MYCARDIUM
PRECISION CARDIAC DIAGNOSTICS

Instructions for Use – 1CMR Pro

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1 PRODUCT DESCRIPTION

1CMR Pro is a software application that can be used as a stand-alone product or in a networked environment, designed to retrieve, locally store, view and analyze Cardiovascular Magnetic Resonance (CMR) images.

Within a clinical or research setting, the user can manually load DICOM files into the ***1CMR Pro*** software for viewing/reporting.

1.1 Intended Purpose

1CMR Pro Software as a Medical Device (SaMD) displays, analyses and transfers DICOM cardiovascular images acquired in Cardiovascular Magnetic Resonance (CMR) scanners, specifically structure, function and flow in the heart and major vessels using multi-slice, multi-phase, multi-parametric and velocity encoded CMR images. It is compatible with 1.5T and 3T CMR acquisitions.

1.2 Indications for use

1CMR Pro is software that displays, analyses and transfers DICOM cardiovascular images acquired in Cardiovascular Magnetic Resonance (CMR) scanners, specifically structure, function and flow in the heart and major vessels using multi-slice, multi-phase, multi-parametric and velocity encoded CMR images. It is compatible with 1.5T and 3T CMR acquisitions.

The intended patient population is both known healthy patients and patients in whom an underlying cardiac disease is suspected. The standard viewing tools are indicated for all patients.

1.3 Clinical Benefits

The primary clinical benefit imparted by ***1CMR Pro*** is to calculate the following measurements of cardiac function accurately and precisely (whilst allowing clinicians to manually adjust measurements):

1. Left and right ventricular ejection fraction, end systolic volumes and end diastolic volumes, stroke volume, cardiac output,
2. Left ventricular mass,
3. Left and right atrial areas,
4. Global longitudinal strain,
5. Mitral annular plane systolic excursion, and
6. Tricuspid annular plane systolic excursion.

1.4 Contraindications, Warnings and Precautions

- ***1CMR Pro*** is a viewing and diagnostic tool.
- Mobile viewing is not supported.
- ***1CMR Pro*** is not indicated for non-CMR images.
- ***1 CMR Pro's*** AI quantitative measurement functionality is not indicated for analyzing CMR images from pediatric populations (age <18), patients with congenital cardiac abnormalities.

- 1CMR Pro is not indicated for use for patients with pacemakers (even if MRI compatible).
- *1CMR Pro* must be used by experienced clinicians as described in section 2.2
- *1CMR Pro* users must read Instructions for Use. The device label states, "By using this software, you confirm with our End User License Agreement." (EULA)
- *1CMR Pro* can be used with non-diagnostic grade monitor or diagnostic-grade radiological reporting monitor, but users – within their clinical accreditation, as ever, should ensure that the number of images they display concurrently, the computer performance, screen size, viewing angles, lighting and their own self-awareness of their attention (fatigue, interruptions etc.) is appropriate for performing clinical reporting

1.5 Guidelines for use

- Following onboarding and authentication, which includes the user agreeing to the EULA covering intended use and misuse including data protection, users are directed to the Instructions for Use for the Application.
- Users can retrieve a version via a web browser.
- Users are then invited to import images in DICOM format.
- Following import of studies, users can view images by study, with multiple windows for different image slices.
- Basic image manipulating tools (all user-controlled) are provided as described in section 1.1, above. The original DICOM image will remain unaltered.

2 RECOMMENDATIONS

2.1 General

Intended patient population include adults of any ethnicity or sex, who have undergone a CMR scan, for any medical indication. No other image acquisitions are approved for viewing in *1CMR Pro*.

2.2 Users

The intended user profile is an "experienced clinician" (Radiologist or Cardiologist) or other licensed professional healthcare practitioner with experience of independent practice and clinical interpretation of CMR images. These clinicians or practitioners will have recognized training for this in their appropriate specialties. Although not essential, these clinicians will typically have formal accreditation with a recognized body (i.e. Level 2 CMR with Society for Cardiac MRI (SCMR), level 2 CMR with the European Association of Cardiovascular Imaging (EACVI), European Society of Cardiac Radiology (ESCR) diploma or other equivalent such experience). Clearly also, trainees aspiring to these accreditations can use the software.

