Instructions for Use

Aireen

Rev.17

Aireen ®
Software version: 2.2

CE 2265

Release date: 03.02.2026

Table of Contents

1. Glossary of terms

Dropzone – a graphically demarcated and grey highlighted area in the application for uploading selected files by dragging them with the mouse.

Dashboard – the initial screen in the application after logging in, which shows an overview of the analyses performed or prepared.

DR – diabetic retinopathy

Report – a document that contains detailed information about the results of the analysis of the patient's eye images.

PDF – a file format for storing documents independently of the software and hardware on which they were captured. A PDF file can contain both text and images, and this format ensures that any document will appear the same on all devices.

Patient ID – an anonymized patient identifier. For example, a non-public ID from a clinical information system.

Aireen Connector – an external application that automatically uploads files to the Aireen cloud application, which can be installed on the camera's computer.

Heatmap – a graphical representation of the areas that contributed to the prediction of the determined result.

Serious incident – any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect, which directly or indirectly led, might have led or might lead to any of the following:

a) the death of a patient, user or other person,
b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
c) a serious public health threat.

Grading of diabetic retinopathy (DR) – classification of disease severity

ICDR – Internal Clinical Diabetic Retinopathy severity scale

Fovea centralis – is the anatomical term for a pit in the macula lutea of the retina, which is the site of sharpest vision.

Optic disc – a pinkish round formation with a variously marked central depression with a diameter of 1.5 mm.

Sensitivity – corresponds to the proportion of positive disease detections by Aireen out of the total number of clinically diagnosed diseases according to specialist medical evaluation.

Specificity – reflects the proportion of patients without a finding of disease using Aireen compared to the total number of patients without clinical symptoms of disease according to specialist medical evaluation.

AMD – age-related macular degeneration

UDI – Unique Device Identifier

API – application programming interface

2. Information on the Instructions for Use

2.1 Purpose

These **Instructions for Use** contain instructions for using the Aireen system in accordance with its function and intended use.

For administrator-level activities and procedures, a separate Administration Manual is available at support@aireen.com.

2.2 Intended population

These **Instructions for Use** are intended for registered users of the Aireen system.

2.3 How to obtain a printed copy of the Instructions for Use

The Aireen system comes with electronic **Instructions for Use**, which are available directly in the application under the **Help** tab, as well as on the website of the manufacturer Aireen a.s. (https://aireen.com).

If you need a printed version of the **Instructions for Use**, please download the PDF version directly from the Aireen application in the main **Help** menu or from the manufacturer's website and print it on a standard and commercially available printer.

You can also contact us at support@aireen.com to request a hard copy. In your request, please make sure to include your login email and the delivery address to which the IFU should be sent.

Aireen a.s. will send you the current printed version of the **Instructions for Use** at its own expense within 7 days of receipt of this request.

3. Symbols used

Caution (Warning) – Indicates a potentially hazardous situation associated with the use or reasonably foreseeable misuse of the system that should be avoided because it could lead to a health hazard or other serious adverse effect.

Manufacturer

Read the electronic instructions for use

Medical Device

Unique Device Identifier

This symbol confirms that the product has been assessed before being placed on the European Economic Area market and meets EU legislative requirements

Additional information for the user

4. Intended purpose

The Aireen system is intended for use by healthcare providers to automatically analyse digital retinal images in adult patients for the purpose of screening of diabetic retinopathy and detecting the presence of age-related macular degeneration signs.

5. Target users

The Aireen system is intended for use by healthcare professionals.

6. Target group of patients

The target group of patients for DR screening are adults diagnosed with type 1 or type 2 diabetes who have not yet been diagnosed with DR.

The target group for detecting the presence of signs of AMD are adult patients aged 50 years and older who have not yet been diagnosed with AMD.

7. Indications

The use of Aireen for diabetic retinopathy screening is indicated for **adults** who have not yet been diagnosed with diabetic retinopathy.

The use of Aireen to detect signs of age-related macular degeneration is indicated for **adults** from 50 years of age who have not yet been diagnosed with age-related macular degeneration.

8. Contraindications

- The use of Aireen is contraindicated for children under 18 years of age.
- Optical media opacification (changes in the cornea, cataract), tremor or narrow pupil due to which an evaluable retinal image cannot be taken.
- Patients in whom ocular fundus imaging for retinal evaluation is contraindicated.
- Previous laser treatment of the retina, injections into the eye, medical history of retinal inflammatory disease or any medical history of retinal surgery.

9. Side effects

The Aireen system is software that analyses digital images taken by another certified medical device. It does not come into contact with the patient or operator in any way. In view of these facts, the risk of any possible undesirable side effects can be excluded.

