AI4CMR Software

User Manual

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SW Version V1.3

Manufactured by

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ISO 13485:2016 Certificate number MD 740465

CE 2797

AI4CMR is qualified as a class IIa medical device. It complies with the requirements of the European Medical Device Regulation MDR 2017/745

MDR Certificate MDR 740464

UKCA 0086

AI4CMR is qualified as a class IIa medical device. It complies with the requirements of the Medical Device Directive 93/42/EEC and UK MDR 2002.

UKCA Certificate UKCA 776320

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Table of Contents

1. Terms and Conditions

This User Manual shall be accompanied by the specific plugin User Manual.
The plugin User Manual describes in more detail the features and steps necessary to interact with the AI4CMR service. For clarification purposes only, we present an example of a possible sequence of steps to interact with AI4CMR.

1.1   Intended use

AI4CMR is an image analysis software for post-processing of cardiac magnetic resonance images (CMR), which are used for the assessment of cardiac diseases.

AI4CMR uses artificial intelligence and is intended to automize cardiac segmentation allowing instantaneous quantification of ventricular volumes, myocardial mass, ejection fraction of heart ventricles and to automatically assess left ventricle wall motion.

AI4CMR shall be used by qualified medical professionals, experienced in examining and evaluating magnetic resonance images as a support tool that provides relevant clinical information.

AI4CMR can be integrated with DICOM viewers through a standard communication protocol.

The software is not intended to determine or recommend a course of action or treatment for a patient.

AI4CMR software does not preclude the analysis of the reporting physician. The cine sequences analysed by AI4CMR are only a part of the complete CMR exam and all the data should be integrated with other sequences and the clinical background of the patient to conclude the CMR exam.

The reporting physician holds the responsibility for validating the data provided by the AI4CMR software and performing the final interpretation of the CMR exam.

1.2   Intended users

AI4CMR is a medical device and shall be used by qualified medical professionals, experienced in examining and evaluating magnetic resonance images.

1.3   Conditions for use

AI4CMR is a cloud-hosted service. The system shall be used in association with a third-party DICOM Viewer, which provides the interface between AI4CMR and the intended users (Medical professionals), Software Developers, and Others.

Patients will not be in direct contact with AI4CMR. The CMR images acquired for the patient are fed from the MRI Scanner or PACS (picture archiving and communication system) to the third-party DICOM Viewer.

This system context and interfaces to third-party systems are represented in the diagram of Figure **1**. The AI4CMR system boundaries, are defined by the box "AI4CMR".

The integration between AI4CMR and the DICOM Viewer is established using plugins that implement a standard communication protocol.

The communication between AI4CMR and the third-party system is initiated by the third-party system which posts a request to the AI4CMR in a networked environment. AI4CMR will validate and process the request and return a response via the same medium.

The patient data is anonymized by the third party before being sent to AI4CMR.
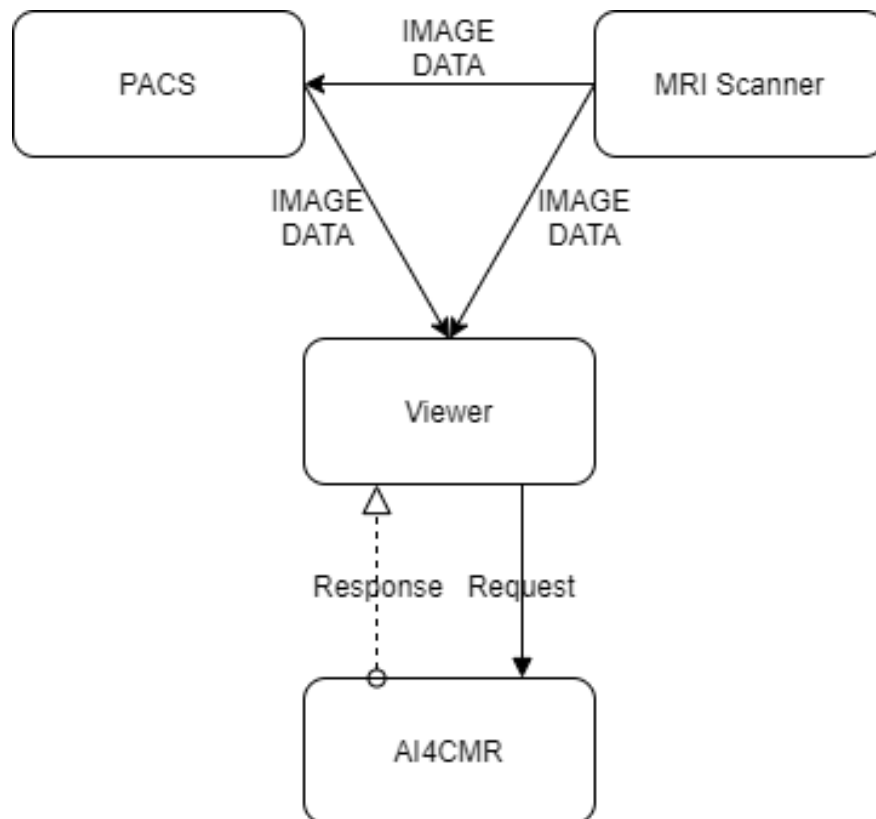

