



AEYE-DS User Manual

AEYE-DS User Manual
Software Version 5.00
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Rx Only
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- Company confidential -



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1. Manufacturer Information

AEYE Health

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New York, 10166

For questions or help, please contact AEYE Health at +1 (866) 262-7343 or info@aeyehealth.com.

2. Indication for Use

AEYE-DS is intended for use by health care providers to automatically detect more than mild diabetic retinopathy (mtmDR) in adults diagnosed with diabetes who have not been previously diagnosed with diabetic retinopathy. AEYE-DS is indicated for use with the Topcon TRC NW400 or the Optomed Aurora retinal imaging camera.

3. Contraindications

AEYE-DS exclusion criteria apply to subjects with the following conditions:

- Vision loss that cannot be corrected (e.g., with eyeglasses), blurred vision, or floaters.
- Diagnosed with macular edema, severe non-proliferative retinopathy, proliferative retinopathy, radiation retinopathy, or retinal vein occlusion.
- History of laser treatment of the retina or injections into either eye, or any history of retinal surgery.
- Contraindicated for fundus imaging:
 - Hypersensitive to light
 - Recently underwent photodynamic therapy (PDT)
 - Taking medication that causes photosensitivity
 - A history of angle-closure glaucoma or narrow anterior chamber angles – in patients who require dilation.





4. Glossary

4.1 Glossary of terms

AAO	The American Academy of Ophthalmology is a global community of eye physicians and surgeons that set eyecare standards
PPP	Preferred Practice Patterns
AEYE-DS Client	The software installed on the users' computer and is used to load images, send them for analysis to the AEYE-DS Service and receive back analyses
AEYE-DS Service	The component of AEYE-DS that resides in the cloud, receives images uploaded via the AEYE-DS Client, analyzes the images using software, and sends back a diagnosis to the Client
AEYE-DS Operator Training Manual	Instruction manual for using AEYE-DS in conjunction with an indicated fundus camera
DR	Diabetic Retinopathy

mtmDR	More than mild diabetic retinopathy: moderate non-proliferative retinopathy, severe non-proliferative retinopathy (NPDR), proliferative retinopathy (PDR), and/or macular edema, as defined in the AAO PPP
NPDR	Non-proliferative diabetic retinopathy
PDR	Proliferative diabetic retinopathy

4.2 Glossary of Symbols

	Warning - indicates a potentially hazardous situation associated with the use or misuse of the device which, if not avoided, could result in serious injury, death, or serious other adverse reaction
	Manufacturer
	Date of Manufacture
	Consult Manual Before Use

5. Warnings and Precautions

5.1 Prerequisites



To operate AEYE-DS safely and according to the intended purpose, the following prerequisites must be met:

- You should have a general understanding of the use of a personal computer running Microsoft™ Windows 7 or newer.
- You should be acquainted with the use of the indicated fundus camera.
- AEYE-DS should be installed according to the instructions in Section 7 of this User Manual.
- You must read and understand the Intended Use, Warnings, and Operating Instructions.

5.2 Warnings



The following warnings apply to all aspects of the AEYE-DS system:

- AEYE-DS is only designed to detect more than mild diabetic retinopathy. AEYE-DS is not intended to detect concomitant diseases, ophthalmic diseases, or other systemic diseases. Patients should not rely on AEYE-DS for detection of any other disease.
- Patients with an AEYE-DS output indicating more than mild diabetic retinopathy should be immediately referred to an eyecare provider for further assessment and treatment that is consistent with the recommendations of appropriate professional entities. In cases where the AEYE-DS test provides no result, the patient should always be immediately re-tested or referred to an eyecare provider. In cases where the AEYE-DS test does not detect the

presence of referable disease, the patient should be strongly encouraged to test again at an appropriate point in the future.

- People with diabetes may be at elevated risk of glaucoma and should be seen by an eyecare provider for glaucoma screening in accordance with recognized patient management recommendations. AEYE-DS does not detect glaucoma.
- Patients should be informed that AEYE-DS does not treat retinopathy and that their images are analyzed to determine whether further examination is needed by an eyecare provider. Physicians should review AEYE-DS results and advise patients of recommended referrals to an eyecare provider for evaluation and possible treatment.
- If AEYE-DS is not able to generate a diagnostic result on a patient who has been pharmacologically dilated, the patient may have vision threatening diabetic retinopathy or other abnormalities including cataract. Such patients should be promptly seen by an eyecare provider for evaluation.
- Patients should be advised to immediately seek an eyecare provider if they experience vision loss, blurred vision, floaters, or any other symptom, as these symptoms require the immediate attention of an eyecare provider.
- Do not use AEYE-DS to test for diabetes mellitus. AEYE-DS is only for use in people already diagnosed with diabetes mellitus.
- It is important for you, the user, to be aware of the limitations of AEYE-DS. AEYE-DS performs computerized interpretation of retinal images. AEYE-DS may fail to detect diabetic retinopathy when the condition exists (false negative) and erroneously indicate that the condition exists when in reality it does not (false positive).
- AEYE-DS is designed to work with good quality, in focus, digital retinal color images of the macula and [optionally] disc. Do not submit retinal color images that are of poor quality, retinal color images that were not taken using an indicated digital fundus camera, retinal images that are not in color, images of other tissues or objects other than the retina, or color images that were obtained by scanning images.
- AEYE-DS is only intended to be used with images acquired with a Topcon TRC-NW400 or Optomed Aurora. Refer to the FDA approved label of the Topcon TRC-NW400 or Optomed Aurora for relevant contraindications, warnings, and precautions.
- Pharmacologic dilation (mydriasis) using a Tropicamide 1.0% solution may be required to capture sufficient quality images in some patients. Refer to the FDA approved label of Tropicamide 1.0% for relevant contraindications, warnings, and precautions.
- The user is responsible for ensuring that the corresponding images and filenames for a particular patient are labeled appropriately to avoid mistaken identity with respect to AEYE-DS results.
- Users should regularly ensure that AEYE-DS Client software is operating on a computer that is free of viruses or malware and is updated with the latest security patches.

6. Product Information

6.1 Device Outputs and Definitions

AEYE-DS will provide one of four diagnostic results:

- 1) More than mild diabetic retinopathy detected: Refer to an eyecare professional
- 2) Negative for more than mild diabetic retinopathy: Retest in 12 months
- 3) Insufficient image(s) quality
- 4) Exam processing cannot be completed

The AEYE-DS device will indicate when image quality is insufficient to perform the diagnosis or when a technical error occurred during the diagnosis process.

Insufficient Image(s) Quality: Fundus images that are not of sufficient quality to rule out disease are indicated with a red frame in the AEYE-DS Client so that relevant images of patients' eyes may be retaken. AEYE-DS will indicate which of the images submitted did not pass its image quality filters so that the user may retake and replace the image(s). Images may be retaken non-mydratically or retaken after pharmacological dilating drops have been administered.



Warning: Patients who receive a result of “Insufficient Image(s) Quality” after following the AEYE-DS imaging protocol should be referred to an eyecare professional for evaluation.

Exam Processing Cannot Be Completed: AEYE-DS will communicate to the user when a technical failure to complete the diagnosis process has occurred. In such cases the user should attempt to resubmit patient images for diagnosis or work to troubleshoot problems that may prevent the AEYE-DS Client from communicating with the AEYE-DS Service.



Warning: Patients who receive a result of “Exam Processing Cannot Be Completed” after following the AEYE-DS imaging protocol should be referred to an eyecare professional for evaluation.

6.2 Limitations

See Contraindications in Section 3.

6.3 Principles of Operation

After installation, the AEYE-DS Client software works in conjunction with the AEYE-DS Service, which analyzes retinal images to produce a diagnosis. To perform an analysis, retinal images are selected using the AEYE-DS Client. The AEYE-DS Client sends the images securely over the internet to AEYE Health servers (AEYE-DS Service) which process the exam images and return the results to the AEYE-DS Client. The results with the clinical decision can then be viewed in the AEYE-DS Client. To perform an analysis, the user must have an active AEYE-DS account and the AEYE-DS Client must be authorized with a registration code, which must be obtained from AEYE Health.

7. Installation



Warning: AEYE Health recommends that installation and system changes be performed by individuals familiar with the IT systems on which the AEYE-DS Client is running.

7.1 System Requirements

To use the AEYE-DS device you will need the following:

1. A computer running a Microsoft Windows Operating System (Windows 7 or newer).
2. A working internet connection.

Specific computer hardware requirements can be found in Section 14 of this User Manual.

7.2 Installation

1. Download the installation package from <https://clinics.aeyehealth.com/client/publish.html>
2. Using the Windows File Explorer, browse to the location on the hard-disk where the AEYE-DS setup.exe has been saved. Double-click setup.exe to launch the installer.
3. Follow the installer prompts to install the software.

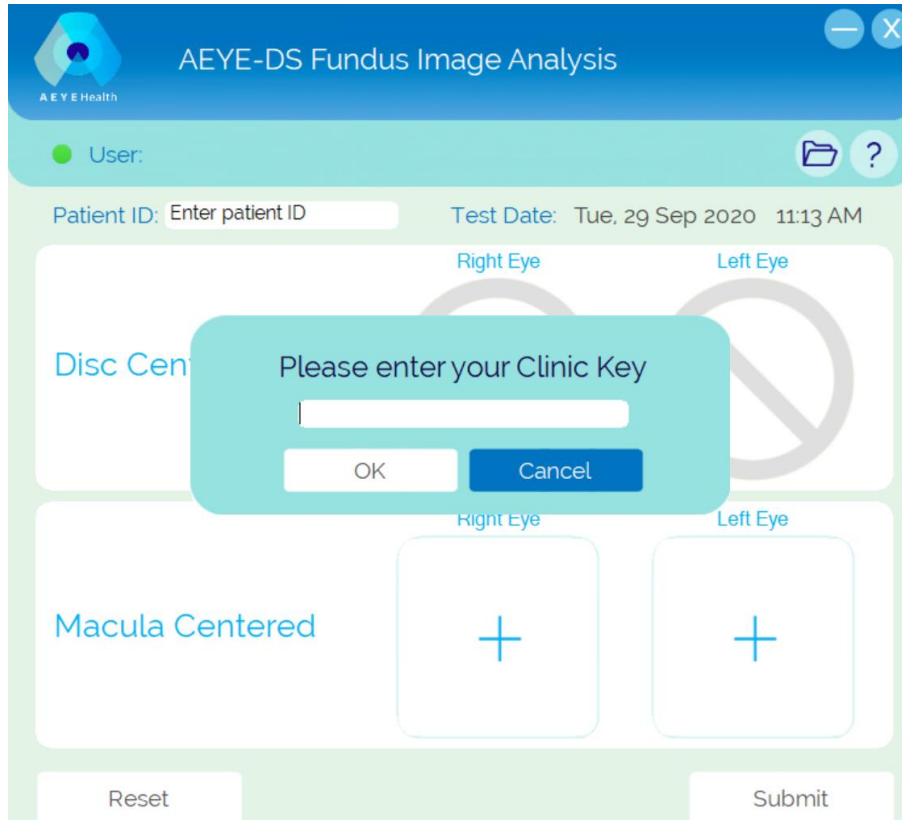
7.3 Registration

A Clinic Key from AEYE Health is required as part of the installation process. Without the Clinic Key the Client will not function. To obtain a code, contact AEYE Health or your AEYE Health representative.

After installation, the AEYE-DS Client can be started by double-clicking the AEYE Diagnostics application from the Windows application menu.

On first execution, you will be required to enter your Clinic Key. An internet connection is required for the AEYE-DS Client to verify this code and register the Client.

AEYE-DS will allow inserting an invalid Clinic Key up to three times, after which it will notify the user to contact AEYE Health.

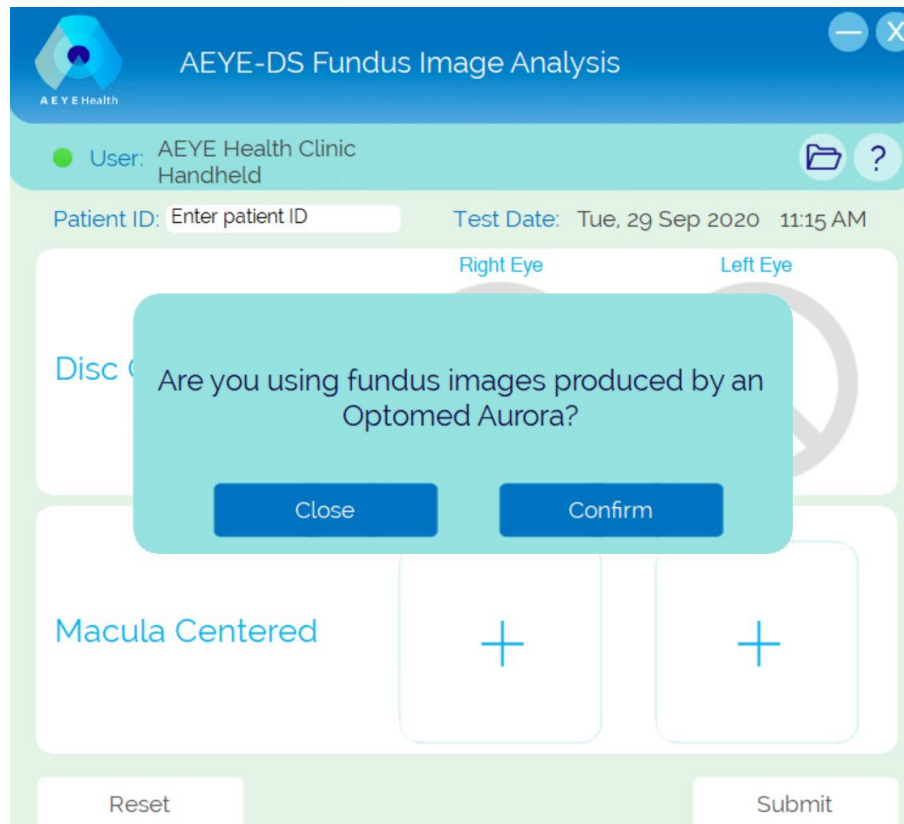


7.4 Getting Started

1. Download and install the AEYE-DS Client.
2. Set up an approved fundus camera to produce fundus images that can be exported to a data storage location accessible to the AEYE-DS Client.
3. Configure the exam space so that minimal light is present.

7.5 Camera Pairing Confirmation

When the AEYE-DS Client is launched, the system will ask to confirm that an indicated fundus camera is paired with the device:



Press “Confirm” to verify that the AEYE-DS is being used with an indicated camera system.

Users will be asked to confirm AEYE-DS is being used with an indicated camera system each time the AEYE-DS Client is started.

7.6 Software Updates

All updates to the AEYE-DS Client will be communicated by AEYE Health to the user via email or phone. Updating the Client requires uninstalling the current version of the client from Windows Settings >> Apps & Features, and then running the setup file for the new Client supplied by AEYE Health.

7.7 Accessing the User Manual and Product Label

AEYE-DS Client comes with an electronic manual that is accessible through the “?” icon located at the top right-hand side of the Client. To open the manual, click the “?” icon. The program will open the manual in a separate viewer window.

AEYE-DS Client has an official product label that can also be viewed from the “?” icon.



8. Image Capture

Images submitted for analysis to AEYE-DS need to be obtained from an approved fundus camera.

8.1 Topcon TRC NW400 with IMAGEnet 6

See Appendix A for instructions.

8.2 Topcon TRC NW400 with IMAGEnet 5

See Appendix B for instructions.

8.3 Topcon TRC NW400 with Lombart DVS

See Appendix C for instructions.

8.4 Optomed Aurora

See Appendix D for instructions.

9. Submitting Images for Diagnosis

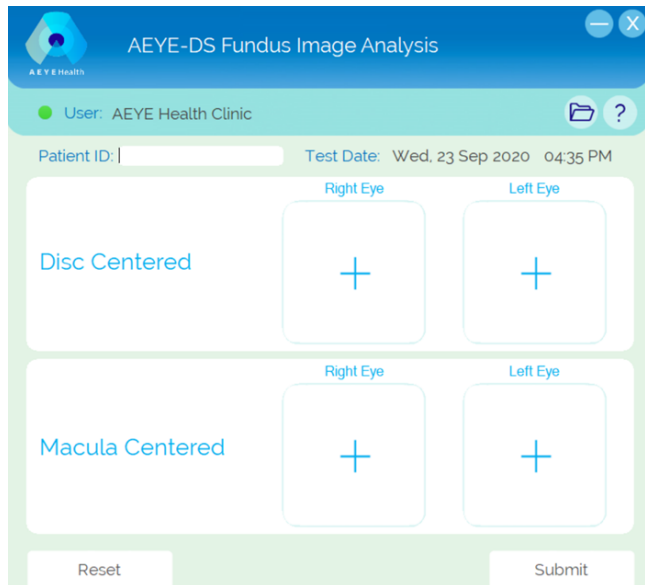
9.1 Submission Criteria

To obtain an AEYE-DS result for a set of patient images, the following prerequisites must be met:

1. AEYE-DS Client is operational.
2. The AEYE-DS Service is available.
3. The computer on which the AEYE-DS Client is installed is connected to the internet.
4. You have an active AEYE-DS account with AEYE Health.
5. Depending on your AEYE-DS Client configuration, there must be a macula-centered for each eye and optionally a disc-centered image for each eye for a total of two or (optionally) four images.
6. All images were obtained from the same patient on the same day, with the same camera.
7. The image file format must be JPEG or PNG.
8. All images should be acquired by a Topcon TRC NW400 or an Optomed Aurora camera.

The AEYE-DS Client must be connected to AEYE servers before submitting any images. This is indicated by the connection status indicator located on the top left of the AEYE-DS Client window. When a connection is available, a green light will appear. When no connection is available, a red will light.