10. Characteristics and clinical benefits of the medical device

Aireen is software application developed using machine learning to automatically detect the presence of potential signs of diabetic retinopathy, age-related macular degeneration and “more than mild” diabetic retinopathy according to the International Classification of Diabetic Retinopathy Severity (ICDR) scale on fundus images of the retina.

Outputs from Aireen:

Indication of diabetic retinopathy (DR):

1. Positive/Negative/Undetermined
    a. Positive indications are completed by classification:
        i. **MORE THAN MILD** (includes levels of severity: **Moderate DR, Severe DR** and **Proliferative DR**)
        ii. **MILD** (includes levels of severity: **Mild DR**)
2. Heatmaps – visualization of the marked areas that contributed to the outcome of diabetic retinopathy
3. Severity of DR for the left and right eye according to the ICDR scale.

Indications of age-related macular degeneration (AMD)

1. Positive/Negative/Undetermined

Screening DR:

- **Sensitivity**: **94.0%**
- **Specificity**: **90.7%**

- **Speed of** automatic image evaluation to detect diabetic retinopathy: **up to 60 seconds** depending on the speed of the internet connection.

Detection of AMD signs:

- **Sensitivity**: **86.9%**
- **Specificity**: **87.9%**
- **Speed of** automatic image evaluation to detect AMD: **up to 60 seconds** depending on the speed of the internet connection.

Clinical benefits of the medical device:

- The medical device is able to increase the availability of screening and detect the signs of DR with a sensitivity of 94.0% and a specificity of 90.7%.
- Early detection of DR helps to maintain a high quality of life for the diabetic patient.
- Early detection of more serious forms of DR.
- The medical device is able to increase the availability of screening for signs of AMD from fundus images and detect signs of AMD with a sensitivity of 86.9% and a specificity of 87.9%.
- Early detection of AMD has the potential to improve the success rate of subsequent treatment, prognosis and brings positive economic implications for disease management.

11. Warnings

Caution!

Abnormalities related to AMD can cause false-positive DR detections and vice versa. In addition, abnormalities related to retinal diseases other than AMD and DR can cause false-positive detections of AMD and DR.

Caution!

A positive Aireen result for DR detects only presence of DR signs. A negative result does not mean that there are no other pathologies present on the patient's retina.

Caution!

A positive Aireen result for AMD detects only the presence of AMD signs. A negative result does not mean that there are no other pathologies present on the patient's retina.

Caution!

Risk of a false negative result for DR or AMD due to data confusion caused by user error. Use extreme caution when entering data (patient ID and images) into the system.

Caution!

Risk of false negative results due to artifacts on the image being evaluated. Pay attention to the quality of the input images for analysis. See chapter for examples of images **15. Examples of images**.

Caution!

Limitations associated with the use of Aireen. In some cases, Aireen may miss the presence of DR signs (false negative result).

Caution!

Limitations associated with the use of Aireen. In some cases, Aireen may miss the presence of AMD signs (false negative result).

Caution!

If the Aireen system is not available, the patient should be referred to an ophthalmologist for a specialist eye examination to screen for DR and detect signs of AMD.

Caution!

If all images uploaded to Aireen are judged by the system to be inappropriate for DR screening, the patient should be referred to an ophthalmologist for a specialist eye examination, see Chapter **8. Contraindications**.

Caution!

If all images uploaded to Aireen are judged by the system to be inappropriate for detecting signs of AMD, the patient should be referred to an ophthalmologist for a specialist eye examination, see Chapter **8. Contraindications**.

Caution!

If an evaluable retinal image cannot be taken to detect signs of AMD, the patient should be referred to an ophthalmologist for a specialist eye examination.

Caution!

If an evaluable retinal image cannot be taken to screen for DR, the patient should be referred to an ophthalmologist for a specialist eye examination.

Caution!

Handle login data in such a way that they cannot be stolen. Do not share your login information with anyone. If your login data is stolen, please contact Aireen a.s. support immediately.

Caution!

Patient should be informed that DR screening with Aireen application is not a substitute for a professional eye examination. In case of known retina pathology, the Aireen examination is not valid and a follow-up by an ophthalmologist is necessary.

Caution!

Patient should be informed that the detection of signs of AMD with Aireen application is not a substitute for a professional eye examination. In case of known retina pathology, the Aireen examination is not valid and a follow-up by an ophthalmologist is necessary.

Caution!

The heatmap only shows the areas that contributed to the prediction of the given result. Some areas shown may not be related to diabetic changes, and not all areas of diabetic retinopathy are highlighted. If the result of the analysis is positive, refer the patient to an ophthalmologist for a specialist eye examination.

Caution!

Before using the Aireen Connector for the first time, make sure that the component uploads images from the correct directory on your computer to the Aireen web application.