Figure 1. High-level representation of the interoperability between AI4CMR and the third-party systems and services.

1.4 Contraindications

AI4CMR is contraindicated to be used for post-processing of all image modalities other than cine CMR.

1.5 Limitations

AI4CMR analysis is limited to cine CMR acquisitions.

Other studies such as Late Gadolinium Enhancement or Perfusion are not covered.

AI4CMR's performance has been tested in three MRI scanner vendors: Siemens, GE Healthcare Systems and Phillips Medical Systems. For new MRI scanner vendors, a message will be returned to the User stating that the vendor is not valid.

AI4CMR's performance has been validated for a range of image characteristics. Cases with image characteristics that are outside the boundaries of the verified performance of the algorithms will be rejected.

1.6 Warnings and precautions

- The physician must always review the cases even when AI4CMR classifies them as normal.
- Quantitative analysis is dependent on the quality and correctness of the image source data acquisition.
- The patient data must be anonymized by the third-party plugin before sending it to AI4CMR.
- The patient data displayed is initially derived from the DICOM information, if available. Editing these values may affect the calculations in all modules. It is the User's responsibility to verify this data before releasing the final results.
- The User must keep a UPS system that provides emergency power when the input power source or mains power fails.
- It is the plugin maintenance team's responsibility to execute the installation procedure to validate the communication between the User and AI4CMR.
- It is AI4MedImaging's responsibility to update/do maintenance periodically to reduce the probability of AI4CMR SW defects.
- At the installation time, a copy of the digital user manual must be copied to the User's network, under the domain of the User's IT Manager.
- In the event of loss of access credentials please follow the procedure in section 4. User account handling.
- Users should read this manual before using AI4CMR.

1.7   Intended patient population

The software analyses images of patients that were examined by CMR imaging.

Age   The use is not recommended for children (age < 18yo) since the clinical evaluation studies targeted a mostly adult population.

Weight   No limitations

Height   No limitations

1.8   Applicable medical conditions

AI4CMR is an image analysis software for the post-processing of CMR images, used for the assessment of the following cardiac diseases:

- Cardiac failure
- Ischemic heart disease
- Valvular heart disease
- Cardiomyopathy
- Cardiac function and morphology
- Hypertensive cardiac disease
- Other pathologies that need assessment of cardiac function and morphology

1.9   Safety Instructions

Software AI4CMR is hosted in a cloud. The intended users interact remotely with the software.

The equipment communicating with AI4CMR shall:
- Be connected to a secure network;
- Have an access control system, to ensure that only accredited users can access the device and the AI4CMR service.

AI4CMR requires that the passwords are different from the username and have at least:
- Eight (8) characters;
- One (1) digit;
- One (1) uppercase;
- One (1) lowercase;
- One (1) special character.

It is highly recommended the usage of anti-virus software in all computers interacting with the AI4CMR to protect against cyber-attacks. Periodic backups are also recommended to make sure that no patient data is lost in an unforeseen event.

2. Conventions and Abbreviations

2.1 Conventions

EDV – End-Diastolic Volume [ml]

ESV – End-Systolic Volume [ml]

SV – Stroke Volume [ml]

EF – Ejection Fraction [%]

Mass – Myocardial Mass [g]

CO – Cardiac Output [L/min]

EDV/BSA – End-Diastole Volume/Body Surface Area [ml/m²]

ESV/BSA - End-Systole Volume/Body Surface Area [ml/m²]

SV/BSA – Systole Volume/Body Surface Area [ml/m²]

Mass/BSA – Myocardial Mass/Body Surface Area [g/m²]

CI – Cardiac Index [L/(min m²)]

BSA - Body Surface Area [m²]

2.2 Abbreviations

ED – End-Diastole

ES – End-Systole

MRI – Magnetic Resonance Imaging

CMR – Cardiac Magnetic Resonance

DICOM – Digital Imaging and Communications in Medicine

HTTP – Hypertext Transfer Protocol

SA – Short-axis

LA – Long-axis

LV – Left Ventricle

RV – Right Ventricle

ICC - Interclass Correlation Coefficient

3. Getting Started

3.1   Notice to the user

Any serious incident that has occurred in relation to the device should be reported to the manufacturer and the competent authority of the Member State in which the user and/or patient is established.

