AI4CMR

Version 2.0
USER MANUAL

AI4CMR

Cardiac MRI reporting:
Simplified. Anywhere. Anytime.

AI4MedImaging

Manufactured by

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ISO 13485:2016 Certificate
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

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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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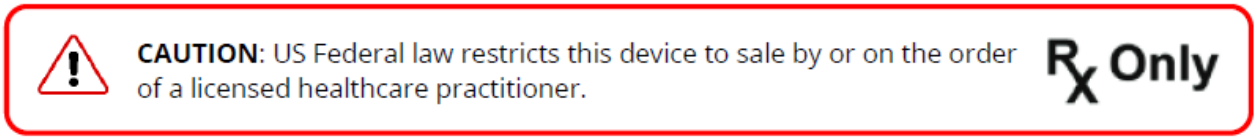

AI4MedImaging shall not be responsible for technical or editorial errors or omissions contained herein.

The information contained herein is subject to change without notice.

The only warranties for AI4MedImaging products and services are described in the express warranty statements accompanying such products and services.

Please contact the manufacturer or authorized representative to request the latest edition of the user manual or consult the latest edition on the AI4MedImaging website.

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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 also supports clinical diagnostics by calculating flow measurements of vascular structures in 2D phase-encoded cardiac MR images

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.

WARNING: * Wall Motion feature is not available for clinical use in the USA. This module is to be used for research purposes only, and not for primary diagnostics and direct patient care

1.2 Indications for use (Unites States)

AI4CMR software is designed to report cardiac function measurements (ventricle volumes, ejection fraction, indices etc.) from 1.5T and 3T magnetic resonance (MR) scanners. AI4CMR uses artificial intelligence to automatically segment and quantify the different cardiac measurements. Its results are not intended to be used on a stand-alone basis for clinical decision-making. The user incorporating AI4CMR into their DICOM application of choice is responsible for implementing a user interface.
AI4CMR also supports clinical diagnostics by calculating flow measurements of vascular structures in 2D phase-encoded cardiac MR images

1.3 Intended users

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

Note: Software Developers interact only for technical Integration and Support.

1.4 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 complete system, including AI4CMR and the third-party systems, as presented in Figure 1, operates as an integrated solution from a clinical workflow standpoint. However, each component is responsible for its own regulatory compliance. Consequently, any DICOM viewer or medical device that interacts with AI4CMR must comply with all applicable requirements under the MDR and another applicable medical device regulations in different markets.

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

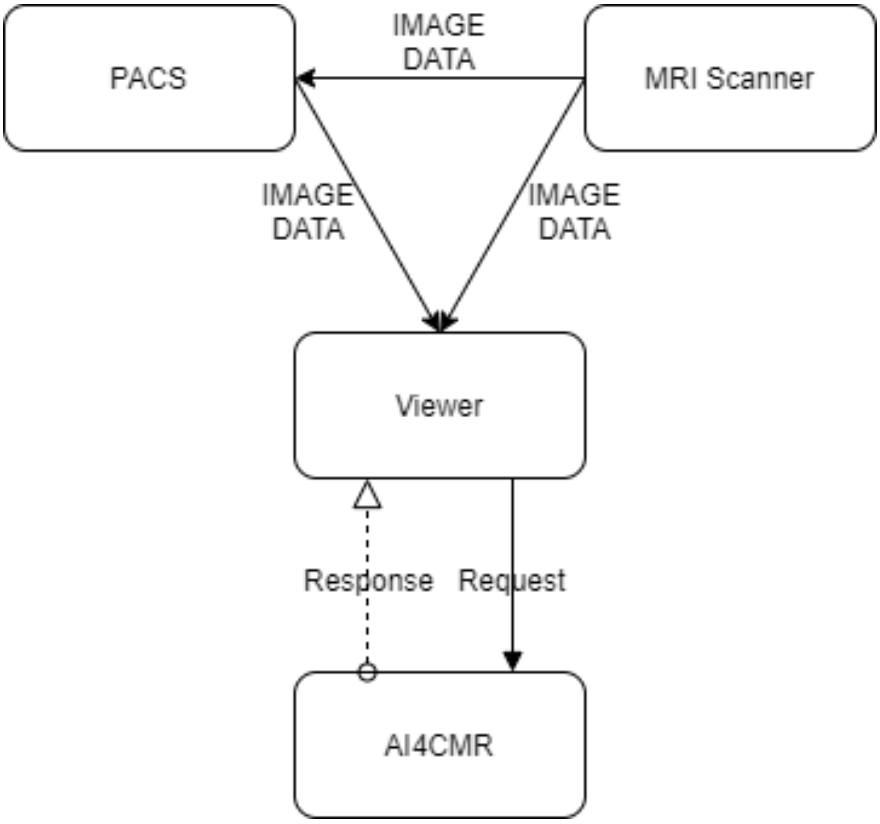

Figure 1. High-level representation of the interoperability between AI4CMR and the third-party systems and services.

1.5 Contraindications

AI4CMR is contraindicated to be used for post-processing of all image modalities other than cine and 2D phase-encoded images of CMR.

1.6 Key Features and Benefits

AI4CMR is intended to support clinicians in the analysis of CMR images. The following benefits may be observed when using the software in accordance with its intended use:

Cine Sequences:

- Fully automated segmentation of left and right ventricles, with possibility of being reviewed in real-time
- Automatic quantification of standard cardiac function parameters:
  - Left ventricle: EDV, ESV, SV, EF, LVM, CO, and BSA-indexed volumes
  - Right ventricle: EDV, ESV, SV, EF, CO, and BSA-indexed volumes.
- High-reliability quantification
- Automatic classification of normal and suspicious left ventricular wall motion*
- Time efficiency, enabling potential reduction of reporting time.
- Compatibility with images acquired from various MRI manufacturers (Siemens, GE, and Philips) - validated across multi-vendor datasets

- Clinical support through standardized, repeatable measurements.

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2D Flow Sequences:

- Semi-automated segmentation of vascular structures via user-placed seed point, with possibility of being reviewed
- Automatic analytical flow quantification, including parameters such as Total Forward/Backward Net Volumes, Regurgitation Fraction, Effective Volume per Minute, Maximum Velocity, Pressure Gradient, and Flow values.
- Clinical support through standardized, repeatable measurements.

General Benefits:

- Cloud-based platform: Offers high availability, scalability, and integration with hospital infrastructure.
- Improves clinical workflow when integrated with PACS or VNAs Viewers (no need for a dedicated segmentation software).
- Interoperability: Communicates with other systems via standard protocols.

1.7 Limitations

AI4CMR analysis is limited to Cine CMR and 2D Phase-Contrast 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.

1.8 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 can introduce patient metadata (cine, cine recompute and flow), It is the User’s responsibility to verify this data before releasing the final results.
- The user is responsible for ensuring the seed point (at Flow) is placed precisely within the intended vessel region of interest and on a structure with adequate signal clarity.
- 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.