Two Images per Eye



AEYE-DS Fundus Image Analysis

User: AEYE Health Clinic

Patient ID: Test Date: Wed, 23 Sep 2020 04:35 PM

Disc Centered

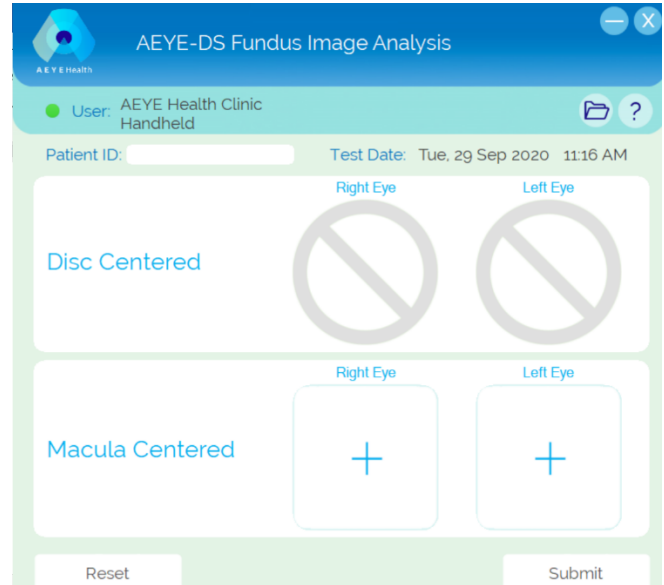
Right Eye Left Eye

Macula Centered

Right Eye Left Eye

Reset Submit

One Image per Eye



AEYE-DS Fundus Image Analysis

User: AEYE Health Clinic Handheld

Patient ID: Test Date: Tue, 29 Sep 2020 11:16 AM

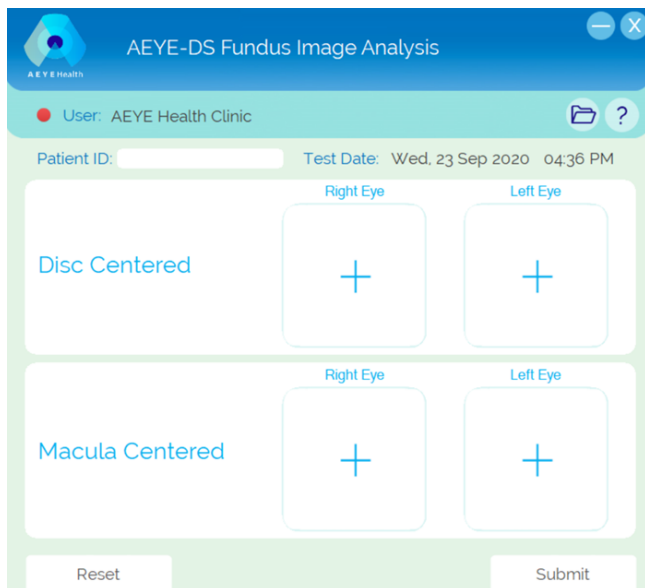
Disc Centered

Right Eye Left Eye

Macula Centered

Right Eye Left Eye

Reset Submit



AEYE-DS Fundus Image Analysis

User: AEYE Health Clinic

Patient ID: Test Date: Wed, 23 Sep 2020 04:36 PM

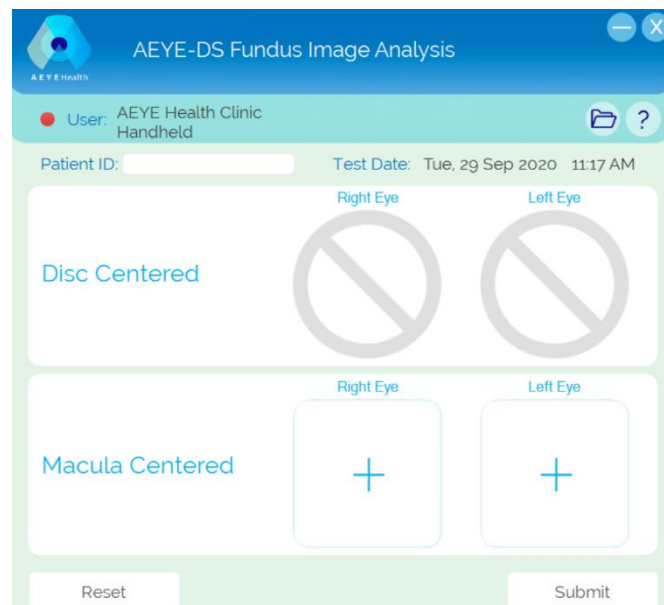
Disc Centered

Right Eye Left Eye

Macula Centered

Right Eye Left Eye

Reset Submit



AEYE-DS Fundus Image Analysis

User: AEYE Health Clinic Handheld

Patient ID: Test Date: Tue, 29 Sep 2020 11:17 AM

Disc Centered

Right Eye Left Eye

Macula Centered

Right Eye Left Eye

Reset Submit

9.2 Selecting and Submitting Patient Images

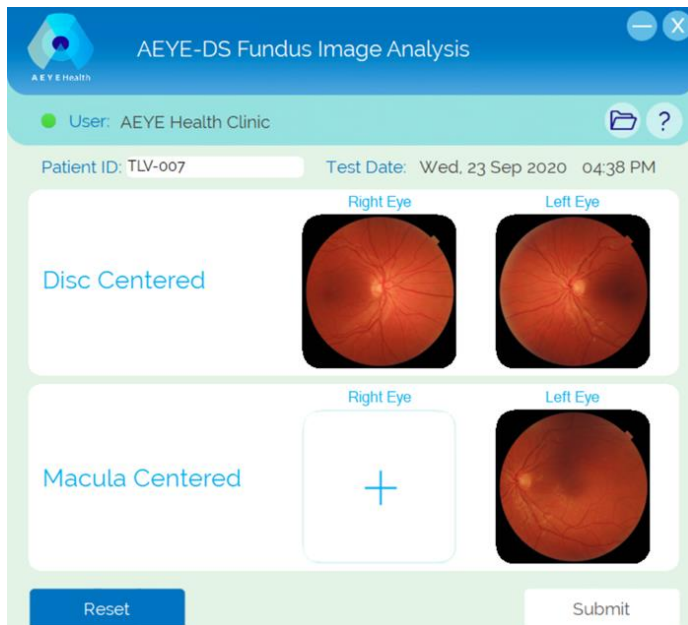
The user will key in a patient ID. Patient ID is mandatory. It is used to identify the patient on the diagnosis report produced by AEYE-DS.

To add patient images, press the “+” button. A Windows File Explorer will open. Select from the File Explorer the relevant image (i.e. Macula Centered-Right Eye, Macula Centered-Left Eye and optionally, disc-centered right eye, disc-centered left eye).



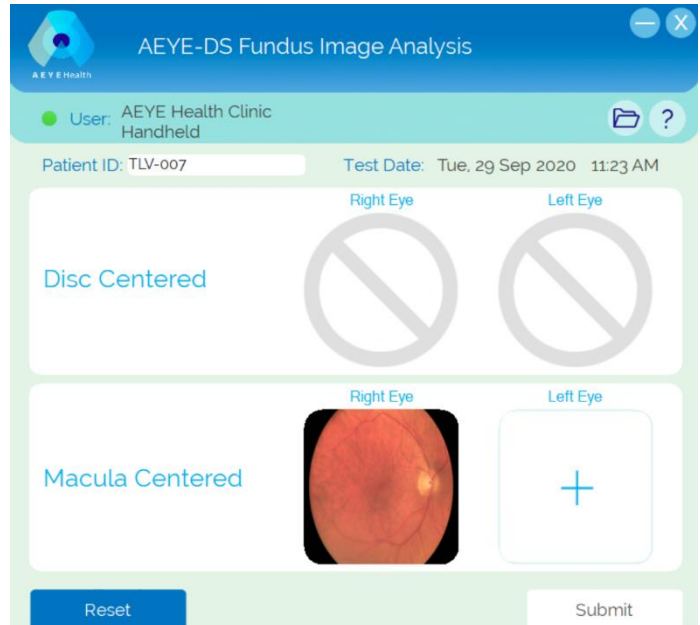
The image file should NOT have a space in its file name.

Two Images per Eye



The screenshot shows the 'AEYE-DS Fundus Image Analysis' window. The user is 'AEYE Health Clinic'. The Patient ID is 'TLV-007' and the Test Date is 'Wed, 23 Sep 2020 04:38 PM'. Under 'Disc Centered', there are two fundus images labeled 'Right Eye' and 'Left Eye'. Under 'Macula Centered', there is a '+' button for the 'Right Eye' and a fundus image for the 'Left Eye'. At the bottom are 'Reset' and 'Submit' buttons.

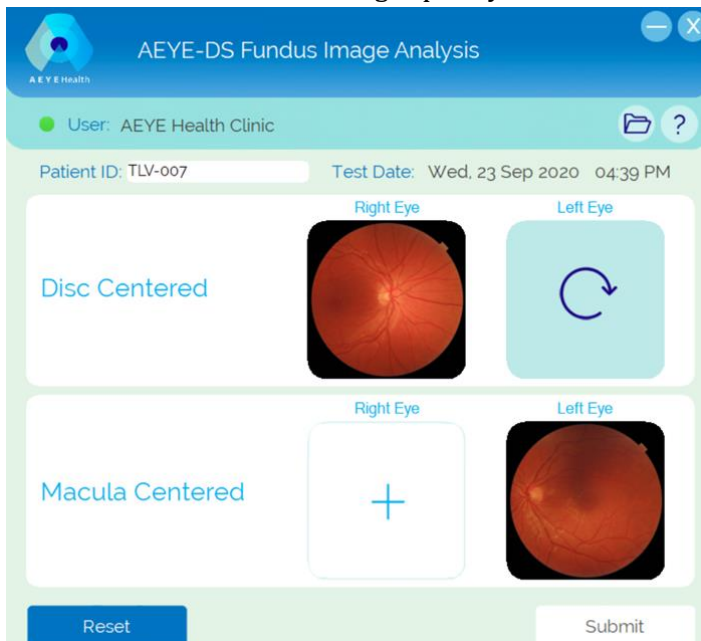
One Image per Eye



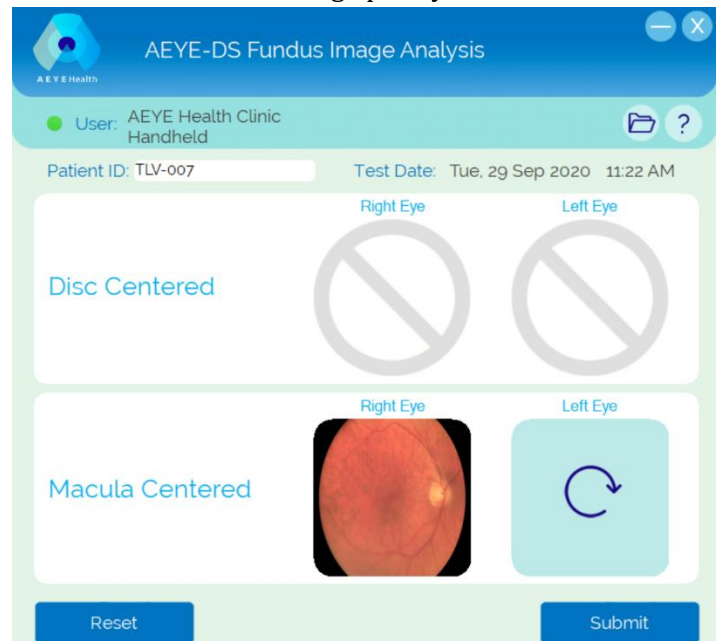
The screenshot shows the 'AEYE-DS Fundus Image Analysis' window. The user is 'AEYE Health Clinic Handheld'. The Patient ID is 'TLV-007' and the Test Date is 'Tue, 29 Sep 2020 11:23 AM'. Under 'Disc Centered', there are two greyed-out circles with diagonal lines, labeled 'Right Eye' and 'Left Eye'. Under 'Macula Centered', there is a fundus image for the 'Right Eye' and a '+' button for the 'Left Eye'. At the bottom are 'Reset' and 'Submit' buttons.

To replace a selected image, hover over the image you want to replace and a “Change” icon will appear. Press the “Change” icon and the File Explorer will open. Select an image from the File Explorer.

Two Images per Eye

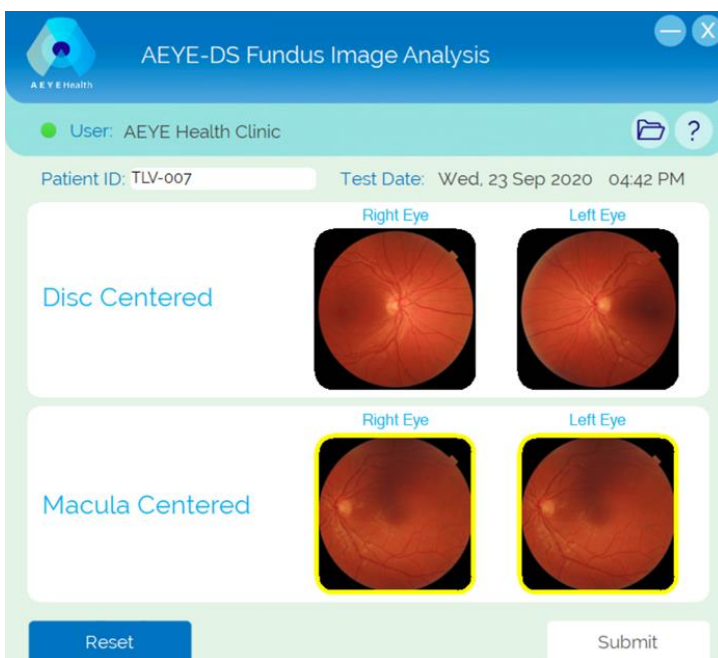


One Image per Eye

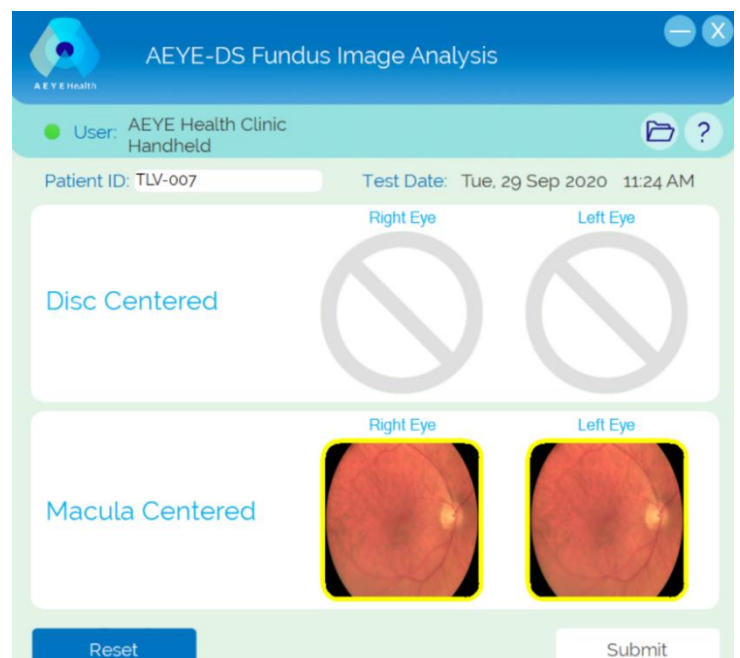


The AEYE-DS Client will detect when the same image file is selected more than once. The Client will mark the duplicate images with a yellow frame. Hovering over the image will display the “Change” icon to allow the user to replace the duplicate image file(s).

Two Images per Eye



One Image per Eye



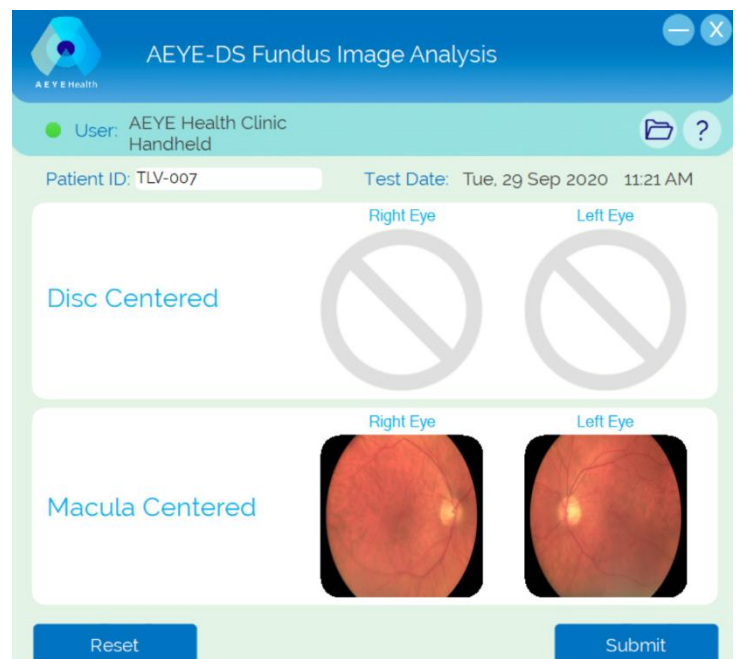
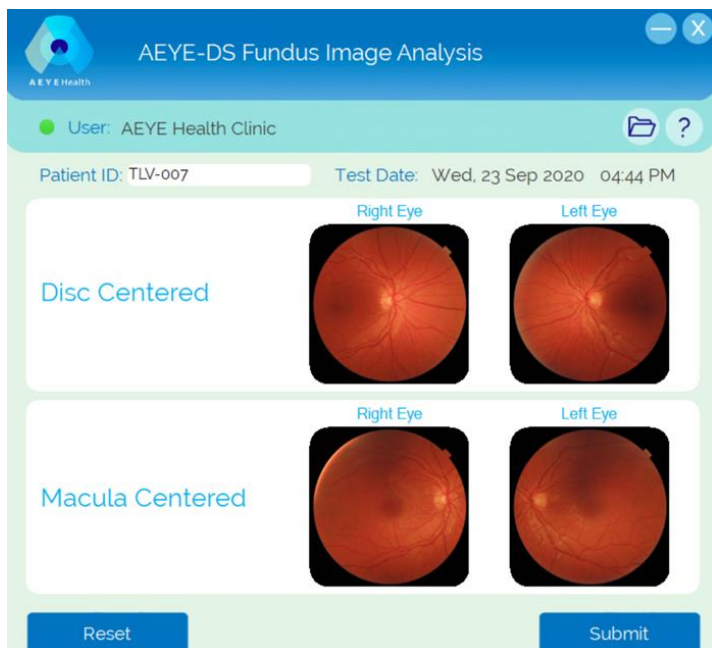
The AEYE-DS Client performs basic checks on the image file name. If the image file name contains text indicating whether the image is of the left or right eye (i.e. L/R or Left/Right) then the AEYE-DS Client will verify that the image file is placed in the appropriate location. If for example an image of the left eye is placed in a location requiring an image of the right eye, then the Client will mark the image with a yellow frame and display the “Change” icon to allow the user to replace the image file.