3.2   System requirements

AI4CMR software runs as a Docker image on the cloud.
The minimum requirements for the ethernet connection are:

- High bandwidth network (50Mbits/s minimum and 100Mbits/s recommended).

3.3   Setup

For customer registration, the customer environment shall be informed to AI4MedImaging: MRI scanner vendor, PACS vendor and version, Viewer vendor and version and third-party plugin ID and version.

A *client_id* and temporary user authentication credentials will be assigned by AI4MedImaging to the customer.

The third-party plugin shall be installed and configured as per its User Manual.

To validate the set-up, the following validation protocol shall be followed:

1. Three clinical cases (hereinafter called gold samples GS1; GS2 and GS3) are delivered to the customer by AI4MedImaging. The samples shall be submitted to AI4CMR through the third-party plugin.

    GS1 case is a valid case with all the mandatory and optional data;
    GS2 case is a valid case with all the mandatory data;
    GS3 case is a non-valid case with missing mandatory data.

2. The results displayed by the third-party plugin for each of the golden samples shall be compared with the following expected results:

GS1:

LV Report		
Classification		Confidence
Normal		0.95
EDV	EDV index	CI
111.58	74.11	3.18
ESV	ESV index	ED frame
36.84	24.47	1
SV	SV index	ES frame
74.74	49.64	12
Mass	Mass index	BSA
78.03	51.83	1.51
EF		CO
66.98		4.78
Final Classification		
Normal		

RV Report		
EDV	EDV index	CI
110.74	73.56	3.10
ESV	ESV index	ED frame
37.72	25.06	29
SV	SV index	ES frame
73.02	48.50	12
EF	CO	BSA
65.94	4.67	1.51

GS2:

A warning shall be displayed stating CO, CI and other indexed volume metrics were not computed since heart rate, height and weight were not given.

LV Report		
Classification		Confidence
Suspect		0.70
EDV	EDV index	CI
209.53	-	-
ESV	ESV index	ED frame
105.66	-	25
SV	SV index	ES frame
103.87	-	9
Mass	Mass index	BSA
139.71	-	-
EF		CO
49.57		-
Final Classification		
Suspect		

RV Report		

EDV	EDV index	CI
191.65	-	-
ESV	ESV index	ED frame
85.05	-	24
SV	SV index	ES frame
106.61	-	9
EF	CO	BSA
55.62	-	-

GS3:
The submission shall be disabled. A warning shall be displayed stating there are missing required fields.

3. The customer's IT Manager must send the validation report to AI4MedImaging's Field Support via email. The report must include:
   - A signed statement by the IT Manager confirming if the validation protocol was successful or if it failed.
   - Screenshots of the results obtained for the 3 golden samples.

4. AI4MedImaging's Field Support must confirm reception and sign the report. If the validation protocol is successful AI4MedImaging will provide the final user credentials to the customer. Otherwise, further support must be offered for problem resolution in articulation with the third-party plugin vendor.

3.4   User Training

After the setup is validated, the users will partake in individual or group training given by AI4MedImaging through the Microsoft Teams platform. The users must be trained before using AI4CMR.

Additional individual/group training or Demos can be requested and scheduled by contacting our Technical Support (Section 5).