3 COMPATIBILITY

Requirement	Minimum Requirements PC	Minimum Requirements Mac
Operating System	Windows 11 64-bit	macOS 14
Network (LAN)	100BaseT	
Network (WAN) for client	10Mbps Downstream; 2.5Mbps Upstream (this is just for downloading the software – all data is kept locally)	
Display	1920x1080 Resolution at 24-bit color	
Processor	Intel Core i5	Apple Silicon M1
Video Card	nVidia or AMD Dedicated GPU	Integrated GPU
Memory	8 GB System 1GB Video Memory	8 GB Unified Memory
Browsers Supported – minimum version	Chrome 120.0.6099.224 Firefox 121.0.1 Edge 120.0.2210.133	Chrome 120.0.6099.224 Firefox 121.2 Safari 17.3

Mobile use (i.e. on phones and tablets) is not supported.

The optimal setup is the best GPU available, for example:

- PC: CPU 8 cores (i7/AMD), 16-32Gb RAM, GPU RTX 4050 or higher
- Mac: M3/M3pro/M3max with 10 or more GPU cores

NOTE: To provide security updates, defect corrections and improved functionality, *1CMR Pro* will be automatically updated occasionally. If the user does not wish to receive automatic updates, then they should email the support team.

4 GETTING STARTED

4.1 Setting up an account

You will need a User Account to start using ***1CMR Pro***. To get a User Account, you should request one from support@mycardium.com. The Company will review your request, and, if granted, will send an email containing a unique URL, a username and a password.

1. Enter your unique URL into a web browser (Chrome, Firefox or Edge on the PC or Chrome, Firefox or Safari on the Mac.
2. You will be presented with a login window. Enter your username and password and click on 'Sign In'.
3. The software will display the following screen:

5 1CMR Pro Image Viewing

5.1 Loading Images

Complete studies can be uploaded by dragging and dropping a folder containing the image DICOM files into the main screen displaying the icon above. Unsupported files will not be loaded correctly and will not display readable images. Supported files showing images which are not cardiac images may be uploaded and displayed. Users of 1CMR Pro should visually check to ensure that they are viewing a Cardiac MR image.

Shortcut keys: Any tab name with an underlined letter can be activated by pressing that letter e.g. View, Scout, Extra etc.

5.2 *All* tab – Viewing an overview of the study

- Select the *All* tab on the *Tab Bar* on the bottom left-hand side of the screen to review a thumbnail summary of the various sequences acquired in this scan.

- *1CMR Pro* will perform smart series classification (this means that heuristic labels are automatically applied to series that the software detects as white blood stack, black blood stack, 4-chamber, 3-chamber and 2-chamber long and short axis cines, Aortic valve short axis and LGE). Heuristic labels can be reassigned manually by dragging the label using your mouse/keypad to a different image.
- Clicking on a thumbnail image will cause it to appear as a preview in the top right of the window. Below the preview, metadata for the selected image is shown. See the Metadata section of the IFU 5.14.
- Within the *All* tab, groups of images can be linked together using the *Group* icon on the bottom right-hand side of the screen.
- By selecting a color within the Group tab and then clicking on individual images/series within the *All* tab, sets of images/cines can be grouped together. You can also select whether to play  , adjust contrast  , zoom  and select phases  together or deselect to enable this to be done separately per image/cine.

- The pre-selected series can be viewed together within the *View* tab. The cascade matrix size can be adjusted at the bottom right-hand side of the screen to view the desired number of series up to a total of 9x3 images. The colors appear on the left-hand series selector. Select a different color group with mouse/trackpad to move between the different colored groups.

Tip: If you want to open two tabs simultaneously side by side, when in multiview, highlight a window and press Shift-shortcut (eg Shift-Quantify).