1.9 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

1.10 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
- Congenital heart disease
- Other pathologies that need assessment of cardiac function and morphology

1.11 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

2.2 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]

TFV - Total Forward Volume (ml)

TBV - Total Backward Volume (ml)

TV - Total Volume (ml)

TNPV -Total Net Positive Volume (PV) (ml)

TNNV - Total Net Negative Volume (NV) (ml)

RF - Regurgitation Fraction (%)

Vol/min- Volume per Minute (Vol/min) (l/min)

Eff. Vol/mi - Effective Volume per Minute (Vol/min effective) (l/min)

Max PG - Maximum Pressure Gradient (mmHg)

Max Vel- Maximum Velocity (cm/s)

Min Vel- Minimum Velocity (cm/s)

Max Mean Vel - Maximum Mean Velocity (cm/s)

Max Flow- Maximum Flow (ml/s)

Min Flow - Minimum Flow (ml/s

2.3 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

TFV - Total Forward Volume

TBV - Total Backward Volume

TV - Total Volume

TNPV -Total Net Positive Volume (PV)

TNNV - Total Net Negative Volume (NV)

RF - Regurgitation Fraction

Vol/min- Volume per Minute

Eff. Vol/mi - Effective Volume per Minute

Max PG - Maximum Pressure Gradient

Max Vel- Maximum Velocity

Min Vel- Minimum Velocity

Max Mean Vel - Maximum Mean Velocity

Max Flow- Maximum Flow

Min Flow - Minimum Flow

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.

AI4CMR Cine:

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:

	EDV (mL)	IEDV index (mL/m^2)	ESV (mL)	ESV index (mL/ m^2)	CO (L/min)	CI (L/min/ m^2)	SV (mL)	SV index (mL/ m^2)	EF (%)	Mass (g)	Mass index (g/m2)	ED frame	ES frame
LV	116.79	77.57	37.87	25.15	5.05	3.36	78.92	52.42	67.58	77.52	51.49	29	11
RV	117.16	77.82	40.70	27.03	4.89	3.25	76.46	50.79	65.26	-	-	29	12

	Value
Classification	Normal
Confidence	0.95
Final Classification	Normal
BSA	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.

	EDV (mL)	IEDV index (mL/m^2)	ESV (mL)	ESV index (mL/ m^2)	CO (L/min)	CI (L/min/ m^2)	SV (mL)	SV index (mL/ m^2)	EF (%)	Mass (g)	Mass index (g/m2)	ED frame	ES frame
LV	219.35	-	110.82	-	-	-	108.53	-	49.48	146.58	-	24	8
RV	203.11	-	91.67	-	-	-	111.44	-	54.87	-	-	24	9

	Value
Classification	Suspect
Confidence	0.69
Final Classification	Suspect
BSA	-

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.

Changes to the plugin (release of new versions) must be communicated to AI4MedImaging and a new validation process might be needed depending on the changes done.

AI4CMR 2DFlow:

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

1. Three clinical cases delivered to the customer (hereinafter called gold samples GS1Flow; GS2Flow and GS3Flow) shall be submitted to AI4CMR 2DFlow through the third-party plugin.

   GS1Flow case is a valid case with all the mandatory data where ascending and descending aorta are identified for analysis.

   GS2Flow case is a valid case with all the mandatory data where the pulmonary artery is identified for analysis.

   GS3Flow case is a non-valid case with missing mandatory data, specifically the VENC value.

   Note: Since 2DFlow submissions require a seed point on the vessels, which influences the final quantification results, the service will automatically position the seed point at a predefined location, overriding any user-defined seed points. This approach is applied solely for validation during the setup phase to ensure reproducibility.

2. The results displayed by the third-party plugin for each of the golden samples shall be compared with the following expected results:
   GS1Flow:

	Volume (L/min)	**Max Velocity (cm/s)**	**Total Forward Volume (ml)**	**Total Backward Volume (ml)**
Ascending Aorta	8.121	190.137	75.851	-0.457
Descending Aorta	3.057	57.813	40.979	-0.601

   GS2Flow:

	Volume (L/min)	Max Velocity (cm/s)	Total Forward Volume (ml)	Total Backward Volume (ml)
Pulmonary Artery	2.178	20.801	36.308	0.0

   GS3Flow: 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.

Changes to the plugin (release of new versions) must be communicated to AI4MedImaging and a new validation process might be needed depending on the changes done.

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-colored boxes include the operations executed on the external DICOM Viewer plugin, to initiate AI4CMR processing (blue boxes).