At any stage in the image selection and placement process, the user can select “Reset”. Pressing “Reset” removes all images and Patient ID information, and allows the user to restart the data entry process for a patient exam.

Once all images are placed in their designated locations, the “Submit” button will become active. Press “Submit” when ready to send the images for diagnosis by AEYE.

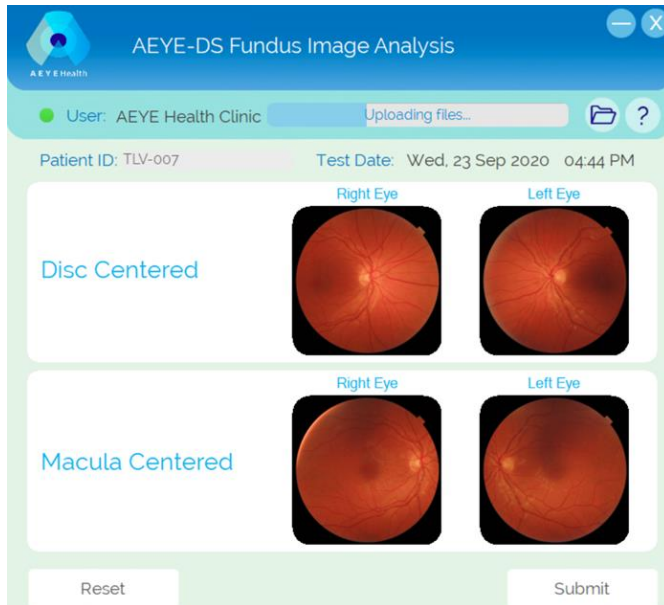
Two Images per Eye

One Image per Eye

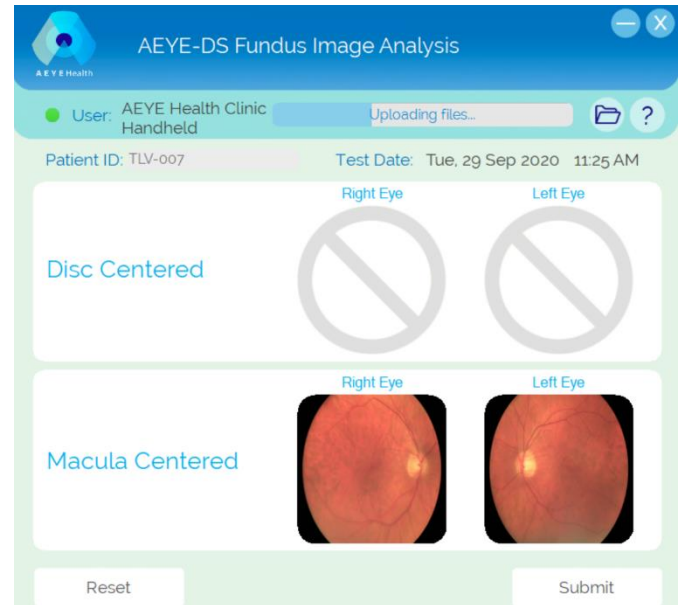


When the exam is being processed by the AEYE-DS Service, a progress bar will appear on the top part of the AEYE Client.

Two Images per Eye



One Image per Eye



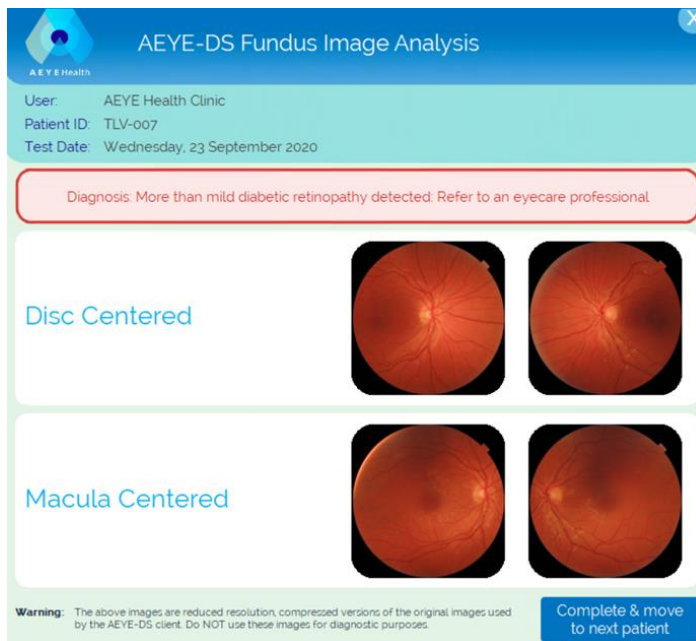
After less than a minute, the AEYE-DS system will generate an output.

9.3 AEYE-DS Outputs

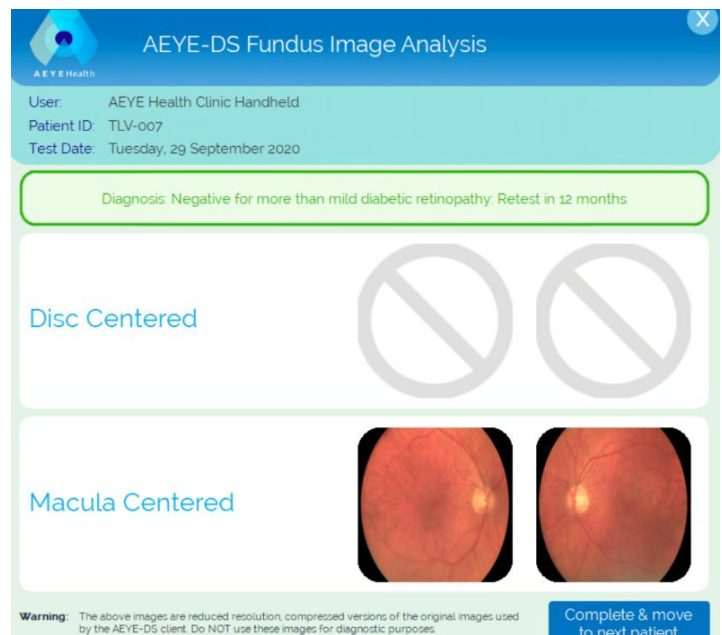
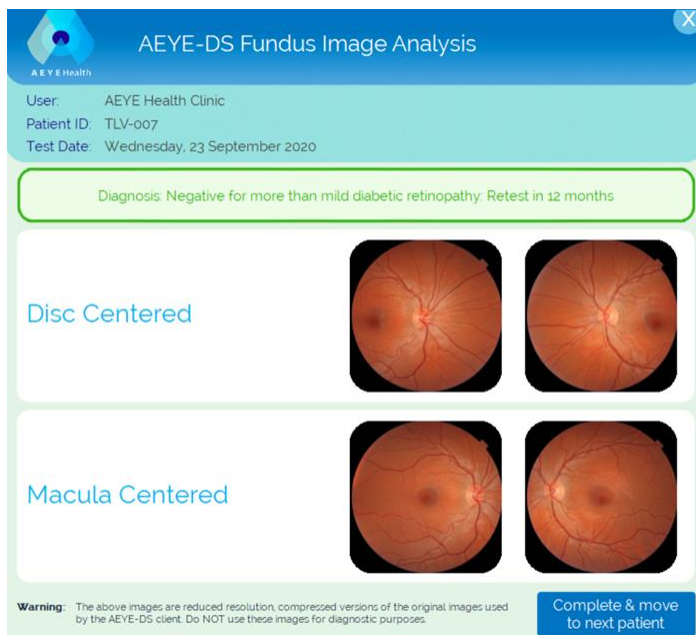
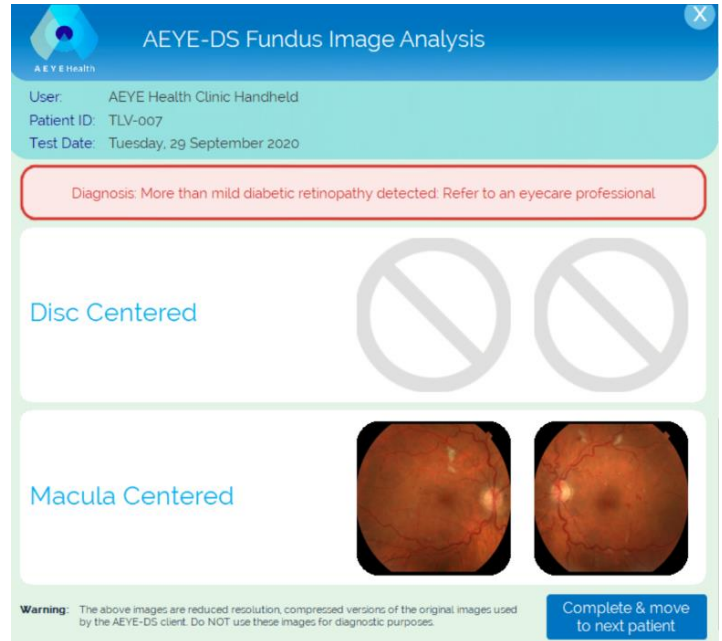
The AEYE-DS Client will output one of four possible results:

1. More than mild diabetic retinopathy detected: Refer to an eyecare professional
2. Negative for more than mild diabetic retinopathy: Retest in 12 months
3. Insufficient image(s) quality
4. Exam processing cannot be completed

Two Images per Eye

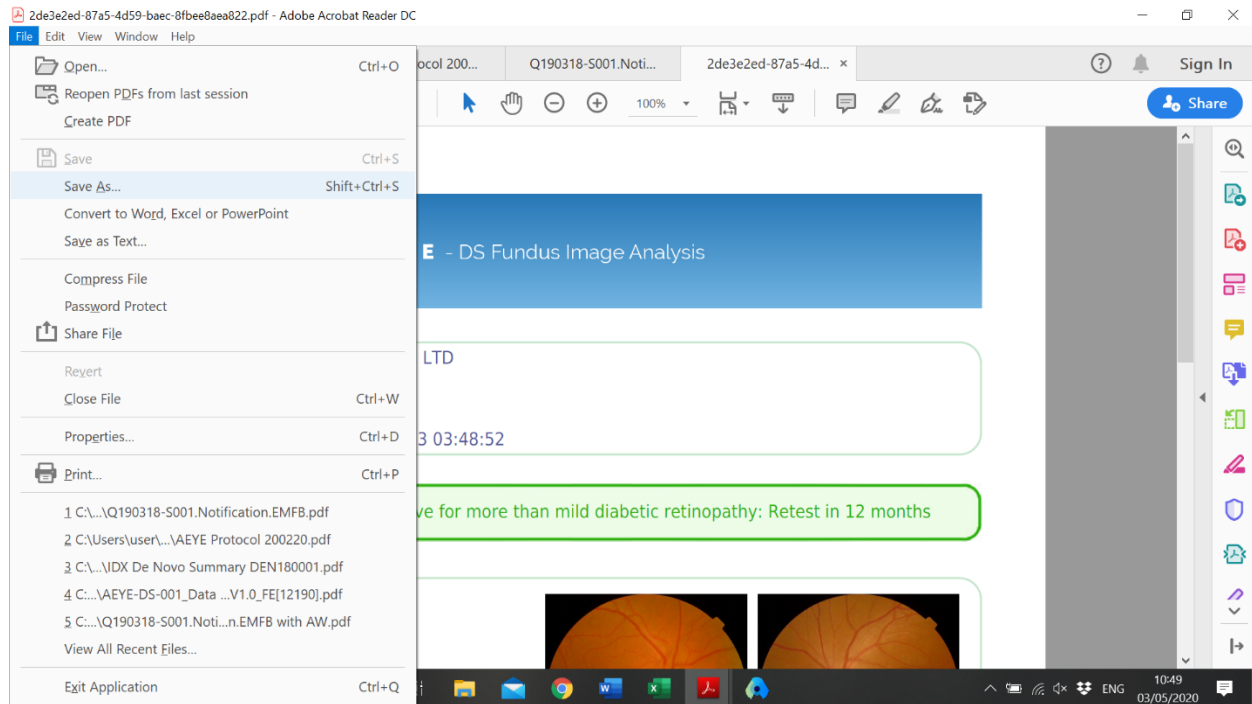


One Image per Eye



If a diagnostic output is produced by AEYE-DS, in addition to its display in the AEYE-DS Client a PDF output report is downloaded and opened using the host computer's default PDF viewer.

Save the PDF diagnosis report in the patient folder by selecting "Save as".

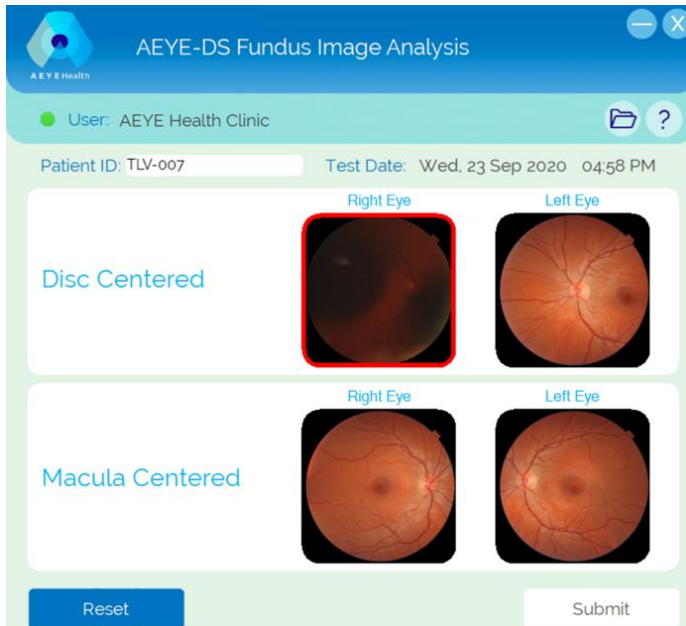


TIP: To retrieve a PDF report produce by AEYE-DS after it has been closed, select the folder icon on the top right of the AEYE-DS Client. When clicked, the Windows File Explorer will open to a folder where all PDF reports are saved there. Report naming convention is aeyehealth_<patient ID>_<date-time stamp>.pdf

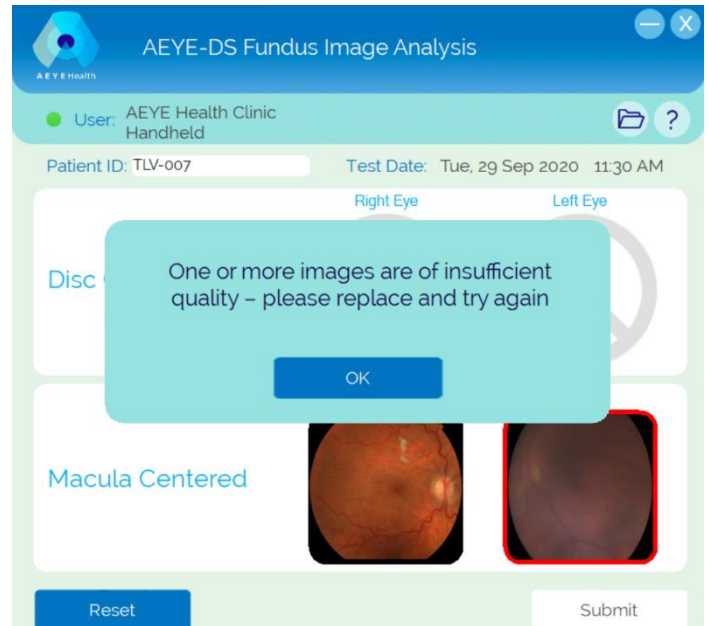
When patient exam is complete, press the "Complete & move to next patient" button to start a new patient exam.

In the case where one or more images were of insufficient quality, no diagnosis will be provided and the insufficient quality images will be highlighted with a red frame. Images can be retaken immediately, while the patient is still at the camera. See section 10 for how to retake and resubmit images in case of insufficient quality.