Caution!

Input images containing burned-in data (such as logos, text, identification information, watermarks, etc.) are not supported as standard. The user is required to check that such data is not contained in the image. The use of such images is only possible after validation and written approval by the manufacturer.

12. Installation

The Aireen software program is an artificial intelligence-based cloud computer program, accessible to healthcare professionals through a URL address and web interface. The Aireen system requires no installation and can be run on commonly available computers connected to the Internet.

The Aireen medical device also supports direct integration via a defined interface – API (Application Programming Interface), which is not covered in this manual. For more information about integration option, please contact us at support@aireen.com.

12.1 Identification of the medical device

On the initial Aireen login screen, a medical device label is displayed at the bottom.

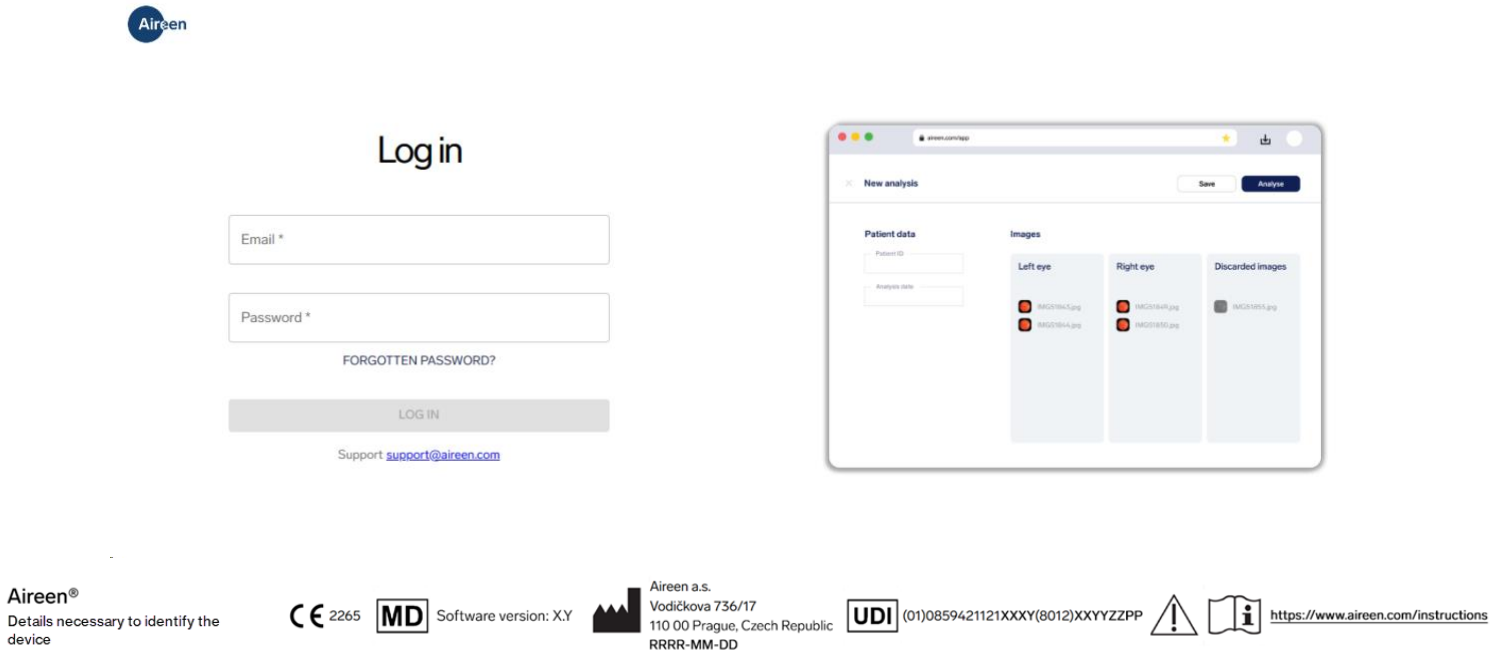


Figure 1: Aireen login screen – medical device label

Details on medical device labelling:

- **YYYY-MM-DD –** date of release of Aireen medical device version X.Y
- **UDI - Unique Device Identifier:**
  - **(01)0859421121XXXY** - UDI-DI code - unique numeric code of the medical device version
  - **(8012)XXYYZZPP** - UDI-PI code - full identification of the medical device including subversion

13. System requirements

The Aireen system can be used on commercially available personal computers with basic software that are connected to the Internet. Supported platforms are: Windows, MAC OS, Linux.