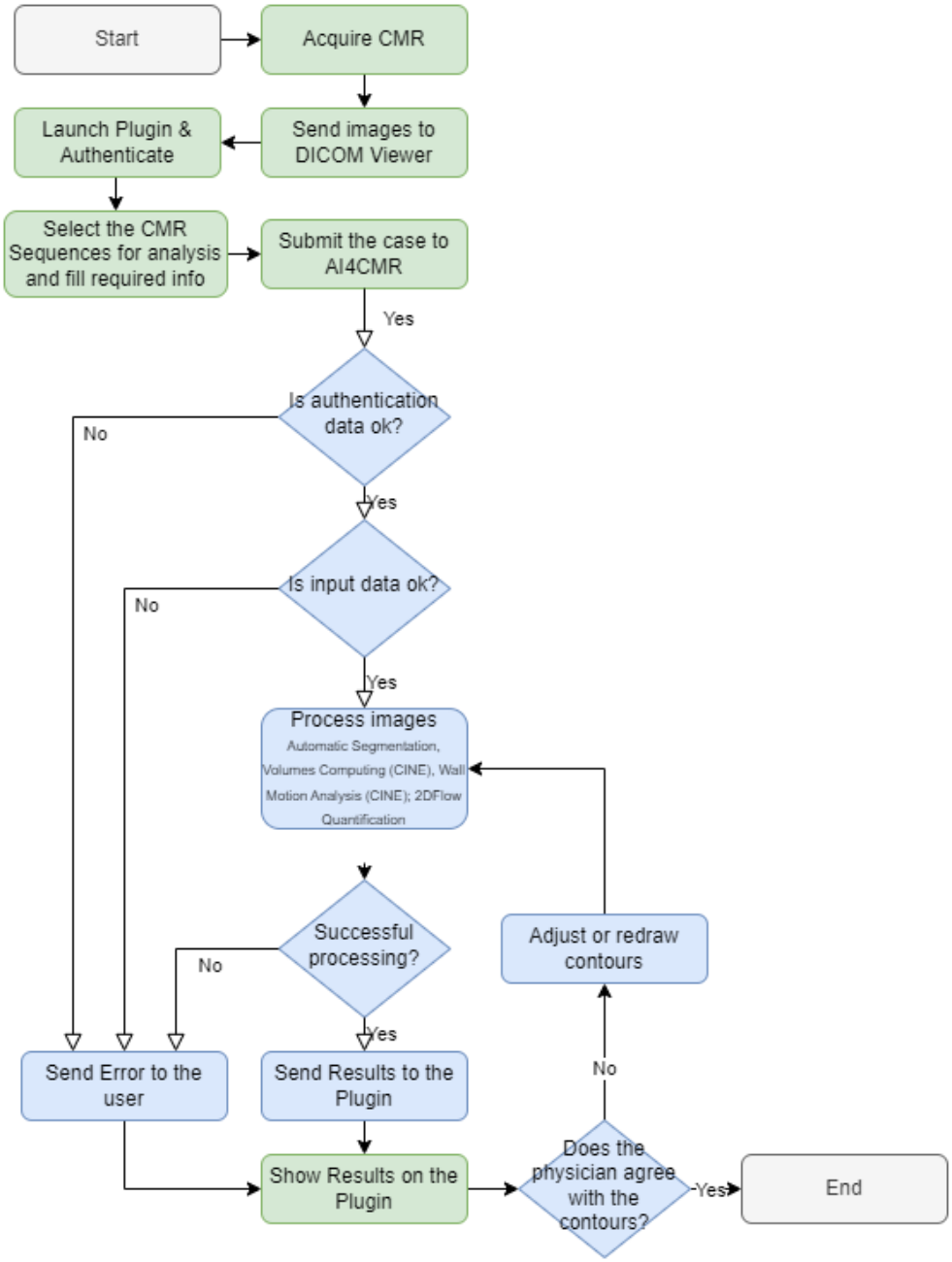

Figure 2. Flowchart of the operating sequence. Green steps are out of AI4CMR's control; blue steps are controlled by AI4CMR.

WARNING: * Wall Motion feature is not available for clinical use in the USA. This module is to be used for research purposes only, and not for primary diagnostics and direct patient care

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 performs one or more of the following actions: Selection of the correct cine sequence planes and other requested patient data Places a seed point at a cardiac vessel structure in magnitude sequences of 2D Flow CMR.	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[1] and completion[2]	AI4CMR
8. The patient data is processed by several AI-based image processing modules (Cine: myocardium automatic segmentation, ventricle volumes computation, wall motion* analysis; Flow: vessels segmentation, flow quantification).	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
11. The user validates the outputs, or adjusts the contours on the dedicates plugin, prompting the recomputation by AI4CMR.	Plugin/AI4CMR

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

Cine:

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.

2D Flow:

- Required:
- Identification of the vascular structures for analisis: vessel name and ROI
    - DICOM 2DFlow data with metadata:
- Pixel Spacing;
- Bits Stored;
- Manufacturer;
- VENC;
- Nominal Interval or TriggerTime or HighRRInterval and LowRRInterval

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]
  - SV/BSA – Systole Volume/Body Surface Area [ml/m²]
  - CI – Cardiac Index [L/(min m²)]
  - BSA - Body Surface Area [m²]
- Case classification*:
  - Wall motion class – normal or suspect
  - Wall motion class confidence
  - Final class – normal or suspect

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- 2D flow vessels contours (coordinates)
- 2D flow Measurements:
  - TFV - Total Forward Volume (ml)
  - TBV - Total Backward Volume (ml)
  - TV - Total Volume (ml)
  - TNPV -Total Net Positive Volume (PV) (ml)
  - TNNV - Total Net Negative Volume (NV) (ml)
  - RF - Regurgitation Fraction (%)
  - Vol/min- Volume per Minute (Vol/min) (l/min)
  - Eff. Vol/mi - Effective Volume per Minute (Vol/min effective) (l/min)
  - Max PG - Maximum Pressure Gradient (mmHg)

- Max Vel- Maximum Velocity (cm/s)
- Min Vel- Minimum Velocity (cm/s)
- Max Mean Vel - Maximum Mean Velocity (cm/s)
- Max Flow- Maximum Flow (ml/s)
- Min Flow - Minimum Flow (ml/s

See Section 3.5.2 for details on outputs validation.

Notice:

For the Case classification:

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.

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3.5.2 Summary of outputs validation

3.5.2.1 Cine:

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 0.83, LV EF is 0.96 and Mass is 0.96. 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 consensus (*)	1.81±17.61	-6.84±17.65	8.36±17.25	3.19±17.37	3.86±5.80

[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.

- Correlation (ICC) in the measurement of RV EDV is 0.97, RV ESV is 0.94, RV SV is 0.82 and RV EF is 0.80. The other volume metrics are arithmetically derived from the previous.
- 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 (*)	1.25±15.99	-13.26±14.63	14.24±15.53	8.34±7.34

(*) The consensus between 2 raters (experts) was obtained by averaging each measurement. The measurements were obtained through a certified software, 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.

3.5.2.2 2D Flow:

The flow quantification performance study was conducted to ensure comparability between AI4CMR and a similar/predicate device, demonstrating a high level of agreement. Vessel segmentation and flow quantification were independent of anatomical structures (e.g., vessel type). The study included 108 independent multivendor samples from real-world cases (covering the ascending aorta, descending aorta, and pulmonary artery) from 66 subjects. These samples were processed by both AI4CMR and the similar/predicate device, and their performance on flow quantification was compared. The key findings were:

- The intraclass correlation coefficients (ICC) for TFV, TBV, and Max Vel were 0.95, 0.82, and 0.95, respectively, highlighting strong agreement in clinically relevant measures.
- The accuracy and precision achieved for TFV, TBV, and Max Vel measurements are given by the bias (mean difference) and the standard deviation:

	TFV (ml)	**TBV (ml)**	**Max Vel (cm/s)**
AI4CMR vs Similar/predicate device	-1.65±9.61	-0.47±2.24	-1.24±15.11

- Statistical comparison between AI4CMR and the similar/predicate device was performed using a paired *t*-test for Max Vel (t = -0.773, *p-value* = 0.445), TBV (t = -1.039, *p-value* = 0.301) and TFV (t = -1.790, *p-value* = 0.076), with all results being non-significant (*p-value* > 0.05).

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 or Guide, 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, there are two options:

- The User shall provide a username and password through the user interface
- The plugin loads credentials/licensing information securely saved in or transmitted by the User's system.

Figure 3. Example of a plugin login window.

Input Data Selection

The input data selection can be done in two ways:

- Manually by the User through the user interface. This option may or may not include automatic prefilling.
- Automatically by the plugin taking advantage of the standard DICOM tags.