Two Images per Eye



One Image per Eye



10. Replacing Images Classified as Insufficient Quality

10.1 Retake Insufficient Quality Images

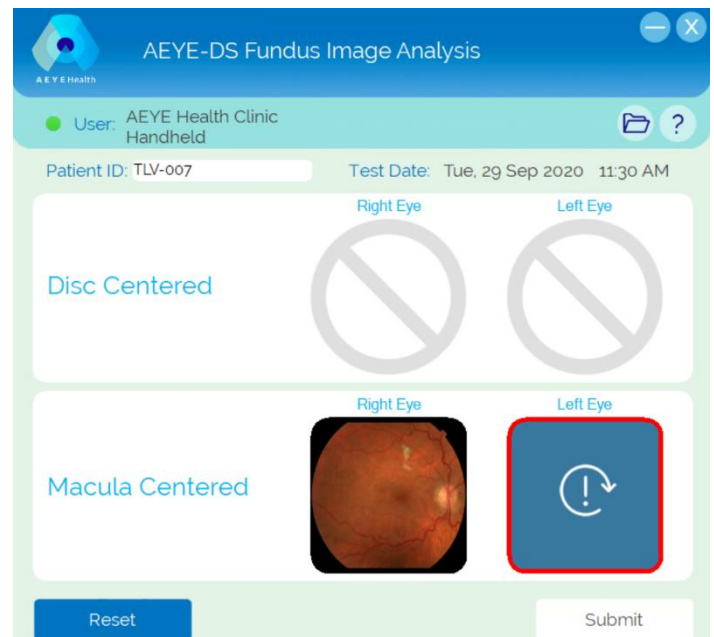
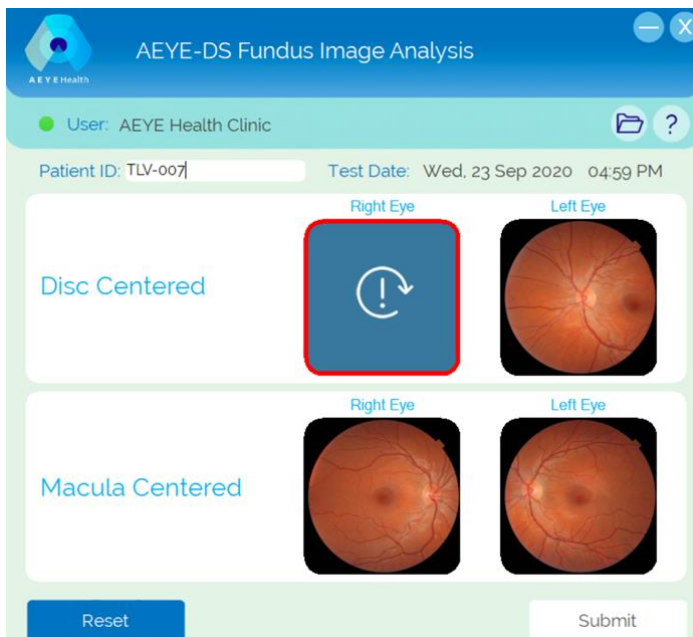
Return to section 8 and **produce** new images only for those images indicated by the AEYE-DS Client as insufficient quality. For example, if the macula-centered image of the right eye was insufficient quality, then **retake** that image only.

10.2 Replace Insufficient Quality Images with New Images

To replace images for an exam with diagnosis “Insufficient image(s) quality”, press the “Change” icon made visible when hovering over the image with the mouse. A File Explorer will open. Select a new image from the File Explorer.

Two Images per Eye

One Image per Eye



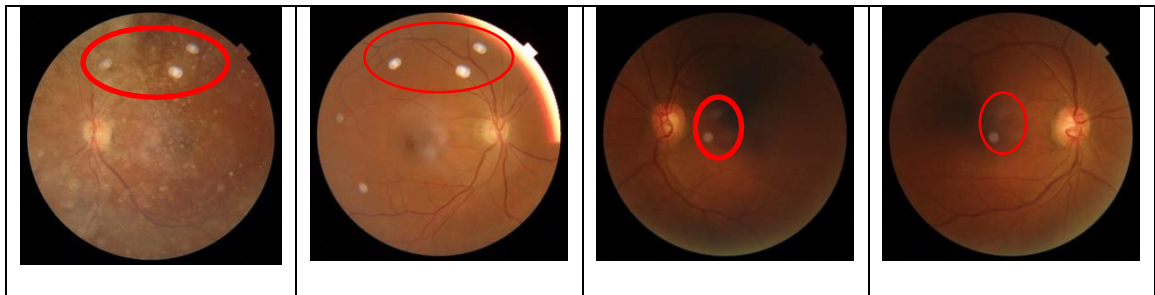
When all the images with a red frame indicating insufficient quality have been replaced, the “Submit” button will become active.

11. Quality Control Guidelines

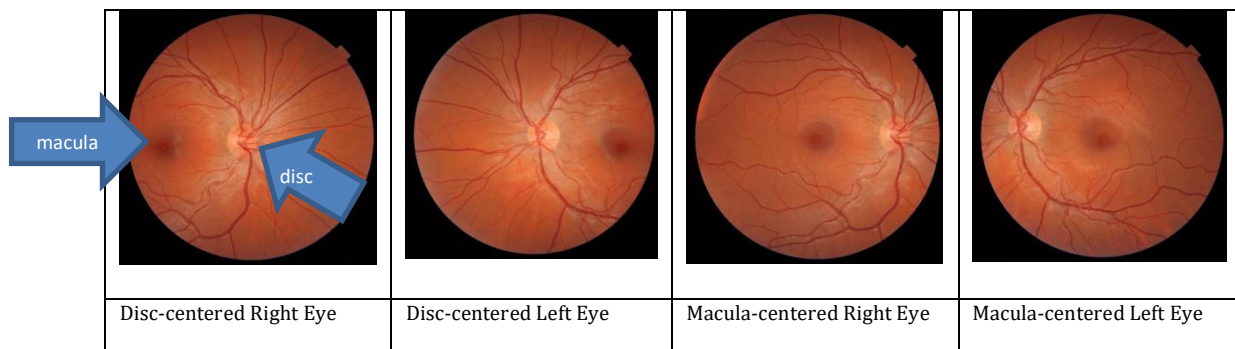
To produce high-quality images, the following guidelines should be followed:

- Images should be taken in a dark room.
- Subjects should place their forehead firmly on the forehead rest.
- Subjects should cover their “other eye” with their hand.
- Subjects should focus on the red dot displayed by the camera.

Review images to determine if they have any visible artifacts as a result of a dirty lens. The Aurora lens should be periodically cleaned to avoid unwanted artifacts.



Macula-centered images (and optionally) disc-centered images should be placed in their designated placeholder in the AEYE-DS Client. The macula is the dark spot in the center of the retina. The optic-disc is the bright circle with veins passing through it. Images of the right eye feature the optic disc to the right of the macula. Images of the left eye feature the optic-disc to the left of the macula.





12. Troubleshooting Q&A

12.1 Connectivity Lost (red indicator light)

In the case of a connectivity problem between the AEYE Client and the AEYE Service (i.e. red indicator light in the AEYE-DS Client), please contact your local IT help desk.

12.2 Retrieving a PDF Report

To retrieve a PDF report produced by AEYE-DS after it has been closed, click on the folder icon located at the top right hand side of the Client, next to the “?” icon. Report naming convention is aeyehealth_<patient ID>_<date-time stamp>.pdf

For all other issues, please contact AEYE Health.

12.3 Common Questions

Q: I can't tell which image belongs to which eye.

A: Looking at the image for the right eye, the optic-disc (bright circle) is to the right of the macula (dark spot). In the left eye, the optic-disc is to the left of the macula.

Q: AEYE-DS Client does not return a response.

A: Please verify that the Windows PC is connected to the internet.

13. Support

For any other questions or inquiries, please feel free to contact AEYE Health:

+1 (866) 262-7343 or info@ayehealth.com



14. Reference Information

Computer requirements

Hardware	Intel architecture
Minimum processor	Pentium 4
Minimum internal memory	2 Gigabytes
Minimum disk space	250MB
Operating system	Microsoft 7 or newer

Supported Camera System(s)

Manufacturer and Model	Topcon TRC-NW400 Optomed Aurora
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Input image specifications

Image file format	JPEG, PNG
Image format	At least 1000x1000 pixels per image

Output specifications

File format	PDF
mtmDR output values	- More than mild diabetic retinopathy detected: Refer to an eyecare professional - Negative for more than mild diabetic retinopathy: Retest in 12 months - Insufficient image(s) quality

15. Software Licensing Information

[EULA PROVIDED SEPARATELY]

APPENDIX A – Topcon NW400 with IMAGeNet 6

Image Capture with the Topcon NW400 and IMAGeNet 6 software.

A.1 Booting the System

Turn on Topcon TRC NW400.

Launch the IMAGeNet software on the connected PC.

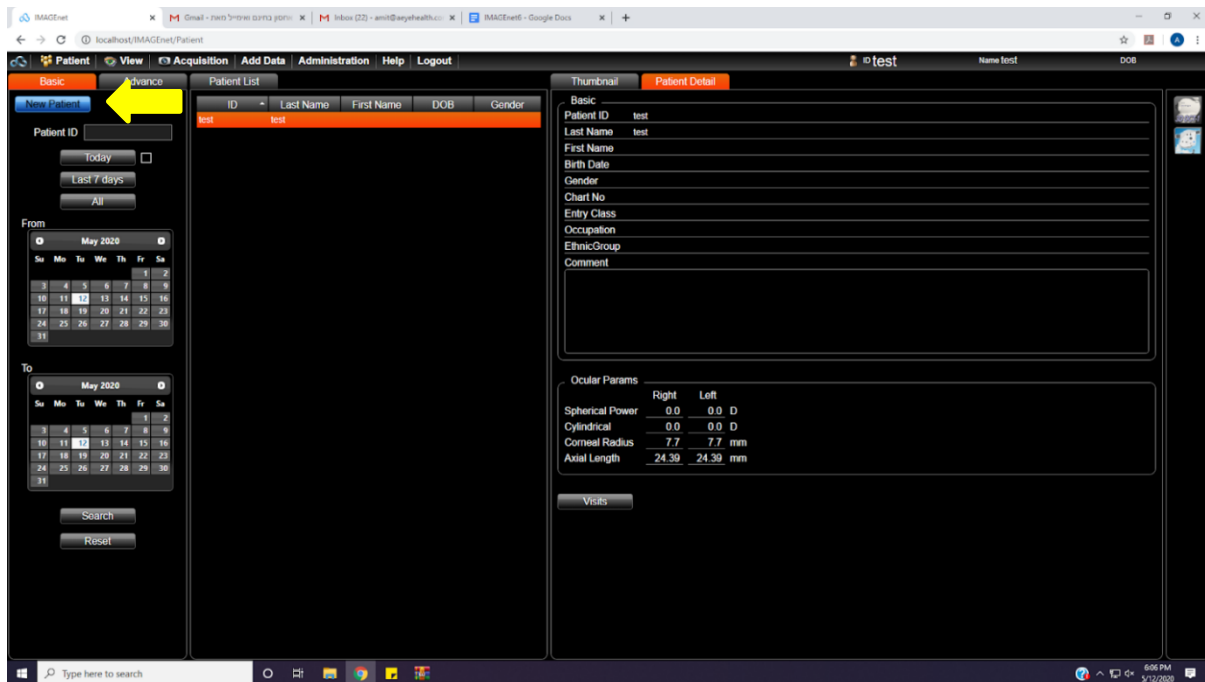
Launch the AEYE-DS Client on the connected PC.

IMPORTANT: Periodically clean the Topcon

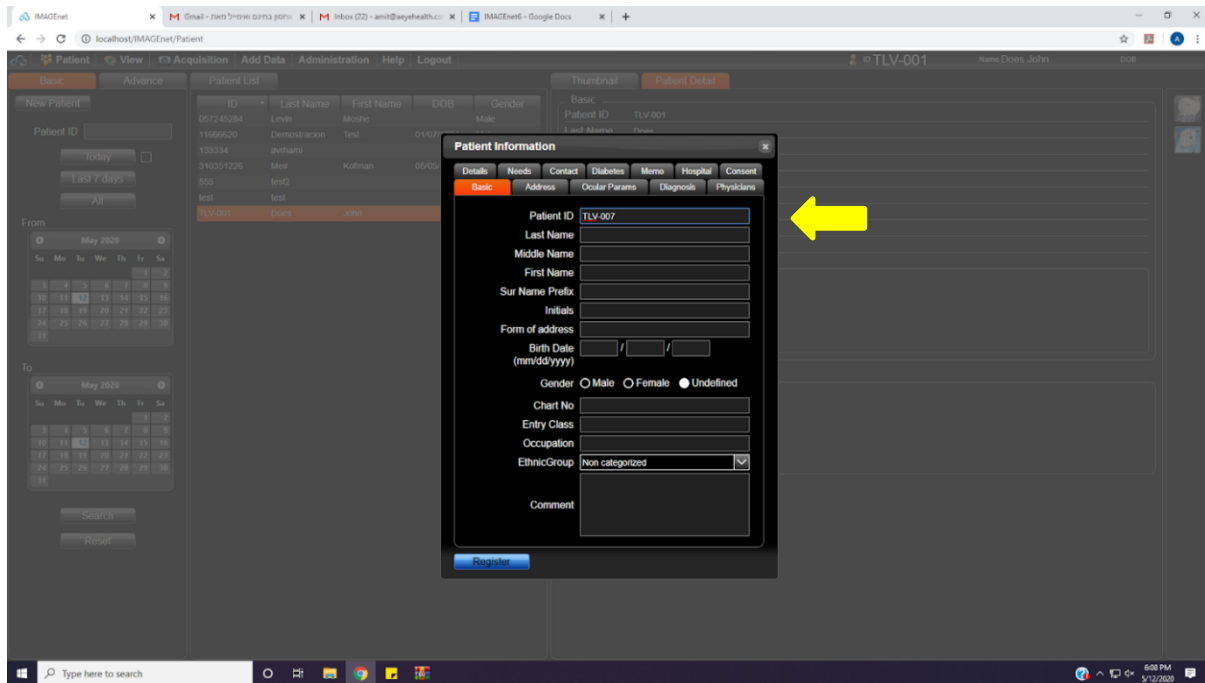
TRC NW400 lens to ensure that image quality is not affected by unwanted artifacts.

A.2 Create a Patient Record in the IMAGeNet Software

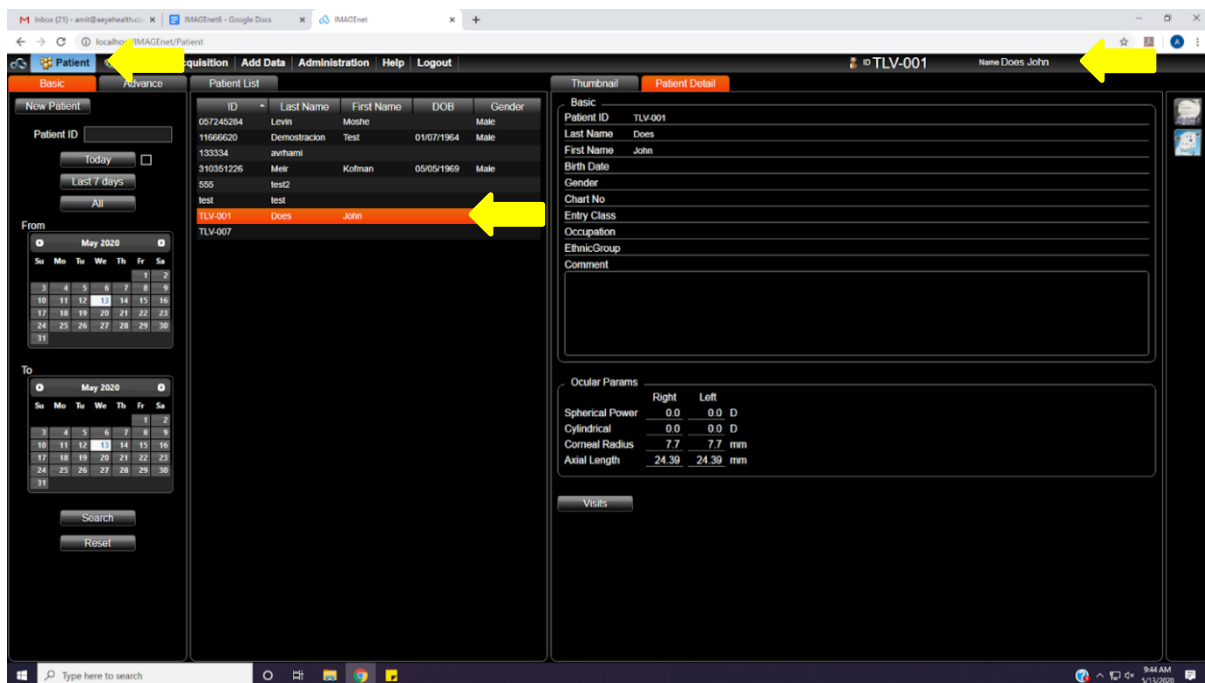
Select “New Patient” to create a new patient record.



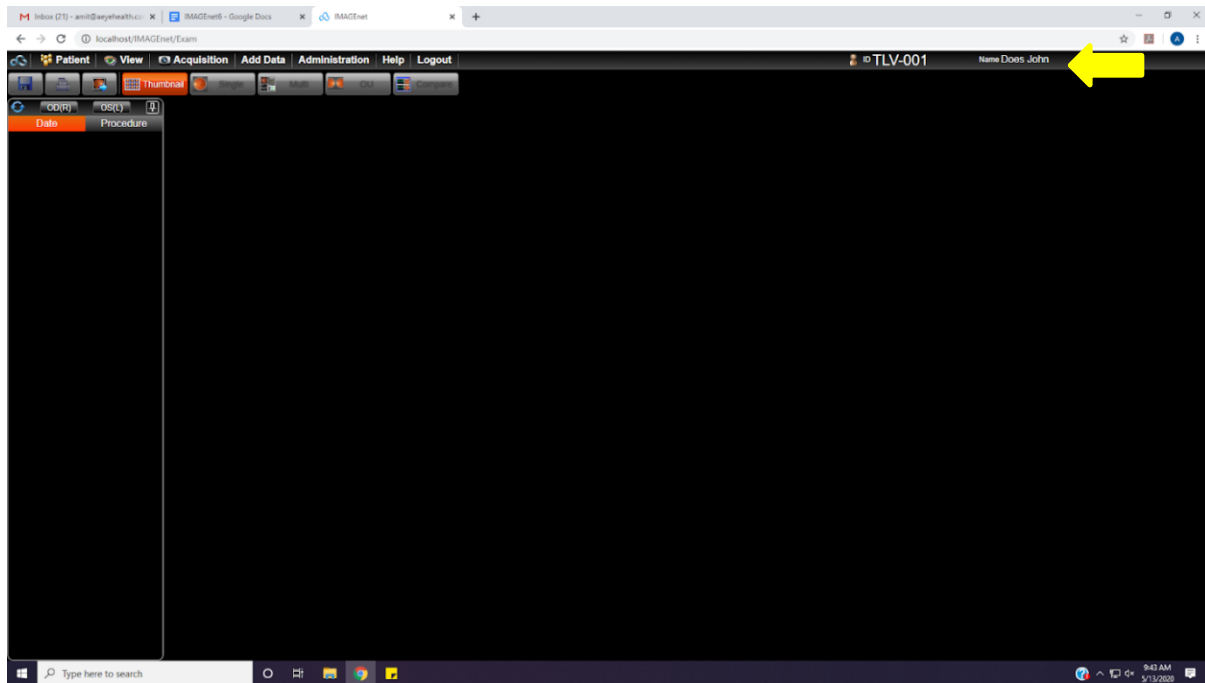
The screenshot shows the IMAGeNet software interface. The 'Patient' tab is selected, and the 'New Patient' button is highlighted with a yellow arrow. The interface includes a 'Patient List' table with columns for ID, Last Name, First Name, DOB, and Gender. The 'Basic' tab is active, showing fields for Patient ID, Last Name, First Name, Birth Date, Gender, Chart No, Entry Class, Occupation, Ethnic Group, and Comment. The 'Ocular Params' section displays values for Spherical Power, Cylindrical, Corneal Radius, and Axial Length for both Right and Left eyes. The 'Visits' button is also visible.