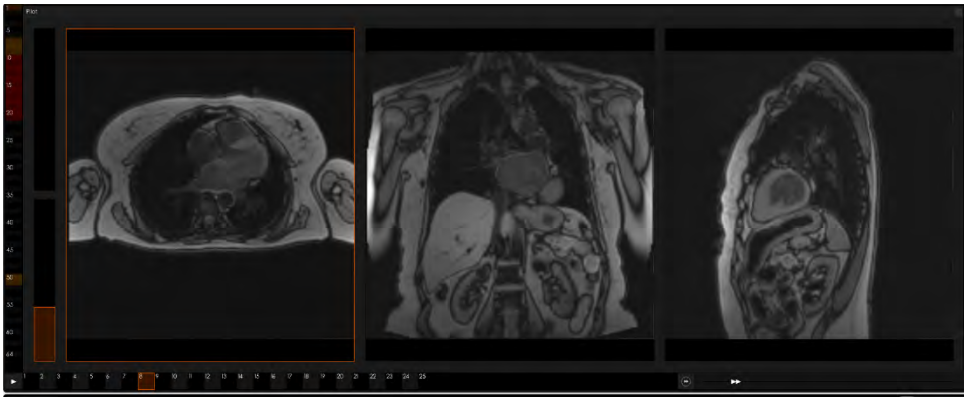
5.3 *View* tab – General Image Viewing

Select the *View* tab to open a series either by selecting it or by pressing the tab key to move along the bottom panel of series labels. Slices are shown along the Y axis and phases along the X axis of the window. You may drag and drop series from the panel on the right into this *View* window.

Shortcut: the view tab can also be selected by pressing “V” (single image by pressing “1”).

5.4 *Scout* tab – Viewing Pilot Images

The Scout tab will display pilot images (without zoom, all pan individually but with zoom and contrast controls linked between images). Use the arrow keys to navigate.



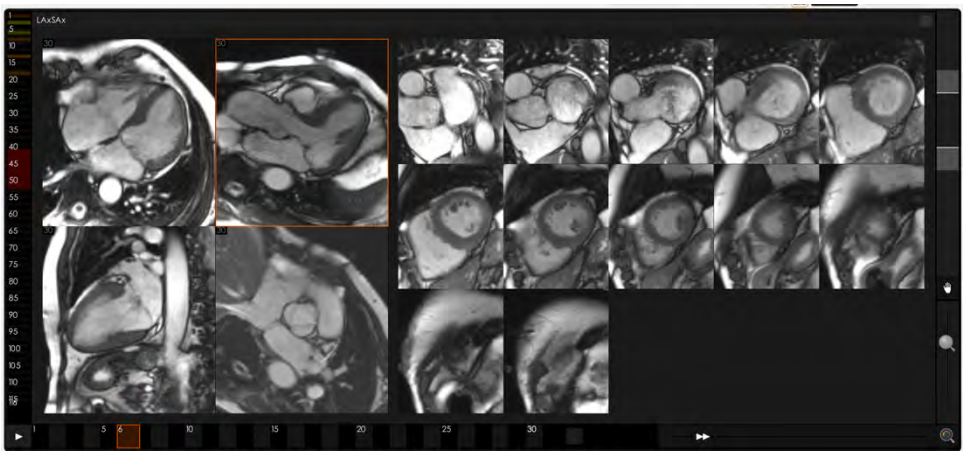
5.5 *Extra* tab – Viewing Extra Cardiac Images

The *Extra* tab shows the white blood and black blood anatomical stacks. These series have labels automatically assigned within the *All* tab, but the heuristic labels can be moved if necessary on the All tab.

Extra tab grouping: The images can pan and zoom in sync but changing contrast is done independently.

5.6 *LAxSAx* tab - Viewing Long and Short Axis Images

The *LAxSAx tab displays* 4-, 3- and 2-chamber long axis and short axis Aortic valve cines on the left-hand side of the screen and the short axis stack on the right-hand side of the screen. These series are automatically identified, and heuristic labels assigned in the *All* tab, which can be manually reassigned if necessary. By default, the short axis stack cines play, pan and change contrast together (all slices change together, rather than individually). The long axis cines play, alter contrast and zoom in sync but pan independently. The *LAxSAx tab* simply displays the cine images, with quantitative metrics available in the *Quantify tab* (see below).