Minimum computer requirements for the medical office include:

- Intel Core i3 processor or higher (including commercial alternatives)
- Working memory (RAM) at least 8 GB
- Software Monitor with 1280×800 px resolution
- Internet connection with a minimum speed of 3 Mbit/s
- Regularly updated and manufacturer-supported Windows, MAC OS or Linux operating system
- Active antivirus protection on your computer
- Updated and manufacturer-supported web browser, preferably Chrome or Edge

For the correct functioning of the software, it is necessary that the current time is set correctly on the client computer (we recommend having the system time synchronization function active in the operating system).

The recommended setting for font size increase (referred to as **Scale** in Windows) in the operating system and also in the web browser is the default value – 100%.

The Aireen system does not require any special storage or handling conditions. System limitations are listed in this chapter and no others are known.

14. Procedure for using Aireen

The procedure for using the application is broken down into the individual points or procedures listed below. But first, open your Internet browser and enter the URL address of the Aireen application: https://app.aireen.com.

14.1 Images and Diagnoses - uploading images and selecting diagnoses to be analysed

On the **Dashboard** screen, click the **[+ NEW ANALYSIS]** button at the top right. The **Creating a new analysis** screen appears with the basic mandatory input field **>Patient ID<**.

The **patient ID** used should be an **anonymized** patient **identifier**. For example, a non-public ID from a clinical information system, the serial number of the patient's chart, etc. Numeric and diacritical characters are supported, including spaces except: # % & { } < > * ? / $! ' : @ + ` | = \ "

The **Images and Diagnoses** screen displays the sections:

1) **Patient data** – patient information entered from the previous point (**Creating a new analysis**)
2) **Selected / Non-Selected Diagnoses** – in this central part of the screen you can select which diagnoses will or will not be performed in the analysis using the checkbox. After checking or unchecking a diagnosis, it will be moved to the **Selected** or **Non-Selected** diagnoses section.
    a. **For each diagnosis there is also information:**
        i. For the right and left eye (R / L), the current number of images that are suitable for the analysis of the diagnosis is displayed.
3) **Images** – in this right part of the screen you upload images to the application for analysis.
    a. Click on the dropzone (a graphically outlined and grey highlighted area in the application for uploading selected files) with the **[UPLOAD IMAGES]** button, after clicking a file selection box will open, select the desired patient images to be uploaded and confirm their selection.
    b. Open an external window (Explorer, Finder) with the desired images and drag them from the external window to the selected dropzone.

After successful insertion of images, they are automatically uploaded to the application, which is indicated by a notification symbol and a message – *e.g. "Adding new images. Current status: 2/3".*

The **Images** section displays information:

1. **Images** – thumbnail preview of the uploaded image with information whether it is the right or left eye. Click on the uploaded image to see a larger view of it.
2. **Name** – the name of the uploaded file (photo).
3. **Status:**
    a. Gradable - image meets the necessary criteria and **is included in the analysis** for all selected diagnoses.
    b. Gradable - image meets the necessary criteria for the analysis of some diagnoses only, **it is included in the analysis**.
    c. Non Gradable - image does not meet the criteria and **will not be included in the analysis**.
    d. Failed - there was an error in the validation of the image and it **will not be included in the analysis.**
4. - the bin symbol allows you to delete an uploaded image.

Input images must meet the following requirements:

- digital 45° fundus image of the eye background taken by a professional certified optical fundus camera;
- a full-colour image with a colour depth of at least 24bit;
- the image contains a fovea and an optical disc;
- image resolution of at least 1650 x 1100 pixels;
- recommended maximum image size is 15 MB;
- JPG, BMP, PNG, DICOM and TIFF format;
- sharp image without unwanted artifacts;
- uploaded image do not contain personal identifiers of the patient in their title or directly on the image (does not apply to anonymized identifiers such as non-public IDs from the clinical information system)

For more information and examples, see Chapter **15**. **Examples of images**

The analysis can be run with a maximum of 10 images that have the status „Gradable“.

14.2 Running the analysis

After validating all uploaded images (if there is at least one of them suitable for analysis), the **[ANALYSE]** button becomes active. Before the final run of the analysis, you can correct the settings of the diagnoses you want to include or exclude from the analysis using the checkbox.

After performing a visual inspection of the data, press the **[ANALYSE]** button to start the evaluation process.

14.3 Evaluation of the analysis

When the analysis is successfully completed, the **Finished Analysis** page displays the result in text and color. **The overall result of the analysis is always displayed at the top of the screen.**

NEGATIVE

Aireen did not detect the relevant presence of potential signs of diabetic retinopathy, age-related macular degeneration.

- **Green color** – analysis did not detect potential signs of the selected diagnosis in either eye.

If the output of the analysis is: **“Aireen did not detect the relevant presence of potential signs of diabetic retinopathy.”**, the patient should continue to be monitored according to current guidelines.