3.5   Software overview

The AI4CMR operating sequence of events is summarized in Figure **2**. The green-coloured boxes include the operations executed on the external DICOM Viewer plugin, to initiate AI4CMR processing (blue boxes).
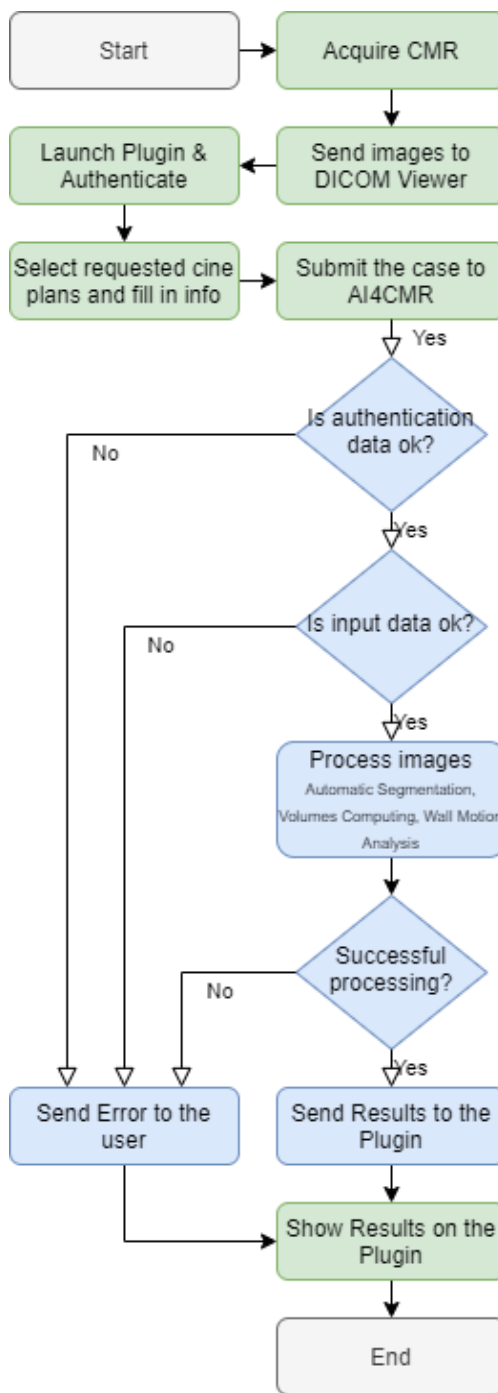
Figure 2. Flowchart of the operating sequence. Green steps are out of AI4CMR's control; blue steps are controlled by AI4CMR.

3.5.1 General operating steps

The general operating steps to use AI4CMR are summarized in the following table:

Operating step	System context
1. The Cardiac Magnetic Resonance is acquired according to standardized protocols	MRI Scanner
2. The images are sent to the third-party software	DICOM Viewer
3. The user launches the dedicated plugin on the third-party software and inserts the user credentials	Plugin
4. The user selects the correct cine sequence planes and other requested patient data	Plugin
5. The user submits the request form to the AI4CMR cloud service	Plugin
6. The request is subject to authentication	AI4CMR
7. The data on the request is checked for sanity and completion	AI4CMR
8. The patient data is processed by several AI-based image processing modules (myocardium automatic segmentation, ventricle volumes computation, wall motion analysis)	AI4CMR
9. The results and log messages (errors, warnings, …) are collected and returned to the plugin via the communication API	AI4CMR
10. The user sees the output of AI4CMR on the dedicated plugin	Plugin

A CMR case to be submitted to AI4CMR shall consist of:

1. Required:
   - DICOM cine SA with metadata:
     - Image Patient Position;
     - Image Patient Orientation;
     - Pixel Spacing;

- Slice Thickness;
- Rows;
- Columns.
  - Patient metadata:
    - Age (on acquisition date);
    - Sex.

2. Optional:
   - DICOM cine 2ch, 3ch and 4ch (recommended);
   - Height, weight, heart rate.

The outputs of AI4CMR consist of:

- Left Ventricle endo and epicardium contours (coordinates)
- Right Ventricle endocardium contours (coordinates)
- Left Ventricle volumes-derived metrics:
  - EDV – End-Diastolic Volume [ml]
  - ESV – End-Systolic Volume [ml]
  - SV – Stroke Volume [ml]
  - EF – Ejection Fraction [%]
  - Mass – Myocardial Mass [g]
  - CO – Cardiac Output [L/min]
  - EDV/BSA – End-Diastole Volume/Body Surface Area [ml/m²]
  - ESV/BSA - End-Systole Volume/Body Surface Area [ml/m²]
  - SV/BSA – Systole Volume/Body Surface Area [ml/m²]
  - Mass/BSA – Myocardial Mass/Body Surface Area [g/m²]
  - CI – Cardiac Index [L/(min m²)]
  - BSA - Body Surface Area [m²]
- Right Ventricle volumes-derived metrics:
  - EDV – End-Diastolic Volume [ml]
  - ESV – End-Systolic Volume [ml]
  - SV – Stroke Volume [ml]
  - EF – Ejection Fraction [%]
  - CO – Cardiac Output [L/min]
  - EDV/BSA – End-Diastole Volume/Body Surface Area [ml/m²]
  - ESV/BSA - End-Systole Volume/Body Surface Area [ml/m²]

- o SV/BSA – Systole Volume/Body Surface Area [ml/m²]

- o CI – Cardiac Index [L/(min m²)]

- o BSA - Body Surface Area [m²]

- Case classification:

  - o Wall motion class – normal or suspect

  - o Wall motion class confidence

  - o Final class – normal or suspect

See Section 3.5.2 for details on outputs validation.