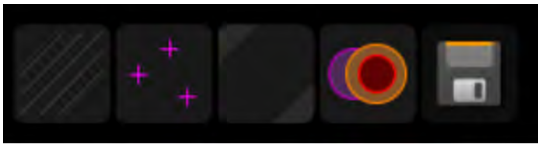


5.7 *Quantify* tab – Volumetric analysis

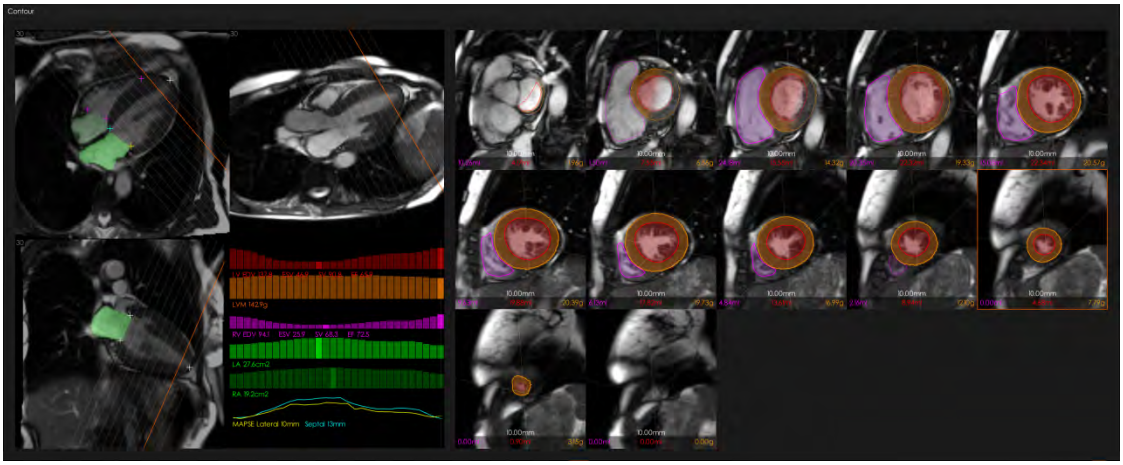
The Quantify tab displays the images identically to the *LAxSAx* tab, but with AI generated contours automatically applied. There are three different machine learning based AI algorithms

delivered within this analysis. Firstly, long-axis function (TAPSE, MAPSE; GLS). Secondly, atrial area (on 4-chamber and 2-chamber). Thirdly, short axis stack contours for LV and RV. The LV contours of the endocardium and epicardium enable quantification of LV mass, end-diastolic and end-systolic volumes for calculation of stroke volume and ejection fraction; the RV contours are of the endocardium for volumetric assessment only. These algorithms use those published by Dr Rhodri Davies (JCMR 2022). Analysis histograms and graphs are presented in the pane where the aortic short axis view is on the LAxSAx tab. Epicardial and endocardial contours are editable, as are the basal LV calipers annotating the mitral valve plane. Select whether to include or exclude papillary muscles in the volumetric analysis. The AI analysis starts automatically after loading the study and relies upon the accurate detection of the relevant sequences using the heuristic labels (which can be manually altered if necessary). This is demonstrated by the *Quantify* tab's loading bar filling in the style of a matrix and is complete when the tab's green dots are full.

Tip: click on the green matrix to pause or restart the AI (useful for slower computers). The AI may pause if the browser detects that another window is maximized on top of the 1CMR.



Other tags toggle on off the short-axis intersection lines, the valve plane tracking points, the base/apex censoring, and the shading. Results may be saved (to your download folder) as a *.csv, but also a diastole and systole image.



5.8 *Gad* tab – Viewing Gadolinium Images

Select the Gad tab to view the sorted LGE images that will automatically populate the respective windows. The column to the left displays the LAX LGE images (4C, 2C, 3C) while the images to the right are the LGE SAX stack. This tab may not detect all LGE images, in which case the images can be grouped in the *All* tab as described above.

Note: this only demonstrates a limited number of images matched by view to the cines. See more using all, 1up single view or multiview and cascade.