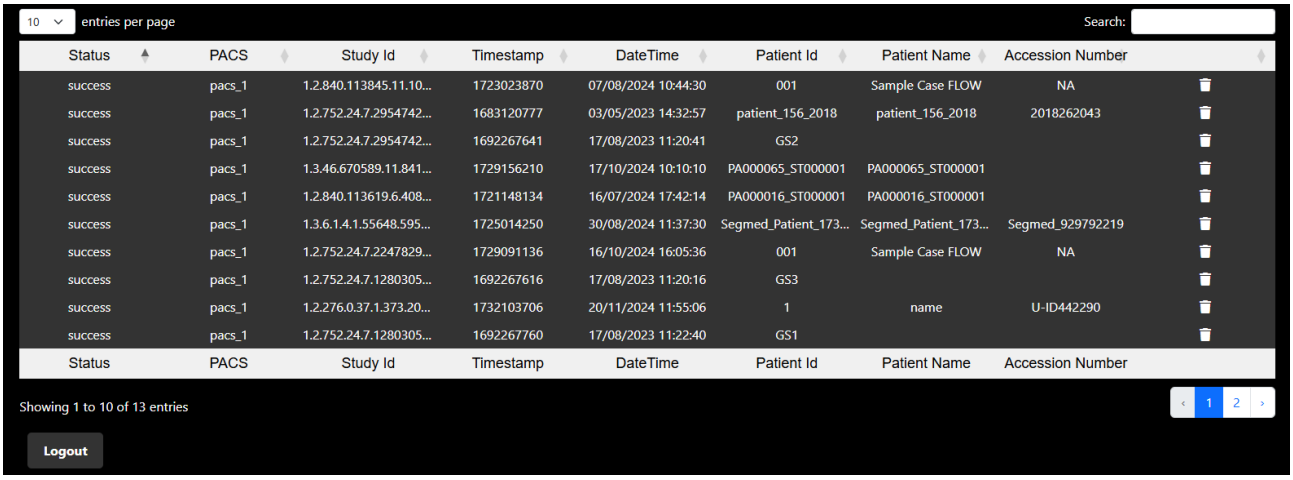


Figure 4. Example of a plugin worklist window.

Form filling

Cine Sequences Analysis

Figure shows an example of an interface for the User to fill in the necessary information. The automation of this step is advised and should allow the edition of the patient metadata (age, sex, heart rate, height, and weight) and the cine slices (cine_sa (SA), cine_2ch (LA 2ch), cine_3ch (LA 3ch), and cine_4ch (LA 4ch)).

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]

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

Error	]1.9479, +∞[	]19, +∞[	]11.2, +∞[	]355.1480, +∞[

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)

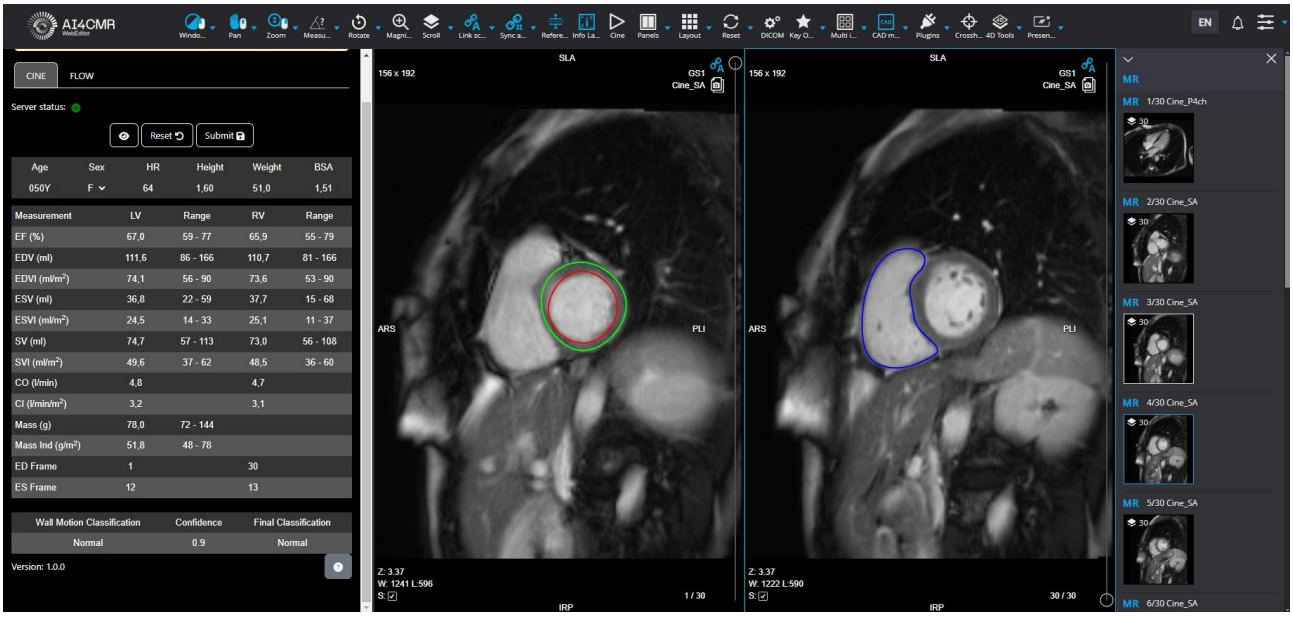


Figure 5. Example of a cine plugin window.

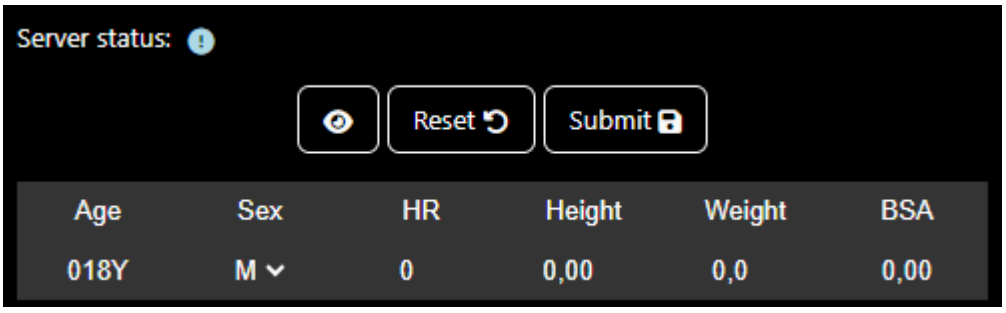


Figure 6. Example of a plugin form filling window.

2D Phase-Contrast Sequences Analysis

AI4CMR 2DFlow's performance has been validated for a range of image characteristics, as shown in the tables[3] below:

Feature	Acceptance	Warning
Pixel Spacing	[1.25, 1.7709]	]- ∞, 1.25[U]1.7709, +∞[
Pixel Intensity	[23.19, 88.55]	]- ∞, 23.19[U]88.55, +∞[

Cases with image characteristics that are outside the boundaries of the verified performance of the algorithms will be processed, but a warning message will be logged to inform that performance can be affected.

In the plugin, the user triggers the AI4CMR 2D Flow to analyze the case by selecting a seed point on the vessels within one of the sequence's magnitude frames to quantify the blood flow of the respective vessel. This allows the tool to quantify the blood flow in the selected vessels. After processing the case, AI4CMR provides the vessels delineation across the entire sequence along with the corresponding flow measurement values.