Notice:
1. **The final case class takes both wall motion classification and ejection fraction value into account. A case is only deemed as normal if both criteria are in the normality range.**
2. **The "confidence" is a probability output (0-1) from the machine learning models used to classify each case. The closer the value is to 1, the greater the confidence in the attributed classification, taking the original training database[1] as a reference.**

3.5.2 Summary of outputs validation

The studies conducted under the clinical evaluation phases showed high agreement between AI4CMR measurements and the human observers in a set of 146 patients:

- Correlation (ICC) in the measurement of LV EDV is 0.99, LV ESV is 0.99, LV SV is 0.81, LV EF is 0.96 and Mass is 0.95. The other volume metrics are arithmetically derived from the previous.

- The accuracy and precision of the measurement of the volume are given by the bias (mean difference) and the standard deviation:

	LV EDV (ml)	LV ESV (ml)	LV SV (ml)	Mass (g)	LV EF (%)
AI4CMR vs rater1 (*)	8.6±17.6	-3.7±17.6	11.7±17.1	1.6±19.6	3.9±5.7
AI4CMR vs rater2 (*)	8.7±17.6	-2.1±17.9	10.8±16.8	3.3±18.4	3.8±5.8

- Correlation (ICC) in the measurement of RV EDV is 0.96, RV ESV is 0.95, RV SV is 0.70 and RV EF is 0.81. The other volume metrics are arithmetically derived from the previous.

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[1] Training database - Neural networks and other artificial intelligence programs require an initial set of data, called training data, to act as a baseline for further application and utilization. AI4CMR has been trained, validated and tested on a split database of around 1000 patients, labelled by experts.

- The accuracy and precision on the measurement of the volume are given by the bias (mean difference) and the standard deviation:

	RV EDV (ml)	RV ESV (ml)	RV SV (ml)	RV EF (%)
AI4CMR vs rater1 (*)	6.9±15.8	-10.9±13.8	17.2±14.8	8.2±7.5
AI4CMR vs rater2 (*)	9.8±16.1	-7.3±14.5	17.1±15.3	7.4±7.5

(*) The raters (experts) used the certified software QMass® by Medis Medical Imaging Systems, which computes the volumes based on the raters' manual segmentations.

- For case classification, the sensitivity is 100%, the negative predictive value is 100%, the accuracy is 76.7%, the positive predictive value is 70% and the specificity is 50%.

No uncertainty/error information is shown in the software together with the LV measurements.

3.5.3 Plugin

AI4CMR is intended to be integrated with a third party DICOM Viewer. The integration is established via a communication protocol implemented by a Plugin. AI4CMR does not have a User Interface. The end-user will interact with AI4CMR via the Plugin's interface.

The Plugin User Manual which accompanies the current manual describes in more detail the features and steps necessary to interact with the AI4CMR service. The Plugin consists of a user interface to help the User create the request form. Different viewers can have different user experiences, but the main idea should be the same.

For clarification purposes, this section provides merely indicative (not binding) examples of what the user experience may be like with a third-party Plugin for AI4CMR.

Login

The first step to use the AI4CMR is to successfully authenticate with the service. To do that, the User shall provide a username and password, Figure **3**.
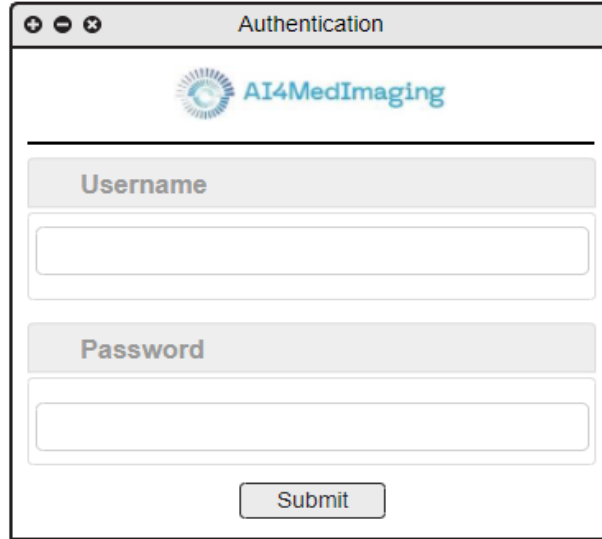
Figure 3. Example of a plugin login window.