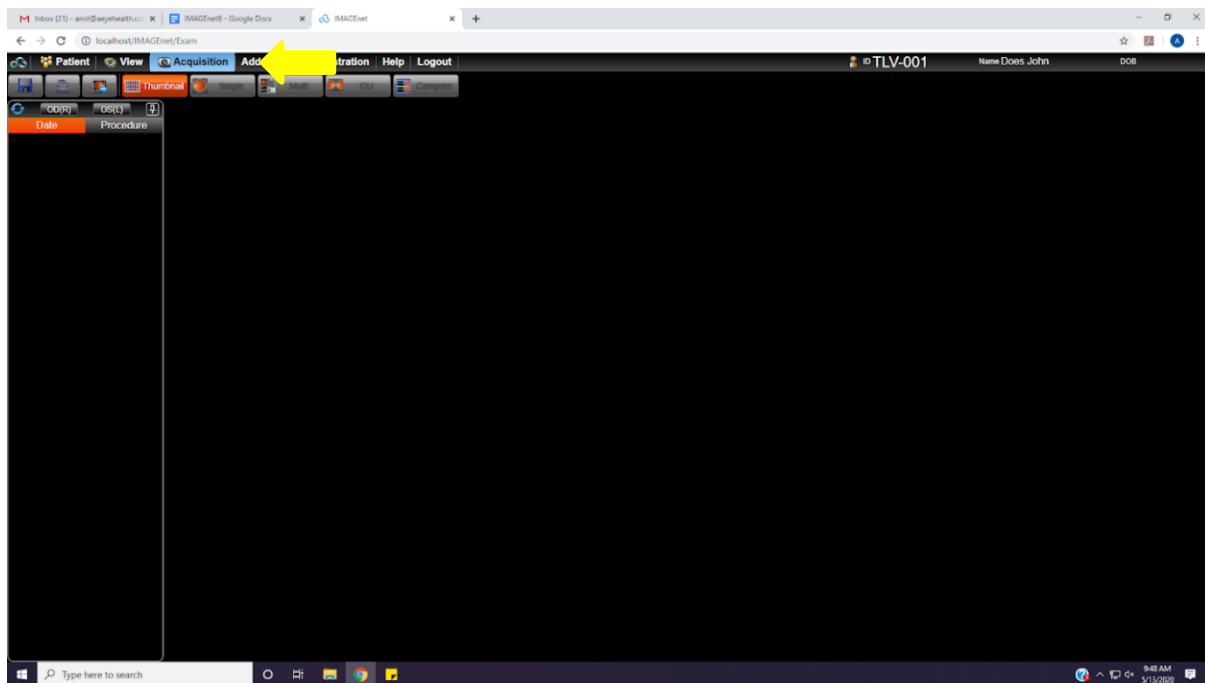
The new patient record should now be visible.

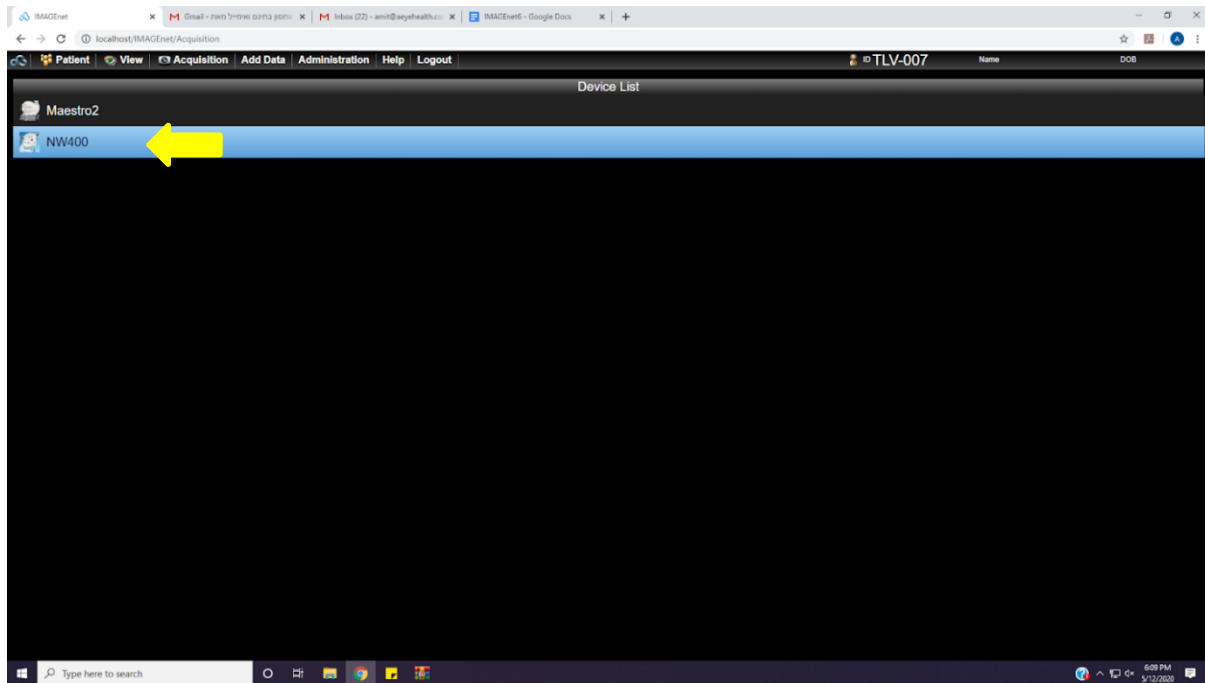


Double-click on the patient item from the list to enter the patient record.



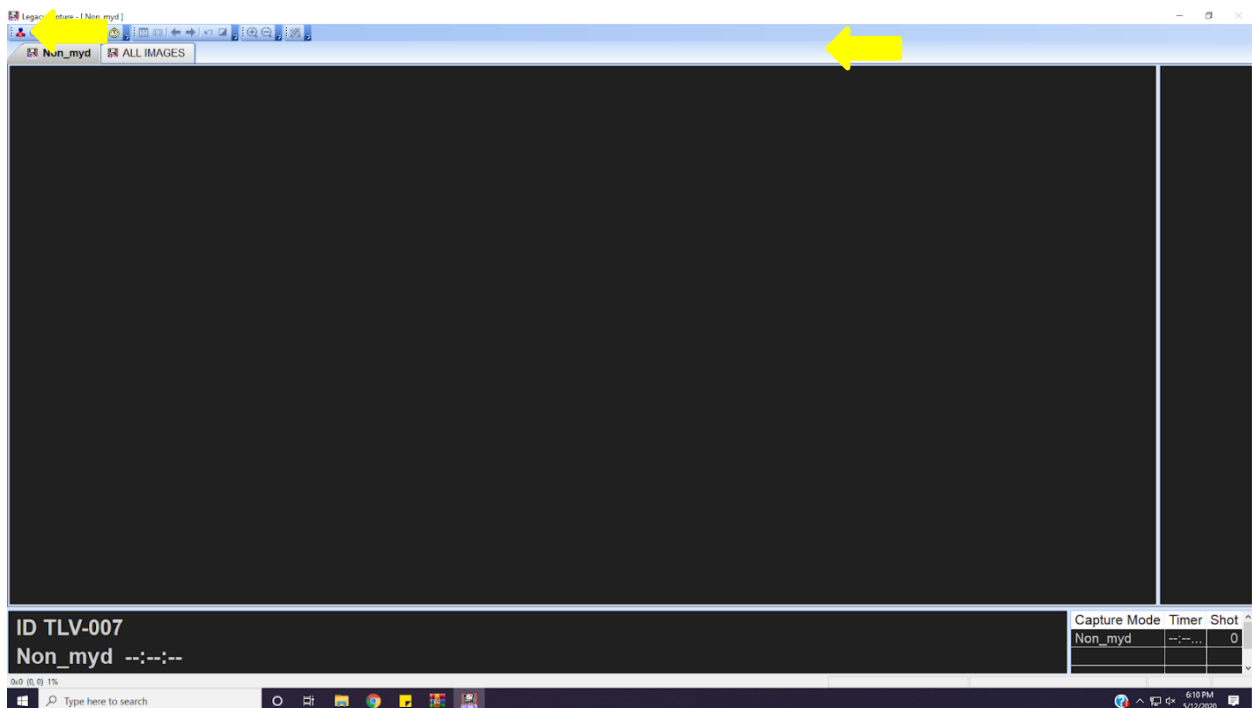
Select “Acquisition” and then the “NW400” to activate the connected camera system.





Activating the connected camera opens the LegacyCapture window.

NOTE: To end the camera session, **press** the patient icon with the X circled in red as shown in the screenshot below. You should close the camera session only if you do not intend to take an image.



A.3 Image Capture with Topcon TRC NW400

On the Topcon touch display, **press** the “Menu” button (top left of the screen) and **select** the “Fundus” option.



Looking at the 5 touch-buttons at the bottom of the touch display:

- **Select** the “OU” option to automatically photograph both patient eyes.
- **Select** “OD” to automatically photograph the right eye only.
- **Select** “OS” to automatically photograph the left eye only.
- **Press** the “Fixation” button to select the desired image center.

“M” centers the image on the macula, “D” centers the image on the optic disc and “C” centers the image between the macula and the disc.

The “Peripheral” touch button should be set to “Off”.



A.4 Taking Macula-Centered Images

Set the “Fixation” option to “M” and select “OU” to photograph both eyes.

Position patient on the chin and forehead-rest of the fundus camera. Patient should remain in this position until the end of the session.

TIP 1: Patient’s forehead should remain firmly pressed against the forehead-rest to ensure the fundus camera can properly focus the image.

TIP 2: Patient should cover their other eye with their hand.

Adjust chin rest position by moving it up/down using the arrows on the Topcon touch display such that the patient's eye vertically centers between the two dotted horizontal lines on the camera display.

Looking at the blue frame on the Topcon touch display, **touch** the pupil on the image of the patient’s eye. This indicates to the camera where the center of the eye is located and allows it to correct its position. **Repeat** this as needed until the eye is centered in the blue square and until the patient can clearly see the green X.

Confirm that the patient is looking for and focusing on the center of the green X, which should become visible as the camera positions itself.

TIP: Patient focus on the center of the green X is critically important for obtaining high-quality images with the proper fixation point.

Select “Capture START” to start the automated image capture process. If the “Capture START” button is not active (no blue frame is visible around the button), then **select** “NW400” in the IMAGENet software. The LegacyCapture window will open on the PC and the “Capture START” button will become active.

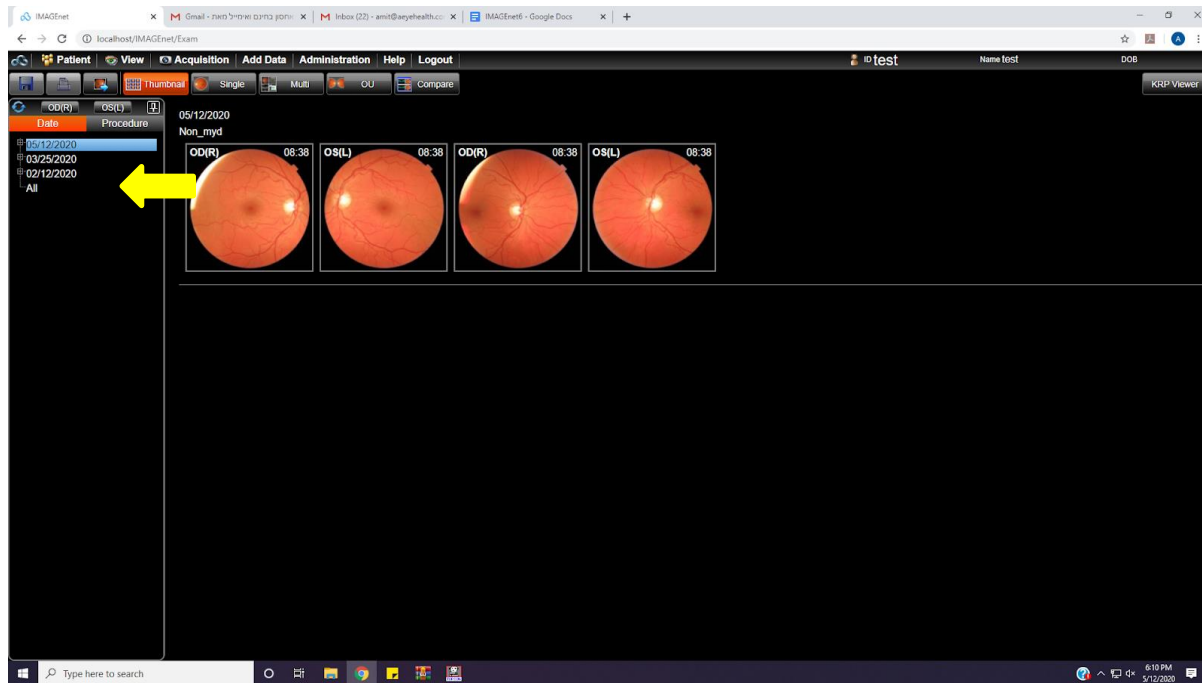
When image capture is complete, **select** “Save” in the LegacyCapture window on the PC. Selecting “Save” saves the images and closes the image capture window.

IMPORTANT: Image file names contain a timestamp that corresponds to the date/time of their save operation. Saving multiple images at once will result in all saved images having the same timestamp in their filename. Using this timestamp can help the operator identify whether the images are disc or macula-centered. For example, if you start with disc-centered fixation (and save the images) and then move on to macula-centered fixation (and save the images) then the images with disc-center will have an earlier timestamp.

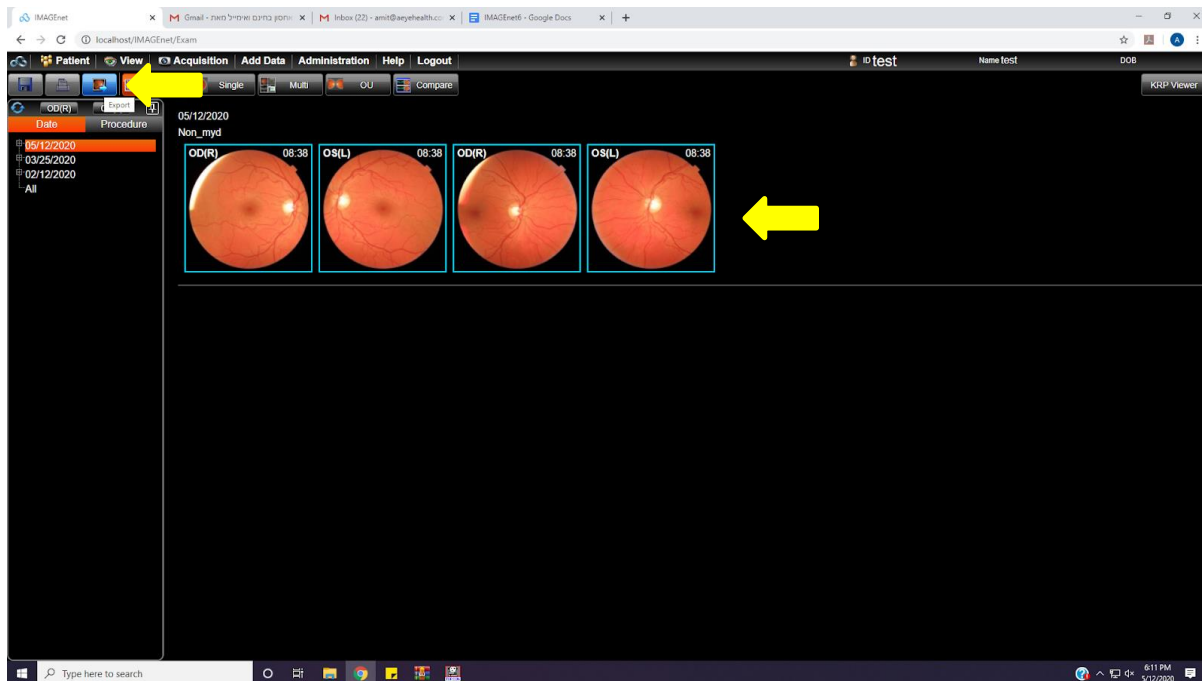


A.5 Export Images from the IMAGENet Software to a Folder

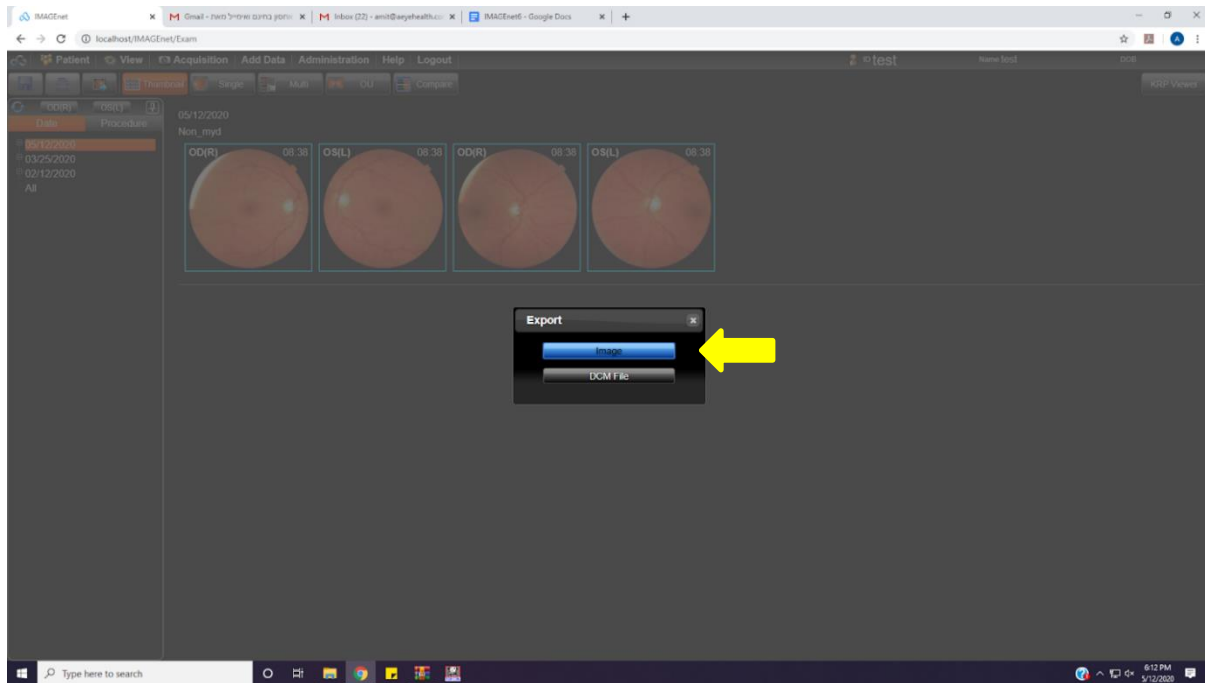
In the patient record in the IMAGENet software, **click** on the date of the exam. The exam images will appear on the screen.