If the output of the analysis is: **“Aireen did not detect the relevant presence of potential signs of age-related macular degeneration.”**, the patient should continue to be monitored according to current guidelines.

POSITIVE

Aireen detected the presence of potential signs of diabetic retinopathy, age-related macular degeneration. A professional ophthalmological examination is recommended.

- **Red color** – analysis detected the presence of potential signs of the selected diagnose in at least one eye.

If the output of the analysis is: “**Aireen detected the presence of potential signs of diabetic retinopathy. A professional ophthalmological examination is recommended.”**, the patient should be referred for a specialist eye examination to confirm the diagnosis and possibly determine the therapeutic course of action.

If the output of the analysis is: “**Aireen detected the presence of potential signs of age-related macular degeneration. A professional ophthalmological examination is recommended.”**, the patient should be referred for a specialist eye examination to confirm the diagnosis and possibly determine the therapeutic course of action.

UNDETERMINED

Aireen did not detect the relevant presence of potential signs of diabetic retinopathy, age-related macular degeneration. However, the results of the analysis are valid for only one eye.

- **Orange color** – Aireen was unable to analyse both patient's eyes.

If the output of the analysis is: “**Aireen did not detect the relevant presence of potential signs of diabetic retinopathy. However, the results of the analysis are valid for only one eye.”**, the patient should be referred for a specialist eye examination or the Aireen analysis should be repeated immediately to obtain a diagnostic result for both eyes.

If the output of the analysis is: “**Aireen did not detect the relevant presence of potential signs of age-related macular degeneration. However, the results of the analysis are valid for only one eye.”**, the patient should be referred for a specialist eye examination or the Aireen analysis should be repeated immediately to obtain a diagnostic result for both eyes.

Press the **[DONE]** button to close the analysis and move to the default **Dashboard** screen.

14.4 Analysis result report

To view the analysis report, click on the **[REPORT PREVIEW]**. The analysis report „***Aireen Report***" **contains the resulting report in text form with a description of the diagnoses analyzed.**

According to the configuration of the Department, the report is accompanied with the Grading of diabetic retinopathy (DR) - it is a classification for determining the severity of the disease. According to ICDR, diabetic retinopathy is categorized into the following categories for positive findings.

The final status for a positive finding of the presence of diabetic retinopathy is defined:

- **POSITIVE|MORE THAN MILD –** includes levels of severity:
  Moderate DR, Severe DR and **Proliferative DR**
- **POSITIVE|MILD –** includes the level of severity: **Mild DR**

and is accompanied by the **DR Grading category** (according to the ICDR classification) with a graphical miniature of the determining result in the histogram

DR Grading Categories *ICDR Classification reported on the PDF report*	**Description**
No DR	No diabetic retinopathy found
Mild DR	Only microaneurysms
Moderate DR	Multiple microaneurysms, bleeding, hard exudates and mild retinal edema
Severe DR	Significant bleeding, venous abnormalities and intraretinal microvascular abnormalities
Proliferative DR	Neovascularization of the retina or optic disc, bleeding into the vitreous and retinal detachment

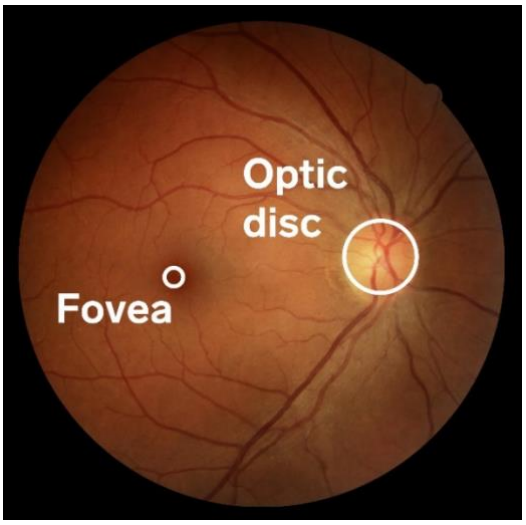
Based on the configuration of the Department, the PDF report also displays the **Analyzed Images** section, including a visualization of the marked areas that contributed to the diabetic retinopathy result. From the report preview, it is also possible to download the PDF document to the computer- using the **[DOWNLOAD REPORT]** button and, if necessary, print it using the **[PRINT REPORT]** button (keyboard shortcut >> **CTRL+P.** The file name corresponds to the template: *Aireen_{ID Pacient}_{RRRR-MM-DD}.pdf*.

14.5 Downloading the report

You can download the resulting PDF report of the performed analysis to your computer using the **[DOWNLOAD REPORT]** button. The report contains information about the result of the analysis, information about the patient (Patient ID) as well as the name of the Provider, the date and time of the examination and the number of analysed images on the right and left eyes.