Form filling

The plugin provides a way for the User to fill in the necessary information to perform a request, as presented in

Figure **4**.

The User shall identify each sequence (SA, 2ch, 3ch, 4ch) and add it to the Plugin (using drag and drop, for example). The SA sequence is mandatory and should always be provided. The LA sequences are optional and can be discarded if they do not exist. The inclusion of the LA views is highly recommended if they are available.

AI4CMR's performance has been validated for a range of image characteristics, as shown in the tables[2] below:

Ranges	Number of Pixel Rows	Number of Pixel Columns	Image Size Values	Slice Thickness Values
Error	]-∞, 140[	]-∞, 140[	]- ∞, 26957[	]- ∞, 7.2[
Warning	[140, 156[	[140, 156[	[26957, 29952[	[7.2, 8[
Acceptance	[156, 320]	[156, 320]	[29952, 102400]	8
Warning	]320, 352]	]320, 352]	]102400, 123904]	]8, 8.8]
Error	]352, +∞[	]352, +∞[	]123904, +∞[	]8.8, +∞[

Ranges	Pixel Spacing Values	Number of Slices	Slice Spacing Values	Pixel Intensity Values
Error	]- ∞, 0.8389[	]- ∞, 8[	]- ∞, 7.2[	]- ∞, 28.0069[
Warning	[0.8389, 0.9322[	[8, 9[	[7.2, 8[	[28.0069, 31.1188[
Acceptance	[0.9322, 1.7709]	[9, 16]	[8, 10]	[31.1188, 273.8040]
Warning	]1.7709, 1.9479]	]16, 19]	]10, 11.2]	]273.8040, 355.1480]
Error	]1.9479, +∞[	]19, +∞[	]11.2, +∞[	]355.1480, +∞[

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[2] The values are the result of a study conducted based on a significative sample of CMR cases.

Cases with image characteristics that are outside the boundaries of the verified performance of the algorithms will be rejected.

Patient metadata shall be filled in by the User if the Plugin does not automatically fill it based on the DICOM information:

- Mandatory:
    - Patient ID
    - Age
    - Sex
- Optional:
    - Heart rate (if not sent to AI4CMR: CO and CI will not be computed)
    - Height (if not sent to AI4CMR: no BSA nor indexed metrics (EDV/BSA, ESV/BSA, SV/BSA, Mass/BSA, CI) will be computed)
    - Weight (if not sent to AI4CMR: no BSA nor indexed metrics (EDV/BSA, ESV/BSA, SV/BSA, Mass/BSA, CI) will be computed)

Figure 4. Example of a plugin form filling window.

Results presentation

After successful processing, the plugin presents the results.

One example of a possible user interface for results reporting is presented in the bottom half of Figure **5** (LV report) and Figure **6** (RV Report).

Figure 5. Example of a plugin form filling and results in the presentation window – LV Report.

Figure 6. Example of a plugin form filling and results in the presentation window – RV Report.

After a failed processing, the plugin presents an error message, so that the user can adapt the request or report a possible problem.

Parametrizations

AI4CMR allows for the change of a set of parameters (wall motion threshold and ejection fraction thresholds). These values should only be changed by the customer's IT Manager and after careful consideration.

Additional fields

Connection status

This field is used to indicate that the AI4CMR service is available. If not, the User can force a connection status update by clicking on the status button.
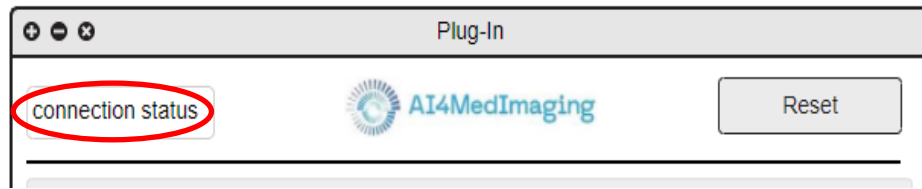
Figure 7. Connection status example.