Select images to be exported (selected images appear with a blue frame) and then select the “Export” icon.

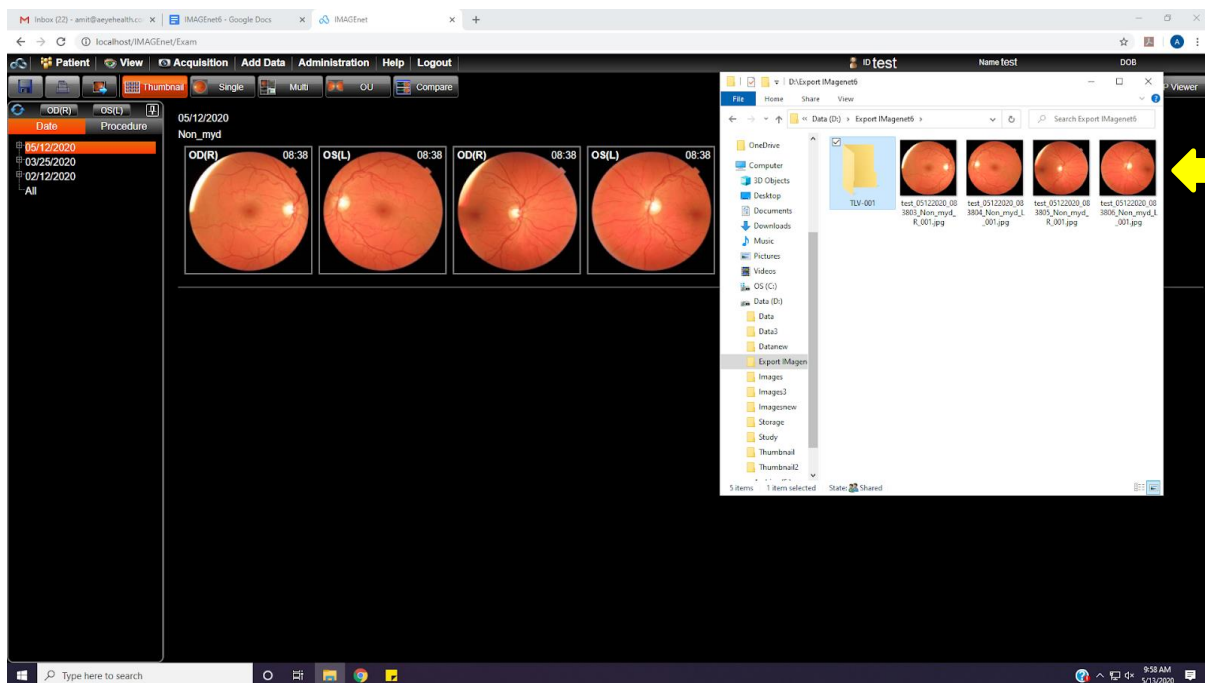


Select “Image” from the Export popup.



Open the configured destination folder on the computer desktop to **verify** that the pictures where exported.

TIP: Set the “View” option in the Windows File Explorer to “Extra large icons” so you can see the actual images.



APPENDIX B – Topcon NW400 with IMAGeNet 5

Image Capture with the Topcon NW400 and IMAGeNet 5 software.

B.1 Booting the System

Turn on Topcon TRC NW400.

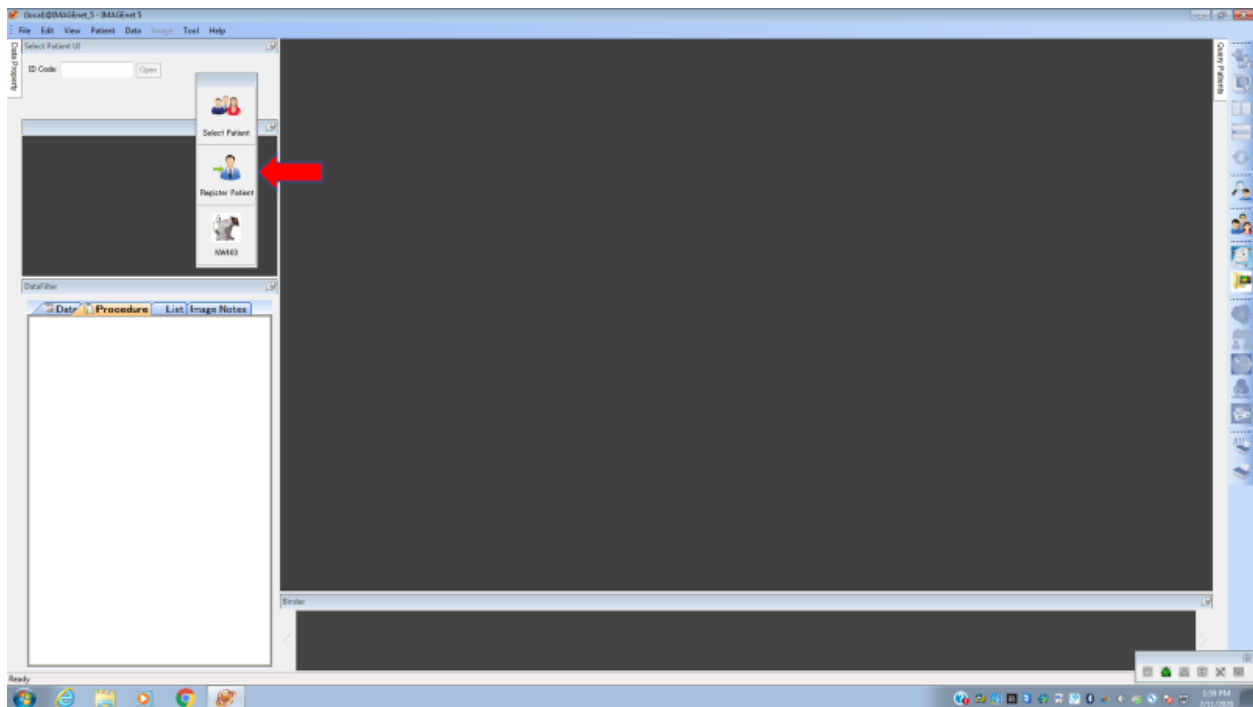
Launch the IMAGeNet software on the connected PC.

Launch the AEYE-DS Client on the connected PC.

IMPORTANT: Periodically clean the Topcon TRC NW400 lens to ensure that image quality is not affected by unwanted artifacts.

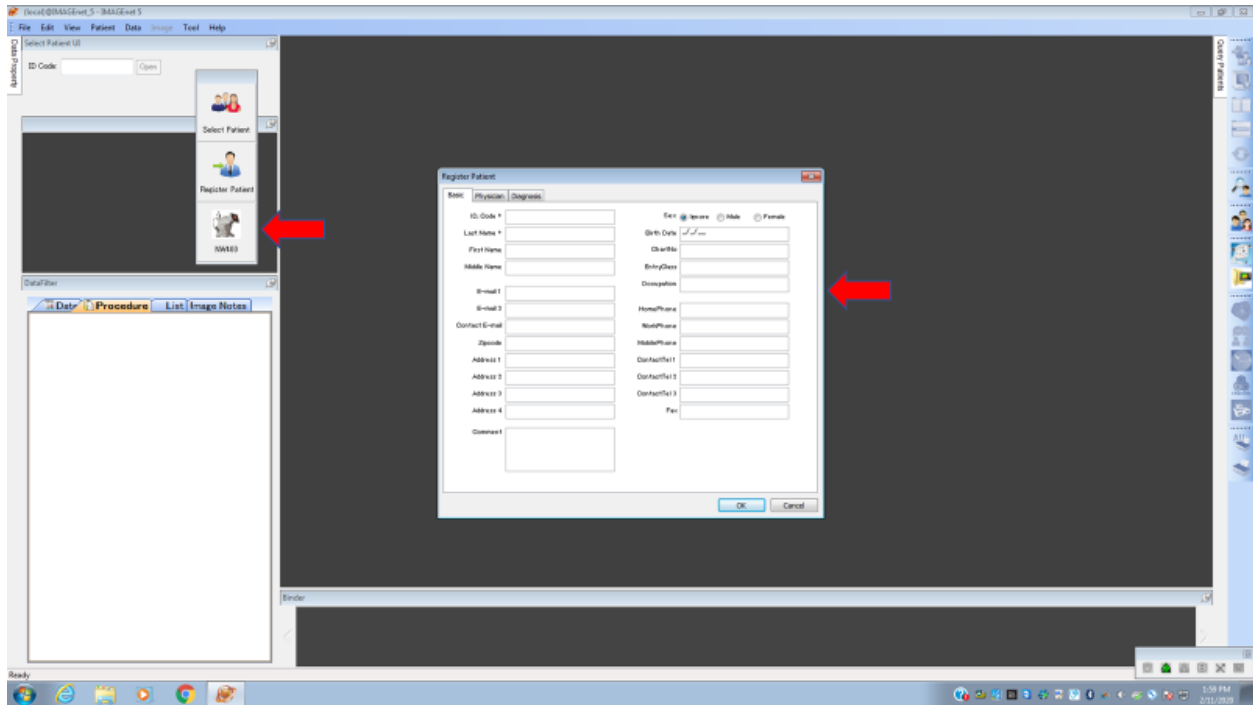
B.2 Create a Patient Record in the IMAGeNet Software

Select “Register Patient” from the IMAGeNet floating menu to create a new patient record.



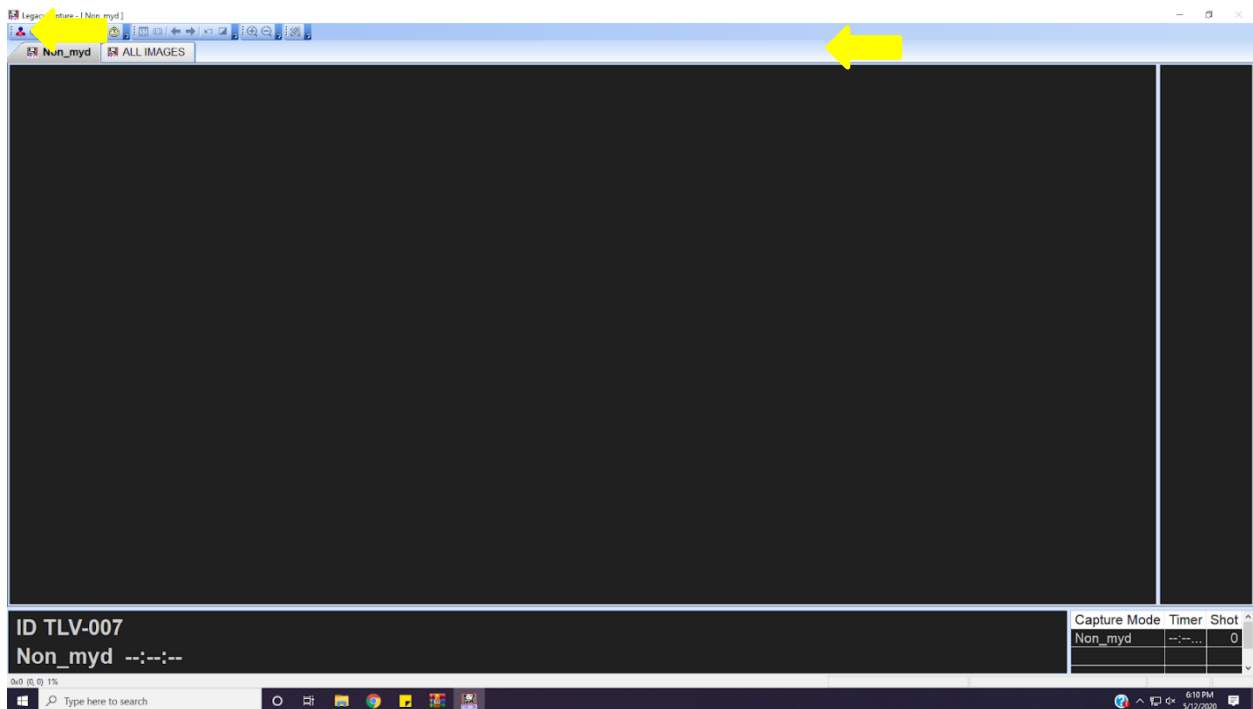
Enter patient details.

Select the NW400 on the floating menu bar to activate the connected camera system.



Activating the connected camera opens the LegacyCapture window.

NOTE: To end the camera session, **press** the patient icon with the X circled in red as shown in the screenshot below. You should close the camera session only if you do not intend to take an image.



B.3 Image Capture with Topcon TRC NW400

On the Topcon touch display, **press** the “Menu” button (top left of the screen) and **select** the “Fundus” option.



Looking at the 5 touch-buttons at the bottom of the touch display:

- **Select** the “OU” option to automatically photograph both patient eyes.
- **Select** “OD” to automatically photograph the right eye only.
- **Select** “OS” to automatically photograph the left eye only.
- **Press** the “Fixation” button to select the desired image center.

“M” centers the image on the macula, “D” centers the image on the optic disc and “C” centers the image between the macula and the disc. For the purpose of this study, select “M” (macula-centered) or “D” (disc-centered) as needed.

The “Peripheral” touch button should be set to “Off”.



B.4 Taking Macula-Centered Images

Set the “Fixation” option to “M” and select “OU” to photograph both eyes.

Position patient on the chin and forehead-rest of the fundus camera. Patient should remain in this position until the end of the session.

TIP 1: Patient’s forehead should remain firmly pressed against the forehead-rest to ensure the fundus camera can properly focus the image.

TIP 2: Patient should cover their other eye with their hand.

Adjust chin rest position by moving it up/down using the arrows on the Topcon touch display such that the patient's eye vertically centers between the two dotted horizontal lines on the camera display.

Looking at the blue frame on the Topcon touch display, **touch** the pupil on the image of the patient’s eye. This indicates to the camera where the center of the eye is located and allows it to correct its position. **Repeat** this as needed until the eye is centered in the blue square and until the patient can clearly see the green X.

Confirm that the patient is looking for and focusing on the center of the green X, which should become visible as the camera positions itself.

TIP: Patient focus on the center of the green X is critically important for obtaining high-quality images with the proper fixation point.

Select “Capture START” to start the automated image capture process. If the “Capture START” button is not active (no blue frame is visible around the button), then **select** “NW400” in the IMAGENet software. The LegacyCapture window will open on the PC and the “Capture START” button will become active.

When image capture is complete, **select** “Save” in the LegacyCapture window on the PC. Selecting “Save” saves the images and closes the image capture window.

IMPORTANT: Image file names contain a timestamp that corresponds to the date/time of their save operation. Saving multiple images at once will result in all saved images having the same timestamp in their filename. Using this timestamp can help the operator identify whether the images are disc or macula-centered. For example, if you start with disc-centered fixation (and save the images) and then move on to macula-centered fixation (and save the images) then the images with disc-center will have an earlier timestamp.

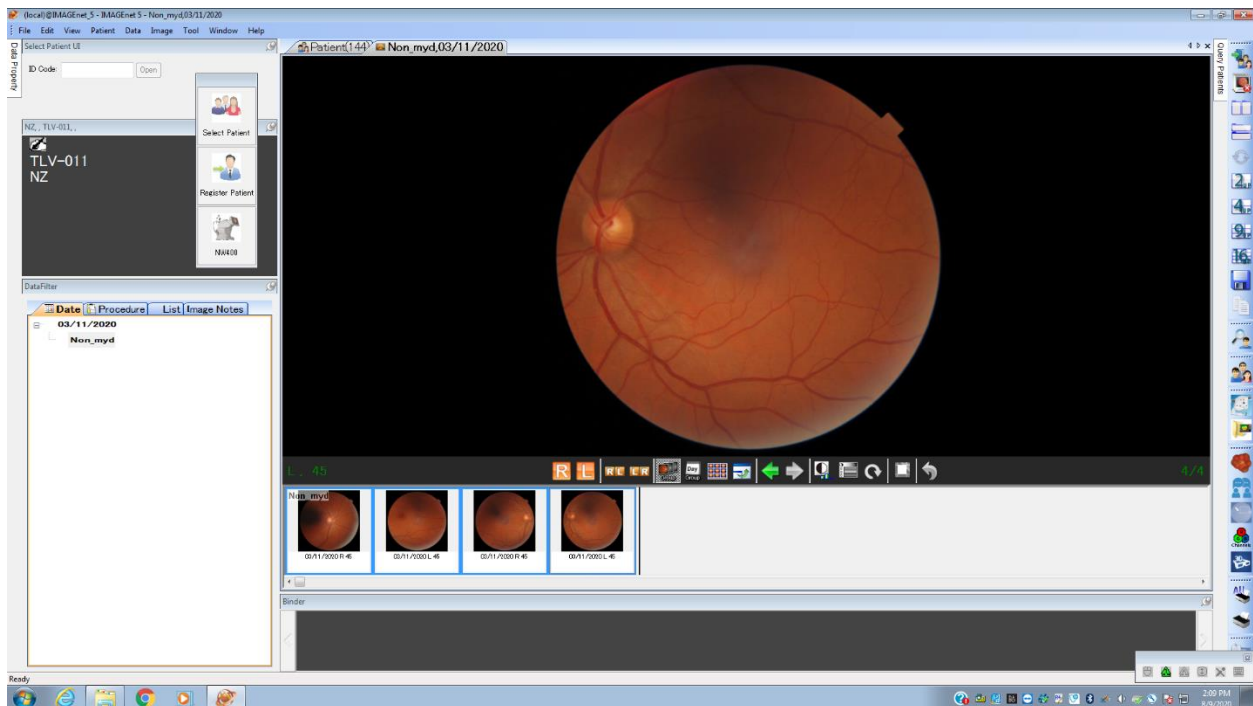


B.5 Export Images from the IMAGENet Software to a Folder

From the patient record on the IMAGENet software and **click** on the date of the exam. A window will open with the exam images.