15 Examples of images

In this chapter we present sample images, both evaluable and unsuitable, from which analysis cannot be performed.



Fovea: is the anatomical term for a pit in the macula lutea of the retina, which is the site of sharpest vision.

Optic disc: a pinkish round formation with a variously marked central depression with a diameter of 1.5 mm.

15.1 Evaluable images

Examples of **suitable** evaluable images of the left and right eyes:

LEFT EYE

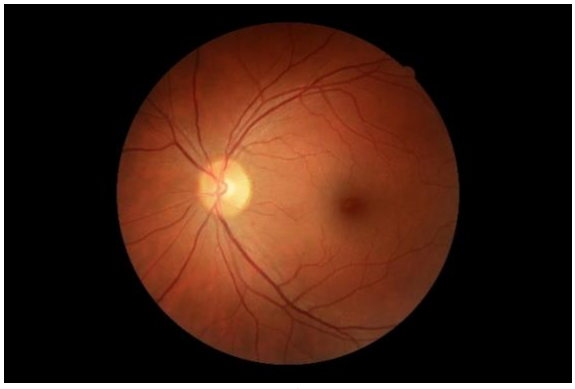


Image example – LEFT EYE

RIGHT EYE

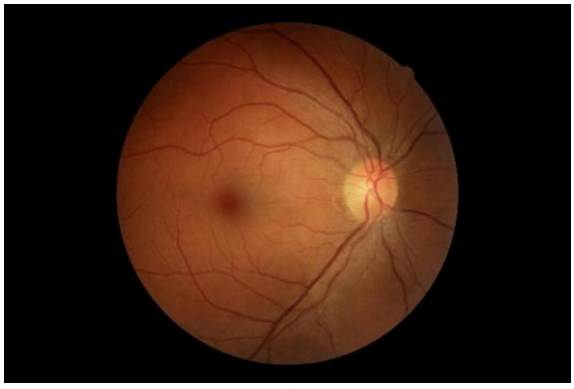


Image example – RIGHT EYE

15.2 Non-evaluable images

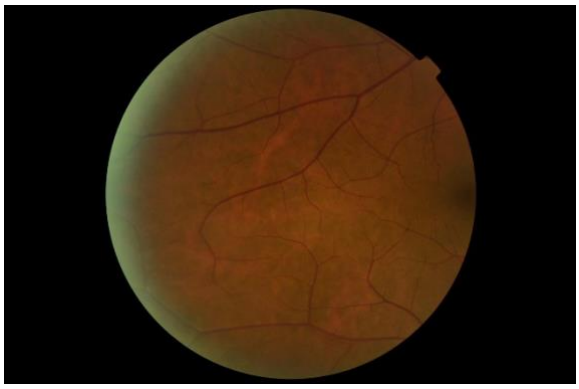
Examples of images that are **not** suitable for analysis. The following are the most common reasons for images that cannot be analysed.

- The image does not include the fovea and optic disc.
- Poor image focus.
- The images always have a stain in the same place – the camera lens needs to be cleaned.

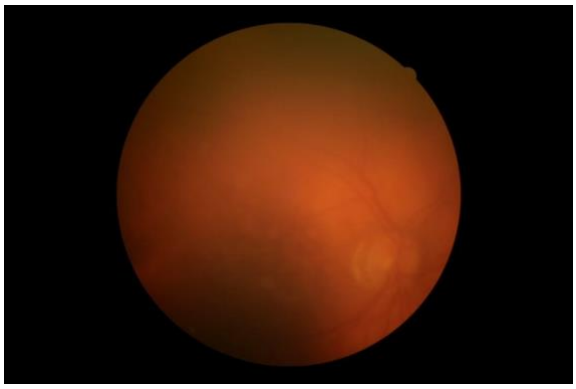
- The patient was not centered during imaging.
- The patient's eyelashes are visible in the image
- The image of the eye was taken when the patient blinked.
- Insufficient focus of the pupils in the image.
- Image degraded by poor lightning conditions (side light, reflection, shadows, etc.)

Graphical examples of non-evaluable images:

