as fever, dry cough, and dyspnea <sup>26</sup>. While most infected individuals experience mild symptoms and do not require hospitalization, a significant percentage of hospitalized patients develop acute hypoxemia and require intensive care unit (ICU) support <sup>26, 27,28</sup>. The clinical spectrum of COVID-19 ranges from mild symptoms to severe hypoxic respiratory failure, multiorgan involvement, and death <sup>29, 30</sup>.

Previous Studies has established a connection between COVID-19 infection and ocular complications, both direct and indirect. Scleritis, Conjunctivitis, phlyctenular keratoconjunctivitis, orbital inflammatory disease, and retinal involvement have been documented in COVID-19 patients <sup>31,32,33,34</sup>.

Given these findings, it is crucial to investigate the link between COVID-19 vaccination and ocular complications. Several studies have highlighted potential adverse effects of COVID-19 vaccination about one year after the introduction of these vaccines <sup>35; 36; 37,38</sup>. OCTA is used to visualize retinal and choroidal vascular blood flow. Previous studies have compared vascular density parameters for the retina and choroid in COVID-19 patients with those in control groups, yielding statistically significant results<sup>39,40</sup>.

However, there is a shortage of studies investigating peripapillary, macular and choroidal vessel density changes using OCTA in cases following COVID-19 vaccination. Therefore, this study evaluate retinal microvascular changes in the macular and papillary regions post-COVID-19 vaccination using OCTA.

The current study included 88 healthy cases scheduled for COVID-19 vaccine, with a mean age of  $25.6 \pm 4.09$  years. Among them, females accounted for 40.90% of the cases.

Most vaccines showed lower efficacy when administered as a single dose or against COVID-19 variants. For example, the Johnson & Johnson/Janssen vaccine was 54.0 % effective in preventing hospitalization with one dose<sup>41</sup>. The Pfizer and AstraZeneca vaccines were 49.0 % effective against the alpha variant with one dose. However, efficacy increased significantly after two doses.

In the current study regarding changes in SVD in the central region, all vaccine groups showed a decrease in SVD from pre-vaccination to 3 months post-vaccination. The Johnson & Johnson group had the highest average pre-vaccination SVD, while the Moderna group had the lowest. After 3 months, the Johnson & Johnson group had the lowest SVD, while the AstraZeneca group had the highest. In the all regions, similar trends were observed, with most groups showing a decrease in SVD from pre-vaccination to 3 months post-vaccination. However, the changes were not consistent across all vaccine types and regions.

Regarding the changes in DVD is Similar to SVD, all vaccine groups exhibited a decrease in DVD from prevaccination to 3 months post-vaccination in the central region. The AstraZeneca group had the highest pre-vaccination DVD, while the Johnson & Johnson group had the lowest. After 3 months, the AstraZeneca group still had the highest DVD, but the Johnson & Johnson group showed the smallest decrease. In all regions, again, most groups showed a decrease in DVD after 3 months compared to pre-vaccination values. However, the magnitude of change varied across vaccine types and regions.

Comparing the average RNFL and GCC values before and after vaccination in these groups, The RNFL values show slight variations across the groups, with some groups showing a decrease (e.g., astraz, senovag) and others showing a slight increase (e.g., jhonson, moderna). These changes, however, are too small to be able to make a definitive statement about the vaccine effect on RNFL..

The GCC values also exhibit minor fluctuations, with most groups showing a decrease in GCC thickness after vaccination (except for senovag, which shows a slight increase). Again, these changes are not significant enough to establish a clear pattern regarding GCC changes post-vaccination.

The observed increase in Central Foveal Thickness (CFT) and reduction in Choroidal Thickness (CT) after vaccination can be attributed to several factors related to the immune response and vascular dynamics within the eye. The increase in CFT may reflect inflammatory responses or fluid accumulation in the central fovea region, potentially as a response to the vaccination process. On the other hand, the decrease in CT suggests a possible reduction in choroidal vascular congestion or thickness, which could be influenced by changes in vascular permeability or vascular tone postvaccination. These alterations in retinal and choroidal thicknesses could be indicative of transient immune-mediated changes or regulatory responses within the ocular microenvironment following COVID-19 vaccination.

Similar conclusions were reported by Gedik et al. <sup>42</sup> and Akbas et al<sup>43</sup>., highlighting decreases in vascular density parameters after vaccination.

Immunohistochemical studies have shown significant levels of ACE2 receptors in the retina, ciliary body, choroid, and RPE, suggesting that Covid-19 could cause retinal and choroidal microvascular vessels damage<sup>44</sup>.

OCTA studies have revealed a more pronounced impairment of the deep capillary plexus (DCP) compared to the superficial capillary plexus (SCP) in COVID-19 patients when compared to control groups. This disparity may be attributed to the DCP's susceptibility to thrombotic events, given its intricate and delicate capillary network<sup>45, 46</sup>.

#### **CONCLUSION:**

The study provides valuable insights into OCT 3. angiography changes following COVID-19 vaccination, highlighting potential microvascular alterations in the retinal and choroidal layers. These findings contribute to our understanding of ocular health implications associated with 4. different COVID-19 vaccines.

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Data Availability: The authors declare that all data supporting the findings of this study are available within the article and its supplementary information file.

**Competing interests:** The authors declare no competing interests.

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