Select the new images captured by clicking on the image with the mouse and holding the 'ctrl' key to enable selecting multiple images. Once the relevant images are selected (selected images are indicated with a blue frame), **select** "Data > Export to Folder" from the top menu.





The images will be sent to a preconfigured folder (typically C:\Users\IMAGEnet\Desktop\Pictures, but location may change depending on the configuration of the software).

Open the destination folder on the computer desktop to **verify** that the pictures where exported.

TIP: Set the “View” option in the Windows File Explorer to “Extra large icons” so you can see the actual images.

APPENDIX C – Topcon NW400 with Lombart DVS

Image Capture with the Topcon NW400 and Lombart DVS software.

C.1 Booting the System

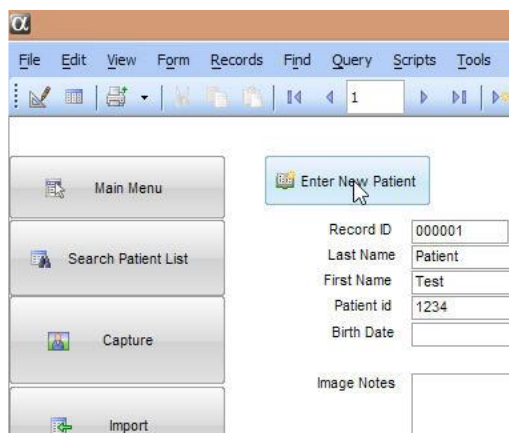
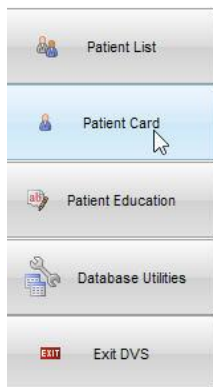
Turn on Topcon TRC NW400.

Launch the DVS software on the connected PC.

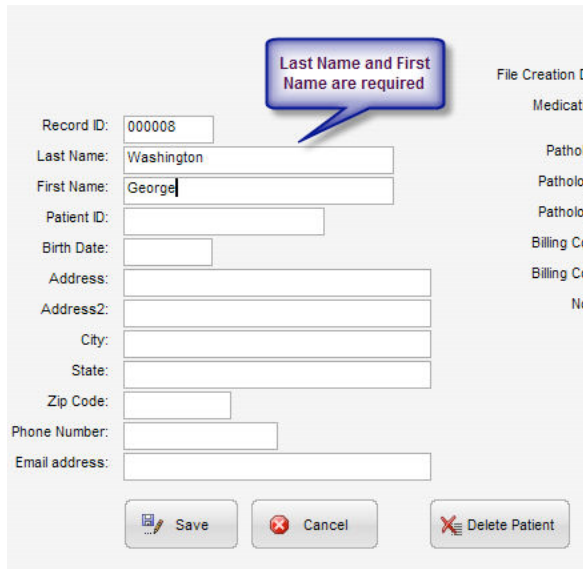
IMPORTANT: Periodically clean the Topcon TRC NW400 lens to ensure that image quality is not affected by unwanted artifacts.

C.2 Create a Patient Record in the DVS Software

From the main menu, **select** “Patient Card” and then “Enter New Patient” to create a new patient record.



Patient Last Name and First Name are required fields.



Last Name and First Name are required

Record ID: 000008

Last Name: Washington

First Name: George

Patient ID:

Birth Date:

Address:

Address2:

City:

State:

Zip Code:

Phone Number:

Email address:

File Creation Date:

Medication:

Pathology:

Pathology:

Pathology:

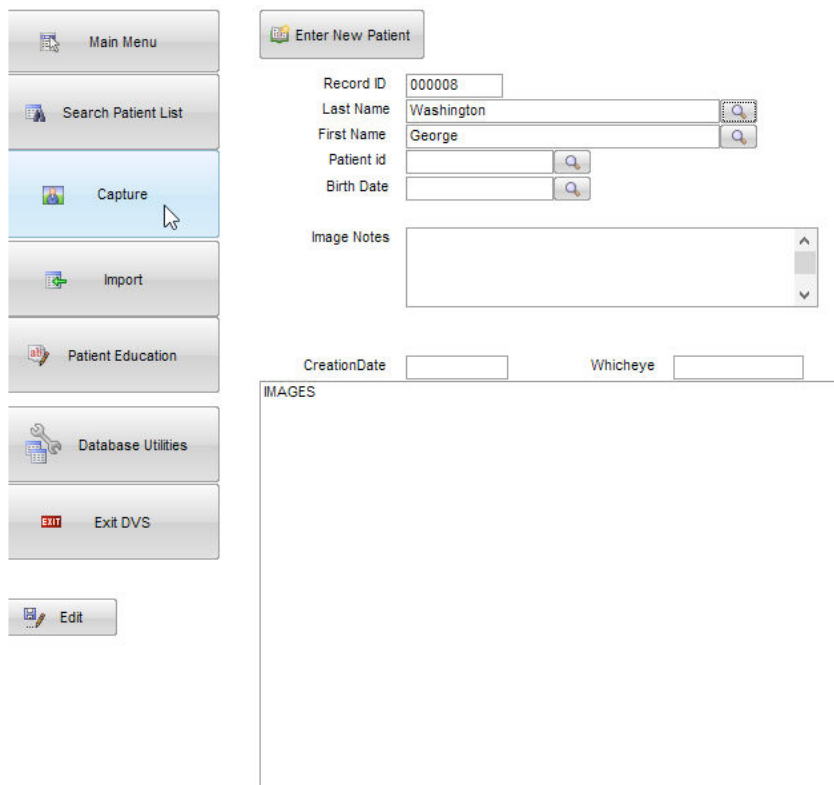
Billing Code:

Billing Code:

No:

Save Cancel Delete Patient

The new patient record should now be visible:



Main Menu

Search Patient List

Capture

Import

Patient Education

Database Utilities

Exit DVS

Edit

Enter New Patient

Record ID: 000008

Last Name: Washington

First Name: George

Patient id:

Birth Date:

Image Notes:

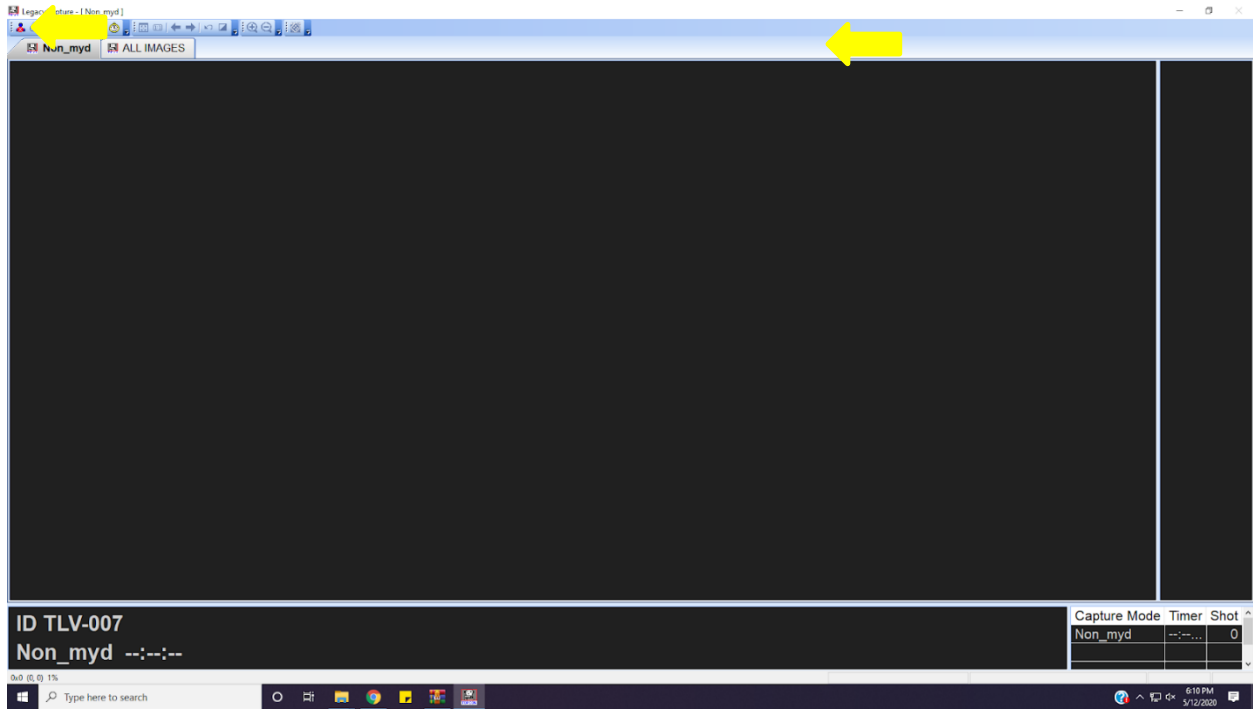
CreationDate:

Whicheck:

IMAGES

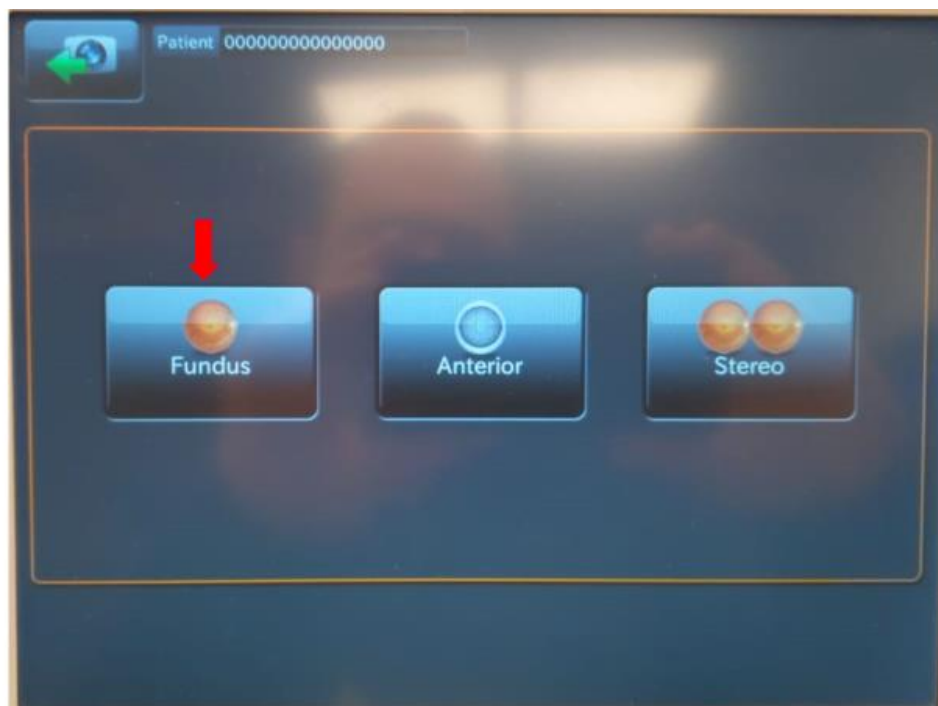
Select “Capture” to activate the connected camera system. Activating the connected camera opens the LegacyCapture window.

NOTE: To end the camera session, **press** the patient icon with the X circled in red as shown in the screenshot below. You should close the camera session only if you do not intend to take an image.



C.3 Image Capture with Topcon TRC NW400

On the Topcon touch display, **press** the “Menu” button (top left of the screen) and **select** the “Fundus” option.



Looking at the 5 touch-buttons at the bottom of the touch display:

- **Select** the “OU” option to automatically photograph both patient eyes.
- **Select** “OD” to automatically photograph the right eye only.
- **Select** “OS” to automatically photograph the left eye only.
- **Press** the “Fixation” button to select the desired image center.

“M” centers the image on the macula, “D” centers the image on the optic disc and “C” centers the image between the macula and the disc. For the purpose of this study, select “M” (macula-centered) or “D” (disc-centered) as needed.

The “Peripheral” touch button should be set to “Off”.



C.4 Taking Macula-Centered Images

Set the “Fixation” option to “D” and select “OU” to photograph both eyes.

Position patient on the chin and forehead-rest of the fundus camera. Patient should remain in this position until the end of the session.

TIP 1: Patient’s forehead should remain firmly pressed against the forehead-rest to ensure the fundus camera can properly focus the image.

TIP 2: Patient should cover their other eye with their hand.

Adjust chin rest position by moving it up/down using the arrows on the Topcon touch display such that the patient’s eye vertically centers between the two dotted horizontal lines on the camera display.

Looking at the blue frame on the Topcon touch display, **touch** the pupil on the image of the patient's eye. This indicates to the camera where the center of the eye is located and allows it to correct its position. **Repeat** this as needed until the eye is centered in the blue square and until the patient can clearly see the green X.

Confirm that the patient is looking for and focusing on the center of the green X, which should become visible as the camera positions itself.

TIP: Patient focus on the center of the green X is critically important for obtaining high-quality images with the proper fixation point.

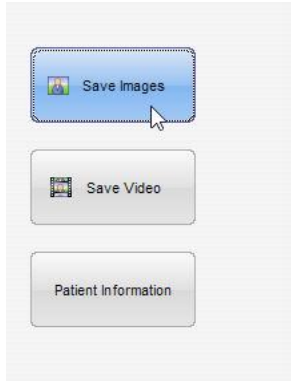
Select "Capture START" to start the automated image capture process. If the "Capture START" button is not active (no blue frame is visible around the button), then **select** "Capture" in the DVS software. The LegacyCapture window will open on the PC and the "Capture START" button will become active.

When image capture is complete, **select** "Save" in the LegacyCapture window on the PC. Selecting "Save" saves the images and closes the image capture window.

IMPORTANT: Image file names contain a timestamp that corresponds to the date/time of their save operation. Saving multiple images at once will result in all saved images having the same timestamp in their filename. Using this timestamp can help the operator identify whether the images are disc or macula-centered. For example, if you start with disc-centered fixation (and save the images) and then move on to macula-centered fixation (and save the images) then the images with disc-center will have an earlier timestamp.

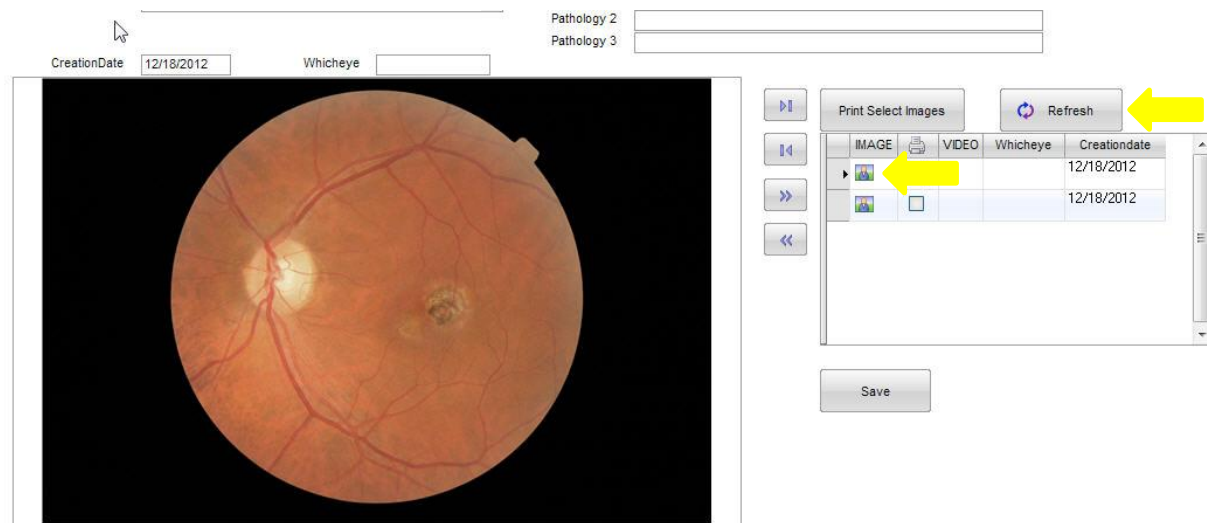


Select also "Save Images" in the DVS software.

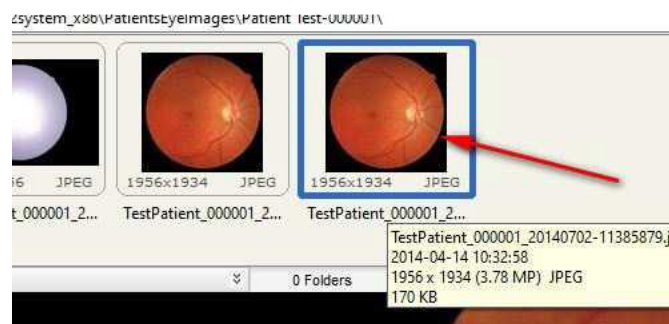


C.5 Export Images from the DVS Software to a Folder

From the patient record, **click** on the image icon to open an image into full screen view. If the most recent images don't show up on the form right away, then click the Refresh button.