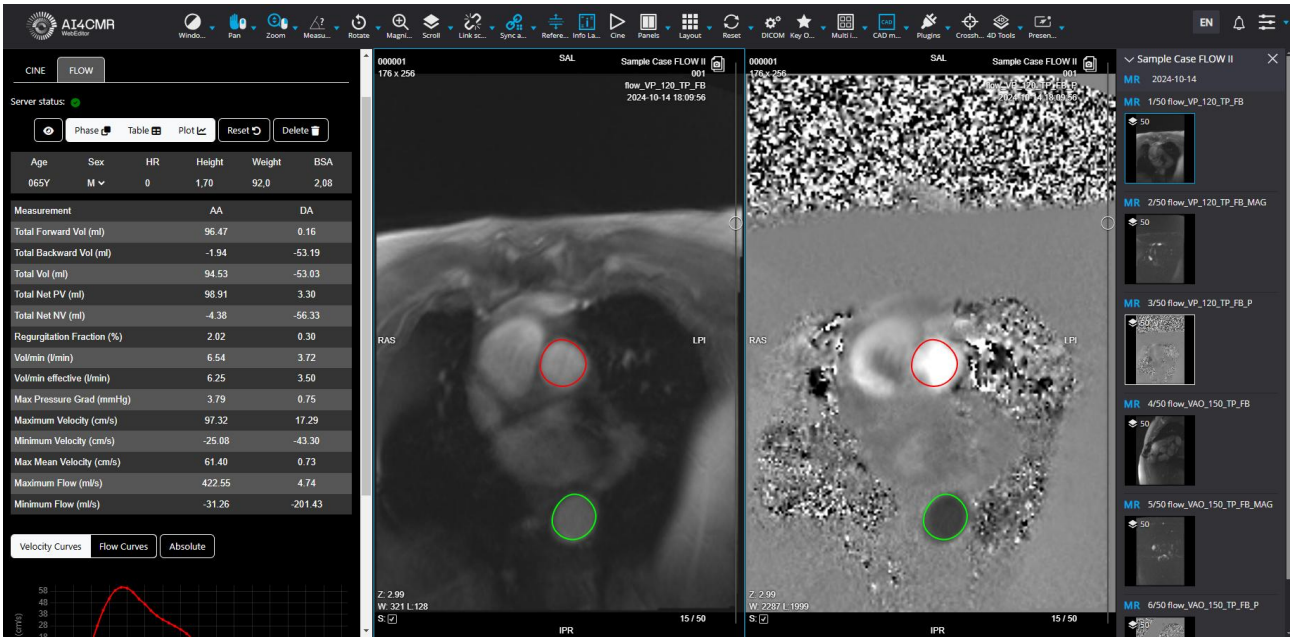


Figure 7. Example of a flow plugin window.

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

Results presentation

After successful processing, the plugin presents the results. The results presentation includes someway to show contours and someway to show numerical values and text. In the case of failure, an error message shall be outputted instead of the results.

Cine Sequences Analysis Results

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

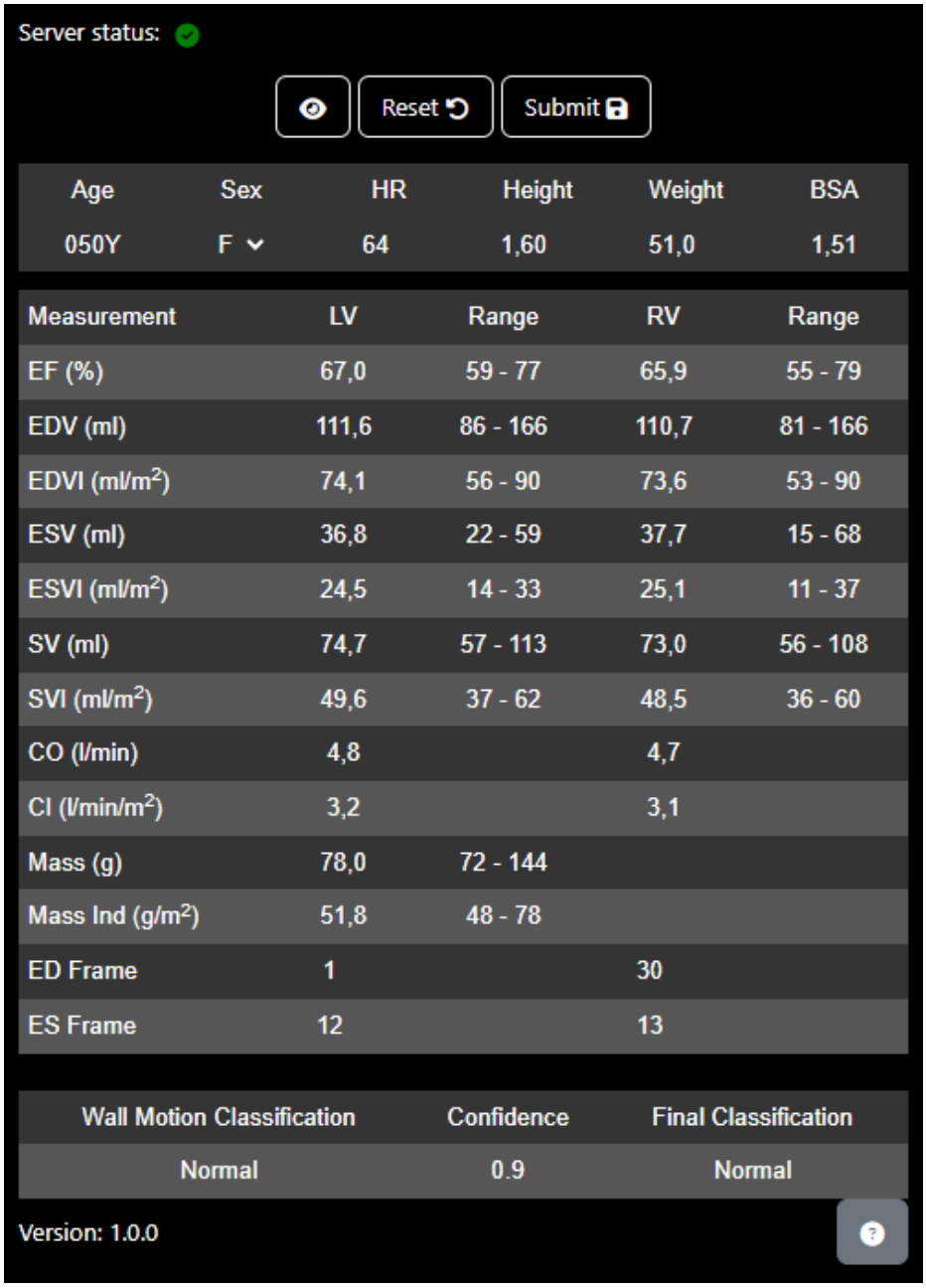
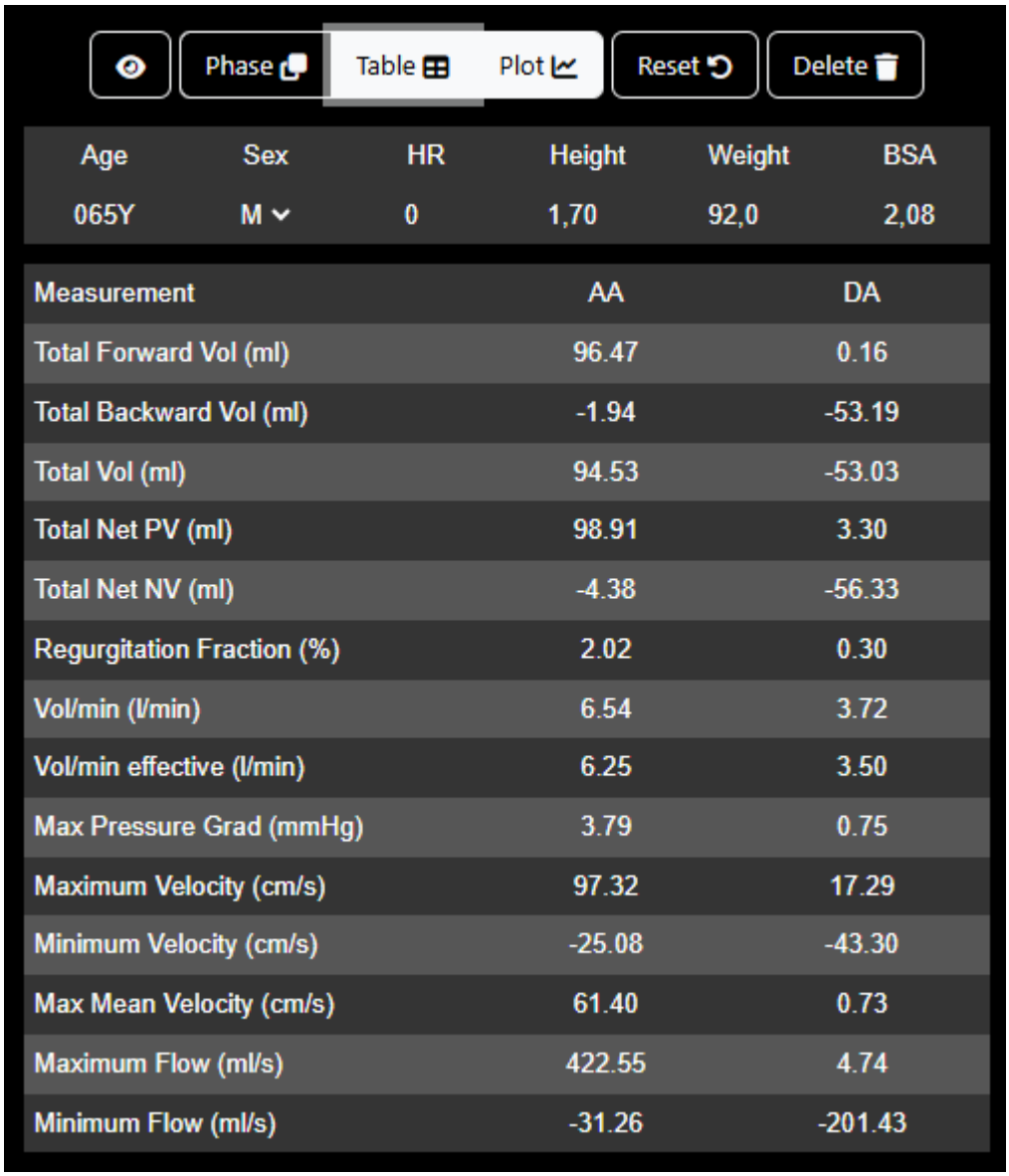