THE IMAGE DOES NOT INCLUDE THE FOVEA AND OPTIC DISC



POOR IMAGE FOCUS



PART OF THE PICTURE IS COVERED WITH EYELASHES

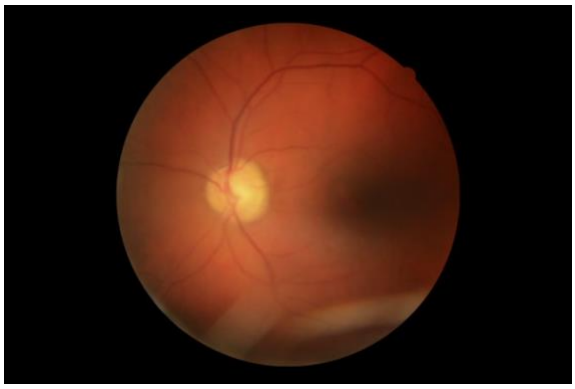
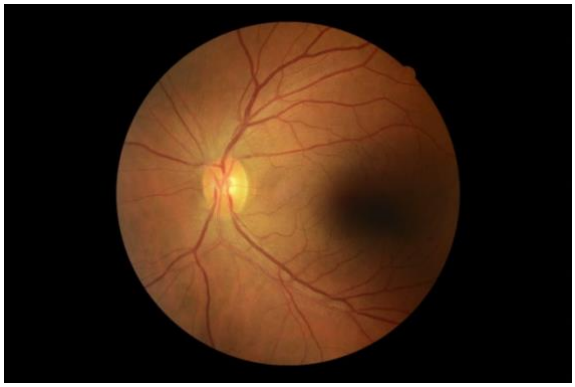
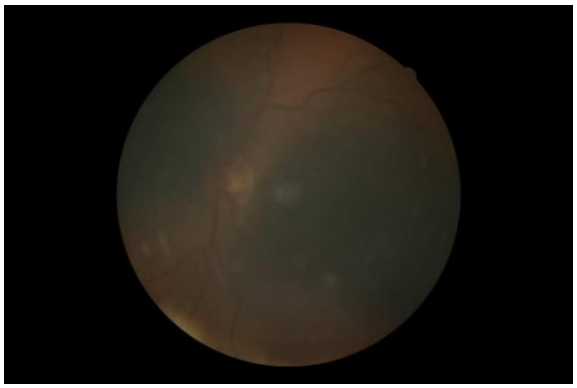