Reset button

The reset button is used to clean all the info from the current request and make it easier for the user to start a new request without cleaning each field individually.
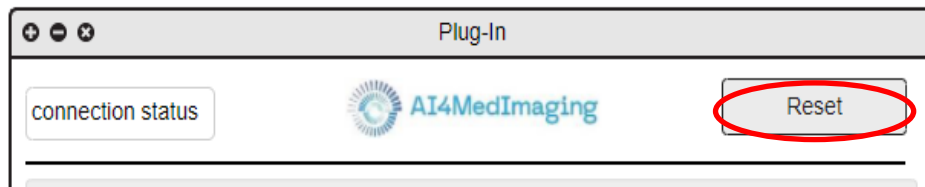

Figure 8. Reset button example.

Info button

This button presents information regarding the plugin and AI4CMR service, such as email, certifications, versions, device labelling and so on.
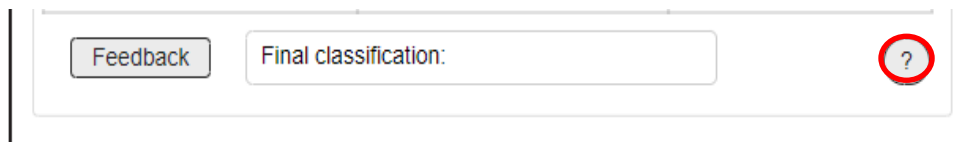

Figure 9. Info button example.

Confidence disclaimer

This button presents information to clarify the wall motion classification results.
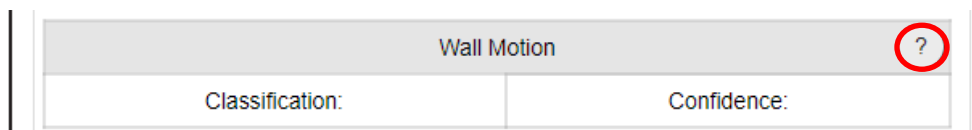

Figure 10. Confidence disclaimer button example.

Feedback button

The User can access plugin support by clicking on this button, which redirects him to feedback email software.
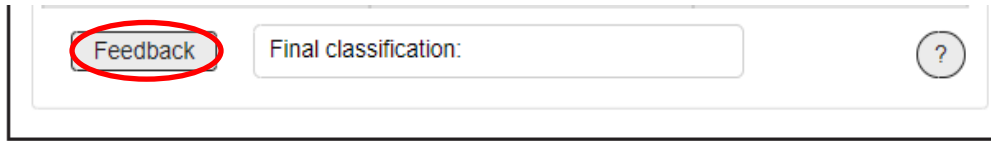

Figure 11. Feedback button example.

4. User account handling

The AI4CMR provides a user account handling page, that allows each user to change their personal information and credentials. To access this functionality, the user should use the following link via the Google Chrome browser (minimum recommended version: 97) or the Safari browser (minimum recommended version: 14.1):

- https://auth.ai4medimaging.com/auth/realms/srerealm/account

4.1 Authentication

To access the account, the user should provide the assigned username or email and password.
<u>Note</u>: the authentication/login window depends on the third-party plugin integration.

Figure 12. User account login page.

After successful authentication the user handling page will be presented, Figure **13**.

4.2 User information handling

After logging in, on the separator "Account" the user can change the email, first name and last name by filling the respective field and clicking on "Save". If these values already exist, they will be presented in the respective field.

Figure 13. User account personal information edit page.

4.3   Password handling

To change the password, the user should log in first and change to the "Password" separator, provide the current password on the "Password" field and the new password on the "New Password" and "Confirmation" fields. After clicking on "Save" the password will be updated.

Figure 14. User account password edit page.

In case of password loss or account compromised, the IT Manager of the User's Institution should contact the AI4MedImaging's Technical Support (see section 5 for details).