Figure 8. Example of a plugin form filling and results in the presentation window – LV and RV Report.

2D Phase-Contrast Sequences Analysis Results

An example illustrating the results of flow measurements is shown in Figure 9, while Figure 10 illustrates the flow and velocity curves.



Age	Sex	HR	Height	Weight	BSA
065Y	M	0	1,70	92,0	2,08

Measurement	AA	DA
Total Forward Vol (ml)	96.47	0.16
Total Backward Vol (ml)	-1.94	-53.19
Total Vol (ml)	94.53	-53.03
Total Net PV (ml)	98.91	3.30
Total Net NV (ml)	-4.38	-56.33
Regurgitation Fraction (%)	2.02	0.30
Vol/min (l/min)	6.54	3.72
Vol/min effective (l/min)	6.25	3.50
Max Pressure Grad (mmHg)	3.79	0.75
Maximum Velocity (cm/s)	97.32	17.29
Minimum Velocity (cm/s)	-25.08	-43.30
Max Mean Velocity (cm/s)	61.40	0.73
Maximum Flow (ml/s)	422.55	4.74
Minimum Flow (ml/s)	-31.26	-201.43

Figure 9. Example of a plugin metrics results in the presentation– 2D Flow metrics Report.

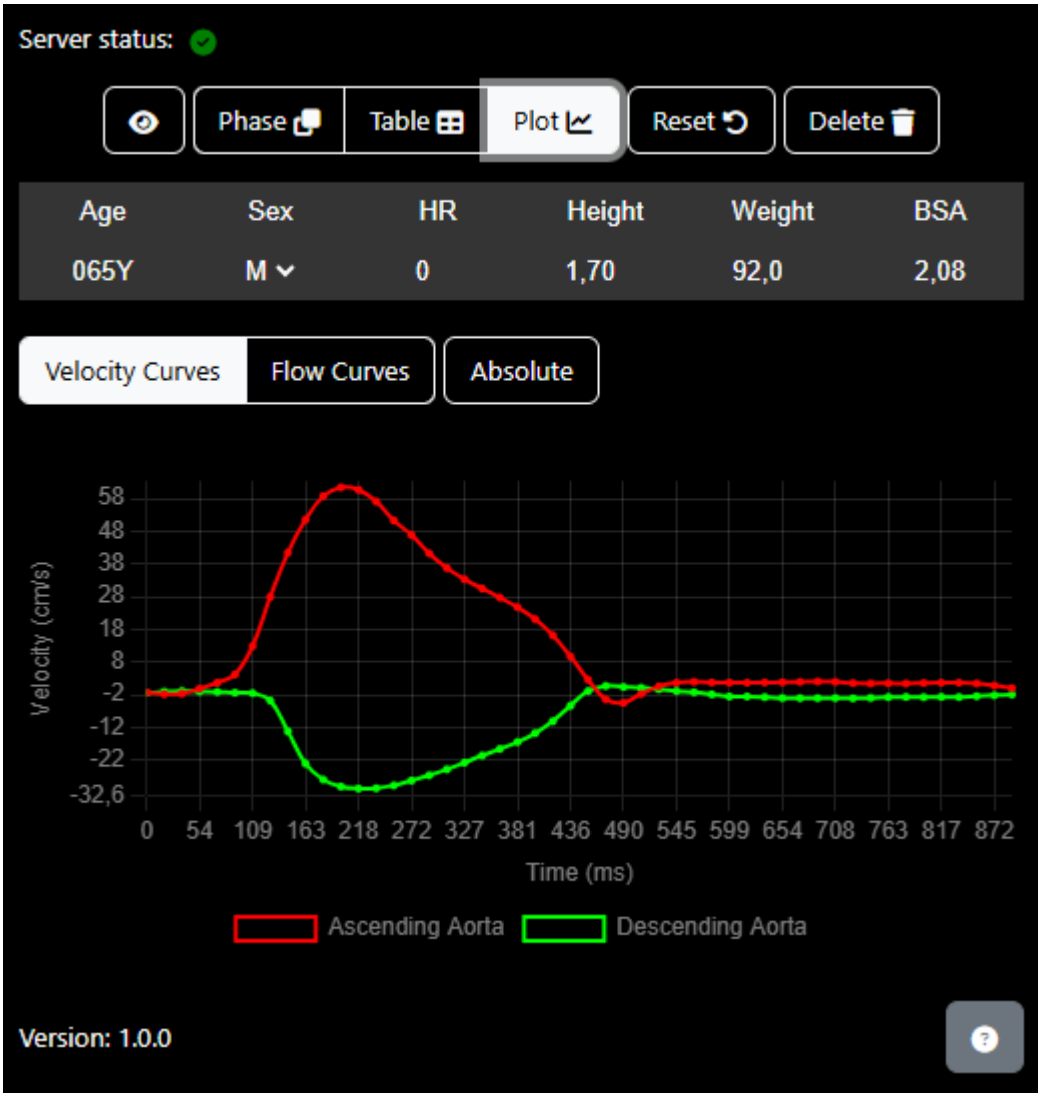


Figure 10. Example of a plugin curves results in the presentation flow window – flow curves

Additional fields

Connection status

This field is used to indicate that the AI4CMR service is available.

If not, the User should be able to force a connection status update. Either by clicking on the status or using any other way. The connection check endpoint of CORE should be used here to test the connection.