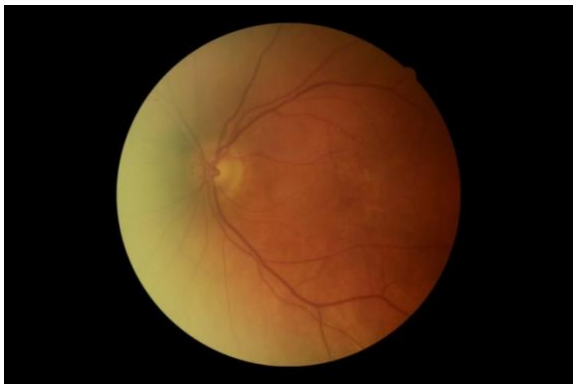
IMAGE WITH VISIBLE SHADOW



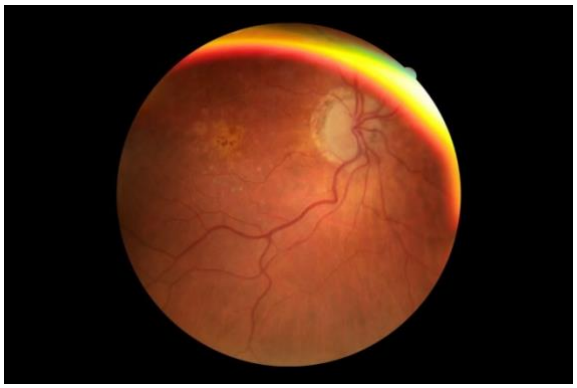
DARK IMAGE



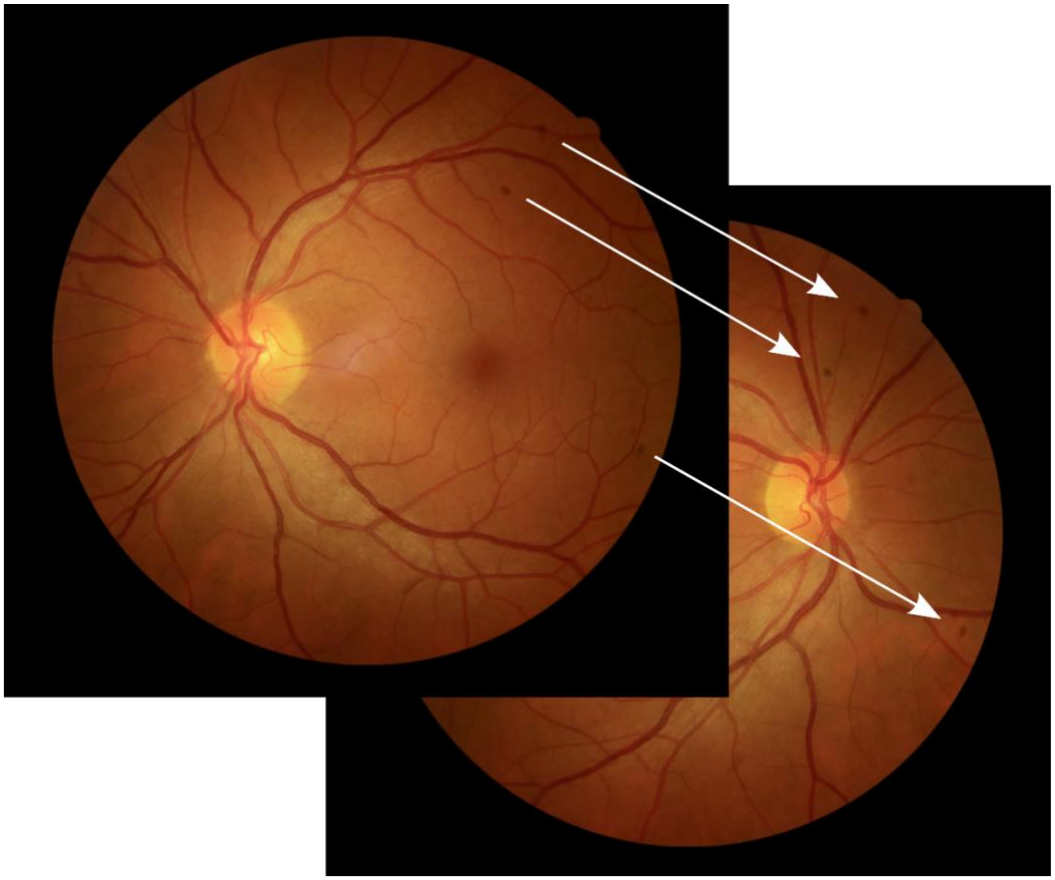
OVEREXPOSED IMAGE



CAMERA REFLECTIONS



REPEATING ARTIFACT – IMPURITY ON THE LENS



16 Forgotten login password

If you forget your password, press the **[FORGOT PASSWORD?]** button on the initial login screen. In the **>Email<** entry field, enter your email address that you normally use to log in to Aireen and press **[SAVE]**.

Within a few minutes, you will receive an email in your inbox containing a unique link to set a new password for your Aireen account. The validity of this link is 15 minutes. In case of any complications, contact technical support using the contact details listed at the end of this manual.

17 Forgotten login name

The login name in the Aireen application is usually an email address. If you forget this login name, contact Aireen a.s.

18 Service and maintenance

The Aireen application does not provide the possibility of independent service by the user. If such service is necessary, Aireen a.s. will release an updated version of this app. With this cloud architecture, the user does not need to install anything on the computer and can automatically access the new version immediately after being published.

19 Instructions for Use – Help

In the main menu under the **Help** option, you will always have the up-to-date **Instructions for Use** for the application. In addition to the scrolling and zooming functions, you can use the **[DOWNLOAD]** button to save a PDF version of the manual on your computer, for example for printing purposes.

20 Clinical results

The Aireen medical device version 1.0 was evaluated in a clinical investigation in 2022. The results of the evaluation for the detection of signs of diabetic retinopathy in the present clinical investigation were compared against the decision of a three-member expert panel and the evaluation was performed on 1,274 patients.

As part of the clinical investigation, the results of the ophthalmologists' evaluations were also compared against the panelists' decisions. **The sensitivity and specificity of the Aireen medical device against the panel was 94.0% and 90.7%, respectively.**

The sensitivity of the ophthalmologists' assessment against the panel reached 90.1%, and the resulting specificity was 76.6%. The data evaluated during the clinical investigation suggested both **higher sensitivity and specificity for the investigational Aireen version 1.0 compared to the ophthalmologists' results**.

The Aireen version 2.0 medical device was put through a clinical investigation in 2024. Results of the investigation for the detection of AMD signs in the subject clinical investigation were compared against the decision of a three-member expert committee and the evaluation was performed on a subject of 722 patients.

The clinical investigation also compared the results of the ophthalmologists' assessments against the committee's decision. **The sensitivity of the Aireen medical device against the committee was 86.9% and the specificity was 87.9%.**

The sensitivity of the ophthalmologists' assessment to the committee was 89.4% and the final specificity was 59.9%. Evaluation of the data collected during the clinical investigation **showed comparable sensitivity and higher specificity in the case of the investigational Aireen version 2.0 than the ophthalmologists' results.**

21 Reporting of serious incidents

Report any serious incident that occurred in connection with the Aireen system to Aireen a.s. and to the competent authority for reporting serious incidents of the Member State in which the adverse incident occurred.

Aireen a.s.
Vodičkova 736/17
110 00 Prague, Czech Republic

Aireen ®
Software version: 2.2

Company website: https://www.aireen.com
Technical and user support: support@aireen.com