4.4   Open sessions

The user has the option to monitor all open sessions associated with his account. That information is accessible in the "Sessions" separator. If any of the sessions open is considered suspect, the user has the option to close it using the "Log out all sessions" button.
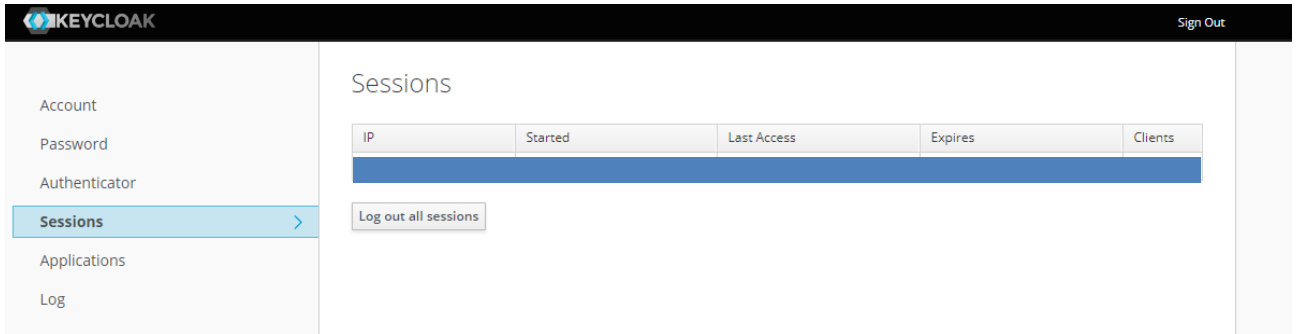
Figure 15. User account open sessions page.

4.5   Logging info

In addition to the open sessions, the user has the option to see all logging events that happen using his account. This information can be accessed on the "Log" separator.
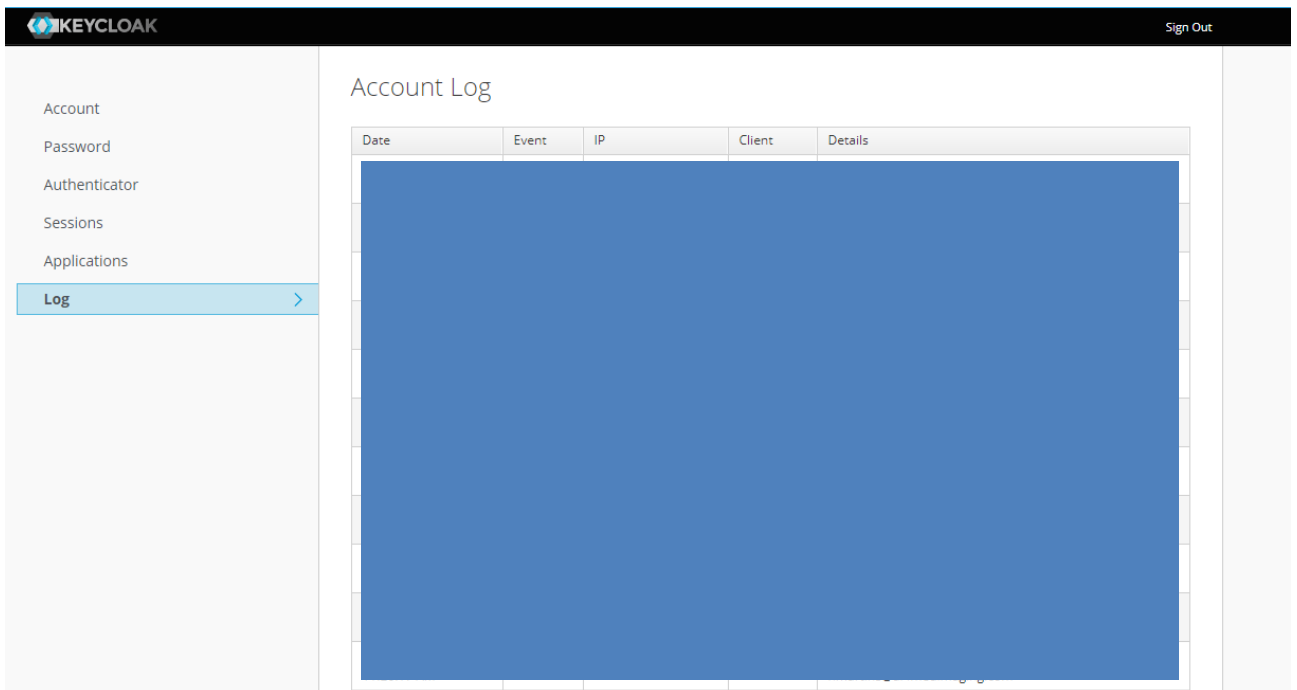

Figure 16. User account access log page.

5. Technical Support

For technical questions, to report a problem, or to request individual/group training or demos, please contact our team by e-mail or website:

AI4MedImaging Medical Solutions S.A.

Rua do Parque Poente, Lote 35
4705-002 Sequeira, Braga
Portugal

Website: https://ai4medimaging.com/

E-mail: support@ai4medimaging.com