Figure 11. 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 12. 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.

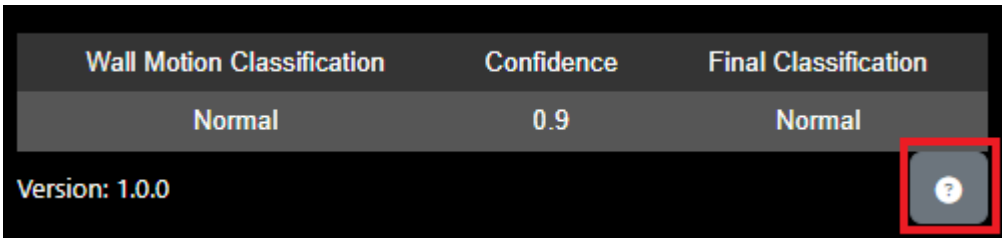


Figure 13. Info button example.

Confidence disclaimer

This button presents information to clarify the wall motion* classification results. When clicked, the button should display the disclaimer text.

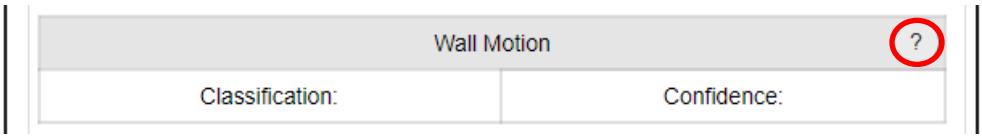


Figure 14. Confidence disclaimer button example.

WARNING: * Wall Motion feature is not available for clinical use in the USA. This module is to be used for research purposes only, and not for primary diagnostics and direct patient care

Feedback button

This button can be used to redirect the User to a feedback webpage, email software, present a mobile number or any other communication way that might fit the task of providing feedback or requesting assistance. The plugin team can also include (or prefill) the message to be sent so that possible problems are easier to track.

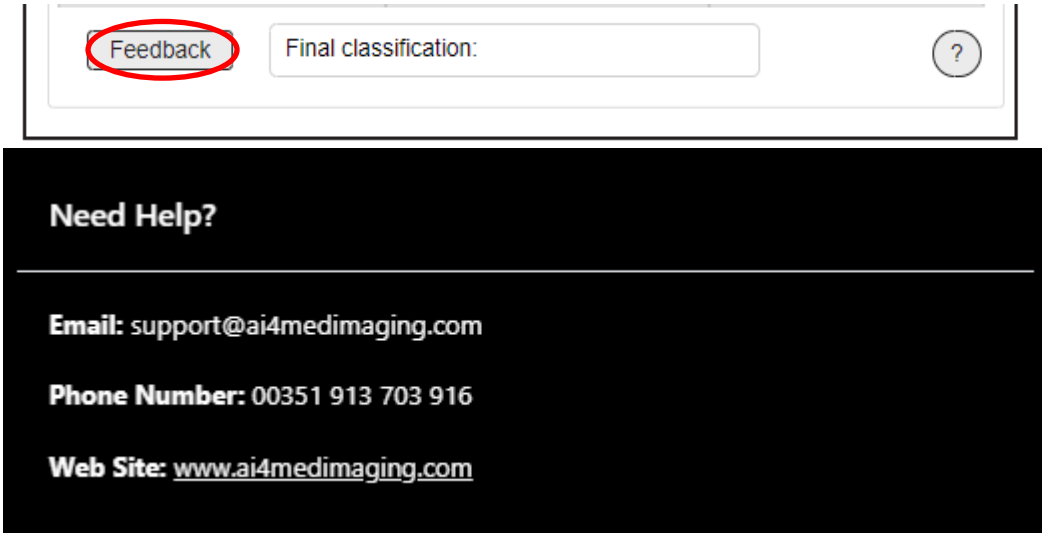


Figure 15. Feedback button example.

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.
Note: the authentication/login window depends on the third-party plugin integration.

Figure 16. User account login page.

After successful authentication the user handling page will be presented, Figure **47**.

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.

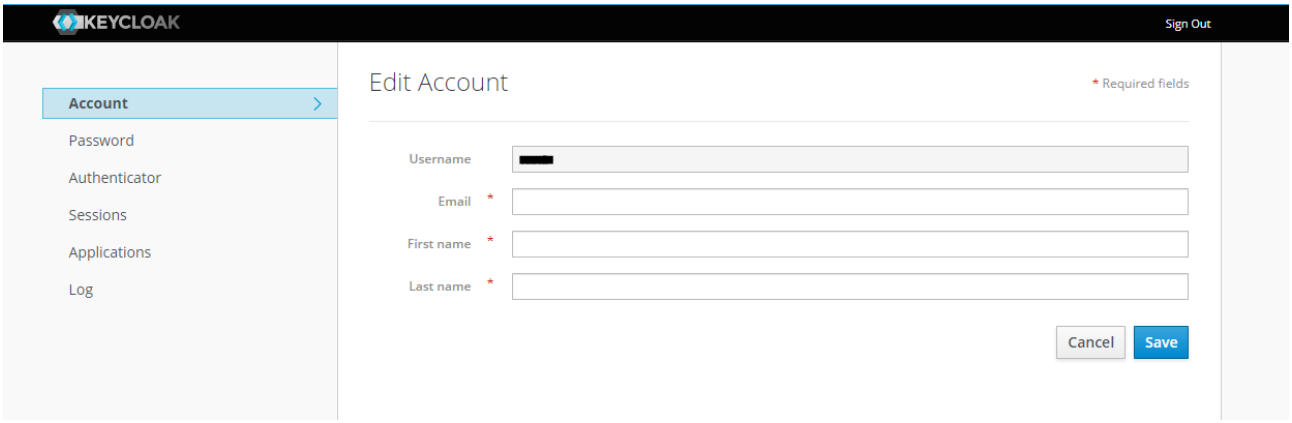


Figure 47. User account personal information edit page.