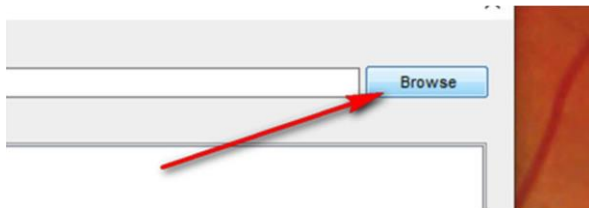


Once the image is open in the viewer, move the cursor to the top of the window until the image explorer bar drops down, showing all images in the patient's folder.

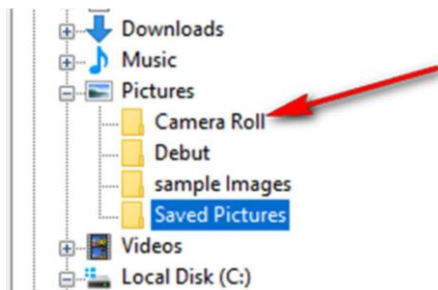


Single click the image you want to export. If you have multiple images to export, hold the Ctrl key down while single clicking multiple images.

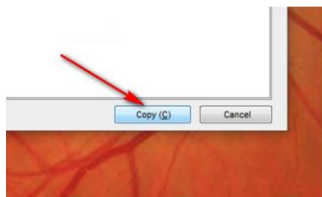
Once you have selected your images, **press** the “c” key on the keyboard (not Ctrl+c). You can also right-click on any one of the images you have selected and **select** “Copy to Folder”.



Once the “Copy” window is open, **click** the “Browse” button to choose the destination folder.



Click the Copy button to export the images.



The images have now been copied to the folder that you have selected.

Once you have selected the destination folder for the first time, that selection will remain in the “History” tab for easy access later. Use the “History” tab to quickly select the destination folder without browsing.



Open the destination folder on the computer desktop to **verify** that the pictures were exported.

TIP: Set the “View” option in the Windows File Explorer to “Extra large icons” so you can see the actual images.

APPENDIX D – Optomed Aurora

Image Capture with the Optomed Aurora fundus camera.

D.1 Setup

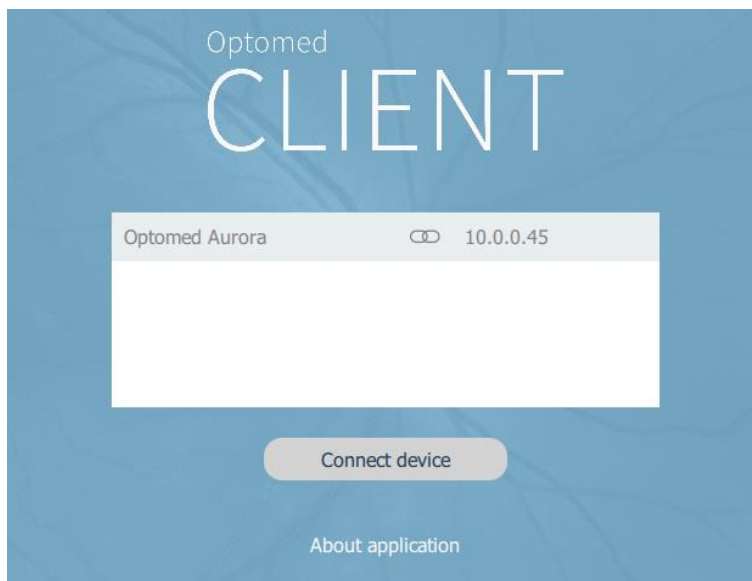
Turn on the Aurora camera using the Power button.

Configure the Aurora camera to connect to the local WiFi:

- Select settings by turning the Optoroller to the gear icon, and then select “Camera”.
- Select the “Wireless” option, and then set the “Wireless On/Off” to “On”.
- Select the “Wireless” option, and then select “Network mode” and set it to “WLAN”. The camera will start looking for available wireless networks and, once it’s done, will display a list of all WiFi networks it was able to locate. Select the relevant network to connect the camera. Input the network password if one is required. Use the camera’s on/off soft switch to move between upper- and lower-case, and the “»” character on the bottom right corner as “Backspace”.

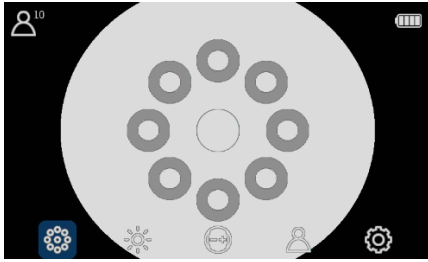
Verify that the Optomed Client is installed on the PC running the AEYE-DS Client. Configure the Optomed Client to save images to a folder on the host PC. See Optomed Aurora User Manual for more information about Optomed Client installation and configuration.

Once the PC and the camera are both connected to the same Wi-Fi network, the Optomed Client running on the PC will display the camera’s name and IP address. The “Connect device” button will become active.



D.2 Camera settings

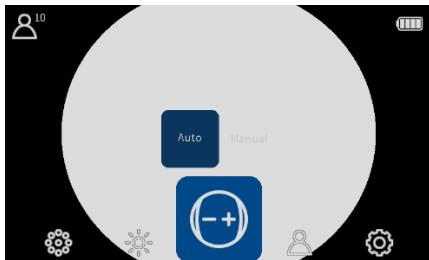
Set Fixation Target to the center (macula centered images).



Set Brightness setting “Auto”.

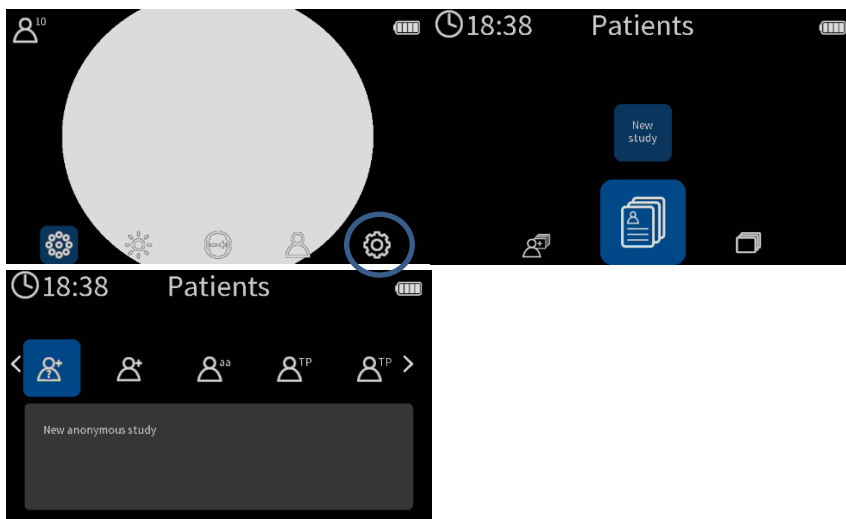


Set Focusing mode to “Auto”.



D.3 Taking images

Create a new study.









Hands-on instructions and demo for aligning the camera and successfully capturing images are available in the instructional video referenced below:

<https://www.youtube.com/watch?v=6LR8e9G9H2A>

Using the on-screen arcs and rectangle as guides, bring the camera into position. Depress the shutter button half-way to allow the camera to focus and then depress the button all the way to take the picture.



When the image appears on the screen, turn the knob one click to display the images quality indicators. Images where at least two quality indicators are green and one yellow should be considered sufficient quality. Insufficient quality images should be retaken.

	Brightness		No reductions in image
	Reflection and shadowing		Some reductions in image
	Sharpness		Much reductions in image

Using the Optoroller, select “Right” or “Left” to indicate whether the image is of the left or right eye. Once selected, the image is automatically saved.



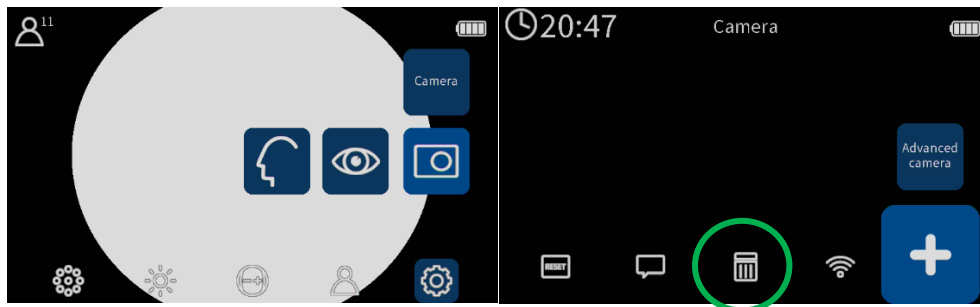
Label the images by appropriately selecting “Left” (OS) or “Right” (OD). This will append an “OD” or “OS” to the file name. If no eye is selected, then a default “IM” will be appended to the file name.

For example, the right eye image file will be OD0108EY.jpg; the left eye image file name will be OS0109EY.jpg.

If the image file is of poor quality, then you can select “Delete” and retake the image.

D.4 Emptying the camera memory card

It is recommended to periodically empty the camera memory after all images have been transferred to the PC. This can be done from the camera menu:



D.5 Transferring Images to the AEYE-DS PC

All images captured by the Aurora camera are automatically transferred via the wireless connection to the host PC where the Optomed Client is installed, and saved to the configured folder. See Optomed Aurora User Manual for more information about configuring a wireless image transfer to a PC.

APPENDIX E – Clinical Study Results

The AEYE-DS device safety and efficacy for automated more than mild Diabetic Retinopathy (mtmDR) detection from digital fundoscopic images was demonstrated in a pivotal clinical study. The study was a prospective, multi-center, single-arm, blinded study. The study was conducted at 8 study sites in the United States (7 sites) and Israel (1 site), with active enrollment from October 2020 through November 2021. A total of 531 subjects were screened and enrolled in the study. The study population represented the target population for the use of this device and consisted of stable, visually asymptomatic subjects who were previously diagnosed with diabetes and had no prior diagnosis of mtmDR. Subjects participated in a routine retinal screening test for diabetic retinopathy (DR) in hospitals, primary care clinics or medical research centers. Patients of both genders, all ethnicities and ≥ 22 years of age were recruited to the study. General patient demographics, medical history, concomitant medications, fundoscopy system used, OCT system used, etc., were obtained for each study subject.

Novice operators, who had not previously performed ocular imaging, obtained fundoscopy images from each eye of the patient, using the Topcon Model NW400 or the hand held Optomed Aurora fundoscopic cameras. Upon submission of the fundoscopy images to the AEYE-DS client software, a diagnostic result (and PDF diagnostics report) of more than mild DR (mtmDR) detected or more than mild DR not detected was produced. A result of 'insufficient quality' was determined if the novice operator reached a maximum of 6 image submission attempts and one or more of the images was still of insufficient image quality. After the novice operator generated an AEYE-DS diagnostic output, each participant underwent additional retinal imaging captured by a professional ophthalmic photographer, to obtain dilated four widefield stereo color fundus images, lens photography for media opacity assessment and macular optical coherence tomography (OCT) imaging. The professional images were sent to an independent reading center where the severity of retinopathy and diabetic macular edema (DME) were determined according to the Early Treatment for Diabetic Retinopathy Study severity (ETDRS) scale. The Reading Center diagnostic results formed the reference standard (ground truth) for the study. As part of the final clinical assessment, each participant was categorized as mtmDR+ or mtmDR-, based on the worst of two eyes. The final clinical assessment based on the worst of two eyes was compared with the AEYE-DS output, at the participant level.

The baseline demographic data and characteristics analysis showed that the mean age was 55 years (range 21-88), 47% were male and 53% were female, 29% were African-American, 39% White and 29% Hispanic or Latino, the remainder were of other racial/ethnic origins. Approximately 95% of the subjects in the study were diagnosed with type 2 diabetes while approximately 5% percent were diagnosed with type 1 diabetes. Duration of diabetes since diagnosis ranged from 1 day to approximately 44 years, with a mean of approximately 10 years (SD=94.8). Most recent HbA1c levels were reported for 446 (86.3%) subjects. HbA1c levels ranged from 5% to 15.6% with a mean of 8.26% (SD=2.15).

The primary efficacy objective of this study was the sensitivity and specificity of the AEYE-DS device to detect mtmDR on digital funduscopy images, acquired by the Topcon NW400 fundoscopy device, based on two macula-centered images (one image from each eye of the patient).

AEYE-DS correctly identified 53 of the 57 fully analyzable subjects with mtmDR+, thus the sensitivity was 92.98% [CI: 83.30%; 97.24%] with a lower one-sided 97.5% confidence bound of 83.3%, which is higher than the pre-defined performance goal of 82%. Sensitivity was identical when calculated for fundus-based mtmDR+ and for multi-modal mtmDR+. Of the 405 fully analyzable subjects who were mtmDR-, according to the Reading Center diagnosis, 370 subjects were correctly identified by AEYE-DS as mtmDR-, based on fundus images alone. Thus, the specificity is 91.36% [CI: 88.22%; 93.72%] with a lower one-sided 97.5% confidence bound of 88.22%, which is higher than the pre-defined performance goal of 87%. Specificity was almost identical when calculated for multi-modal mtmDR-. Therefore, the null hypotheses for sensitivity and specificity were rejected and it is concluded that the study is deemed successful. Positive Predictive Value (PPV) was 60.23% [CI: 49.78%; 69.82%] and the Negative Predictive Value (NPV) was 98.93% [CI: 97.28%; 99.58%]. The PPV was influenced by the actual prevalence of mtmDR+ patients in the pivotal study diabetic population (i.e., 12.3%), as this was not an enriched study.

Further sub-analyses showed that there were no significant effects of sex, race/ethnicity, HbA1c ($\leq 10\%$ vs $>10\%$), age (<55 years vs >55 years), diabetic duration since diagnosis (≤ 10 years vs >10 years, if available) and lens status on sensitivity and specificity. As sequential enrollment provided a sufficient number of mtmDR+ subjects, enrichment was not performed. Therefore, subset analysis by cohort (not enriched, enriched) was not performed.

A handheld camera sub-study was performed at selected sites participating in the pivotal study given the clear benefits of using rapid AI-based diagnostic screening for DR with a handheld camera. Using

a handheld camera is quicker, more convenient and cost efficient and is therefore more likely to be purchased and used in a primary care setting. Subjects participating in the handheld sub study underwent additional fundus imaging, using the FDA cleared Optomed Aurora handheld fundoscopy device. The novice operator obtained two macula-centered images (one from each eye of the patient) using the handheld fundoscopy imaging device, according to a standardized imaging protocol.

The results of sensitivity and specificity based on two fundoscopic images obtained from the handheld fundoscopy (secondary endpoint) were 91.89% [CI:78.70%; 97.20%] and 93.57% [CI: 89.82%; 96.01%], respectively. Since the sensitivity is 91.89% with a lower one-sided 97.5% confidence bound of 78.7%, the point estimate for sensitivity is much higher than the 82%, which was the predetermined acceptable point estimate for a handheld device. The specificity is 93.57% with a lower one-sided 97.5% confidence bound of 89.82%, which is higher than the predetermined acceptable point estimate for specificity of 85%. Therefore, the handheld sub study can be deemed successful for both sensitivity and specificity. The AEYE-DS sensitivity and specificity results using the multi-modal Reading Center diagnosis were virtually identical to the above reported results.

The co-powered secondary endpoints of this study were the sensitivity and specificity of the AEYE-DS device to detect mtmDR from digital fundoscopic images, acquired by the Topcon NW400 fundoscopy device, based on four images (one macula centered image and one optic disc centered image per eye). Diagnostic results and AEYE-DS device diagnostic results and showed a sensitivity and specificity of 94.74% [CI: 85.63%; 98.19%] and 88.64% [CI: 85.18%; 91.38%], respectively. The sensitivity is 94.74% with a lower one-sided 97.5% confidence bound of 85.63%, which is higher than the performance goal of 82%, therefore the null hypothesis is rejected in favor of the alternative hypothesis for the sensitivity. The specificity is 88.64% with a lower one-sided 97.5% confidence bound of 85.18%, which is slightly lower than the performance goal of 87%, therefore the null hypothesis is not rejected in favor of the alternative hypothesis for the specificity. The Positive Predictive Value (PPV) was 54% [CI: 44.26%; 63.44%] and the Negative Predictive Value (NPV) was 99.17% [CI: 97.59%; 99.72%]. Sensitivity and specificity (and PPV and NPV) results were the same when calculated for fundus-based mtmDR+ and for multi-modal mtmDR+. The sensitivity of the AEYE-DS device based on 4 images passed the study performance goals, but the specificity was slightly lower. The implications of the slightly lower specificity mean that more subjects may be determined to be mtmDR+ and sent for follow-up ophthalmic examinations than necessary. As the sensitivity results were successful and even higher than the sensitivity with 2 images, and true-mtmDR+ subjects will not be missed by the AEYE-DS device, the price of a slightly lower specificity based on 4 images is not too high and certainly does not involve any risks. In any case, as the use of

two images is less complicated and time consuming than four images, it is more probable that AEYE-DS device users will rely on the use of 2 (macula-centered) images per eye. For this reason, the Instructions for Use will allow the use of 2 or 4 images per eye to obtain an EYE-DS diagnostic output.

The imageability results from the pivotal study, reflecting data on the usability in the hands of the study novice operators, reported >99% Imageability for the AEYE-DS device using both the Topcon NW400 and the Optomed Aurora fundoscopy cameras.

Usability of the AEYE-DS device was also assessed in a human factors validation study, including User Manual comprehension and usability of the device in the hands of potential users. Once the users underwent initial, one-time training and practice, all users stated that the device was easy and straightforward and all were successful in submitting images for diagnosis and obtaining a diagnosis output result and PDF report. All users stated that the user manual was clear and easy to use.

In summary, the AEYE-DS device using 2 or 4 images acquired from the Topcon NW400 and 2 images acquired from the handheld Optomed Aurora fundoscopy devices demonstrates successful performance, in terms of sensitivity, specificity, PPV and NPV, as well as imageability and usability.