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.

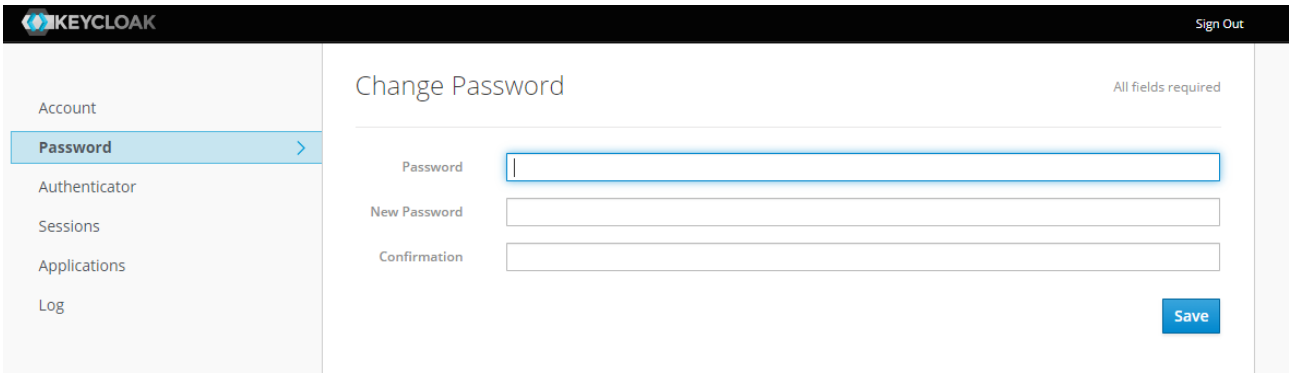


Figure 18. User account password edit page.

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.

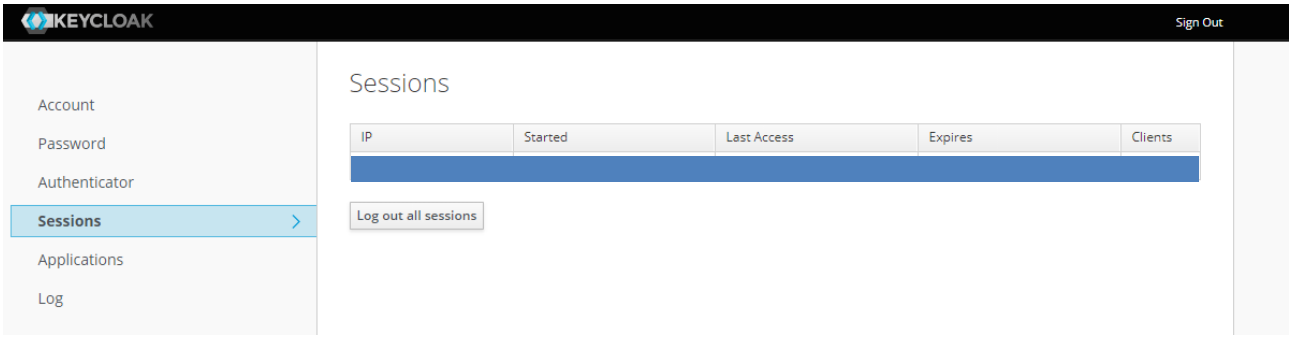


Figure 19. User account open sessions page.

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.

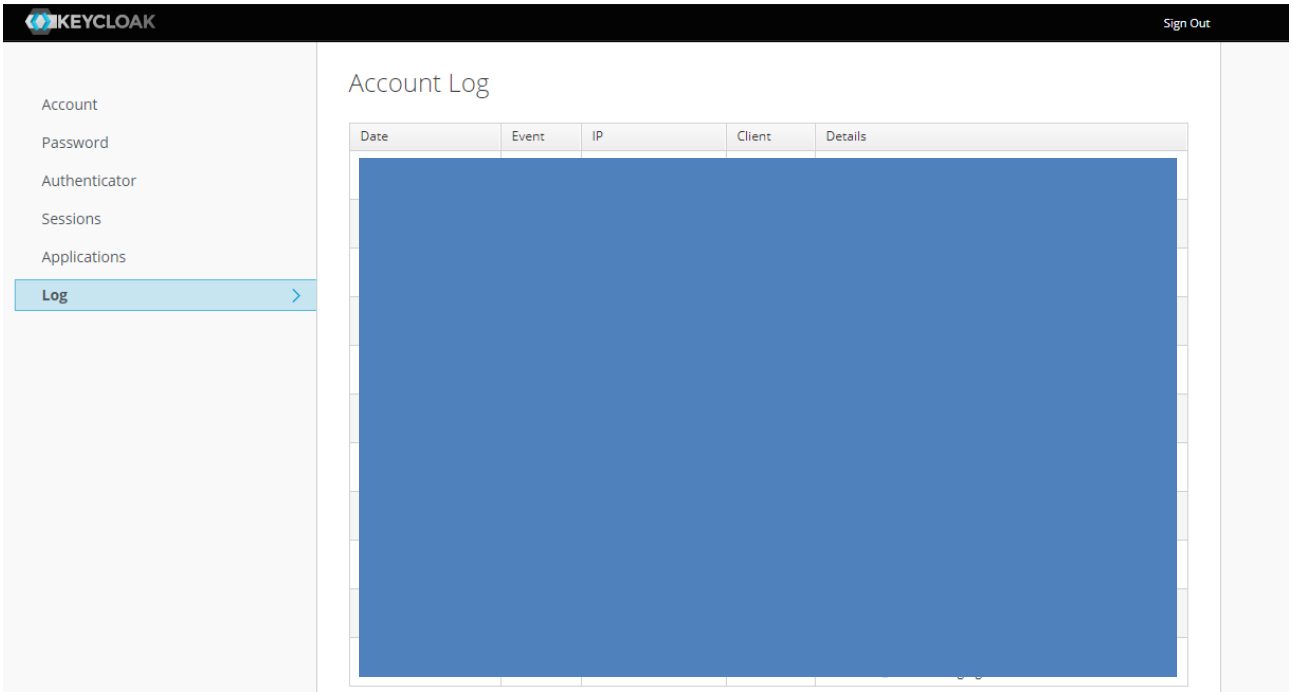


Figure 20. User account access log page.

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:

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Website: https://ai4medimaging.com/

E-mail: support@ai4medimaging.com