5.9 *Perf* tab – Viewing Perfusion Images

Select the *Perfusion* tab to view and play the perfusion images. This will show selected perfusion stacks at stress and rest, with rest images on top and stress images on the bottom. The perfusion images are displayed on the left and any maps on the right, if they have been generated on the scanner.

5.10 *Flow* tab – Viewing Flow Images

Select the *Flow* tab which will display magnitude and phase images. The application of contours is in development, so the *Flow* assessment is currently visual and for research use only.

5.11 *Map* tab – Viewing Map Images

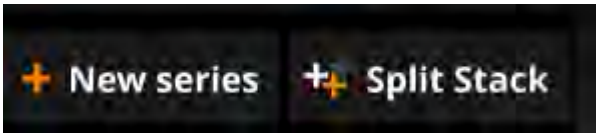
The *Map* tab displays all color sequences eg T1 and T2 mapping sequences, but also any others (R2*, perfusion maps etc). These are automatically identified.

Tip: if you want to quantify an area, after selecting the correct image in Map, go to View (V, 1 or click on the view tab) to display the area/measurement quantification tools.

5.12 3D tab (stack tab)

The 3D tab displays and unfolds all image stacks (perfusion, long axis, short axis etc). This is helpful for seeing stacks not included in other tabs – for example, an RV stack or a congenital heart disease sagittal/coronal/transverse cine stack. It can also be used for occasional stacks where the images are not well displayed elsewhere.

Tip: some DICOM stacks may not sort properly To create new series (displayed in all), the "+new series" and "+Split stack" buttons will resolve this. Then heuristic labels can be moved in the All tab.



5.13 Unseen tab

The *Unseen* tab works similarly to the *All* tab, showing all the study's images, but all sequences that have been reviewed are highlighted in green. This is to highlight any series that have not yet been visualized.

5.14 Control banners

5.14.1 Tab Bar

The *Tab Bar* is found on the bottom left side of the screen. It shows the different tabs that can be selected, all individually described above.

Tip: you can move between them with the keyboard “Tab” key (to go left to right) or “Shift-Tab” (to go right to left)

5.14.2 Frame Selector

The *Frame Selector* runs along the bottom of the displayed images, above the *Tab Bar.* This shows the number of frames in a cine and can be individually selected by clicking on the appropriate numbered frame to highlight this on the main screen - or use the left/right keys

5.14.3 Series Selector

The *Series Selector* runs along the left-hand side of the displayed images. This runs from number one to the total number of individual images/cines (series) acquired. By selecting a number on the *Series Selector* within the *All* tab, the individual image/cine is then displayed within the *View* tab. The up/down arrow keys can also be used.

5.14.4 Header

The *Header* displays the 1CMR Pro logo and the patient's demographic details as inputted onto the scanner. This includes the patient's name, sex, age, unique identifier, date of birth, scan date and the total number of series.

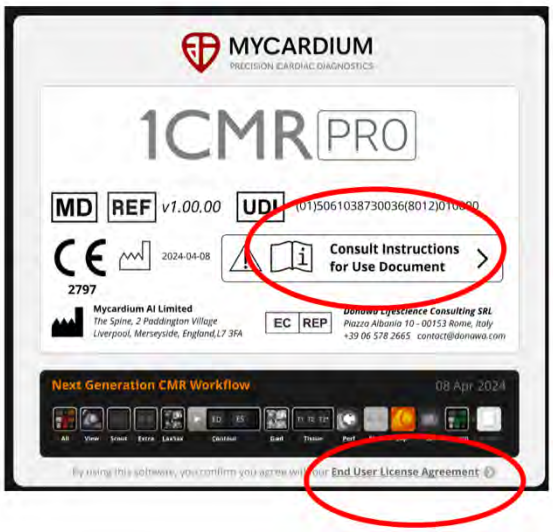
5.14.5 Operations Banner

The *Operations Banner* is displayed on the top right-hand side of the screen.

Hover your mouse over any button and a tooltip displays the function
ID: temporarily anonymise your screen (turn on/off the header with patient details)
Show/hide text overlays
Show/hide contours
Show/hide images
Show/hide original pixels (interpolation on/off)
Screen grab (capture movie if movie playing)

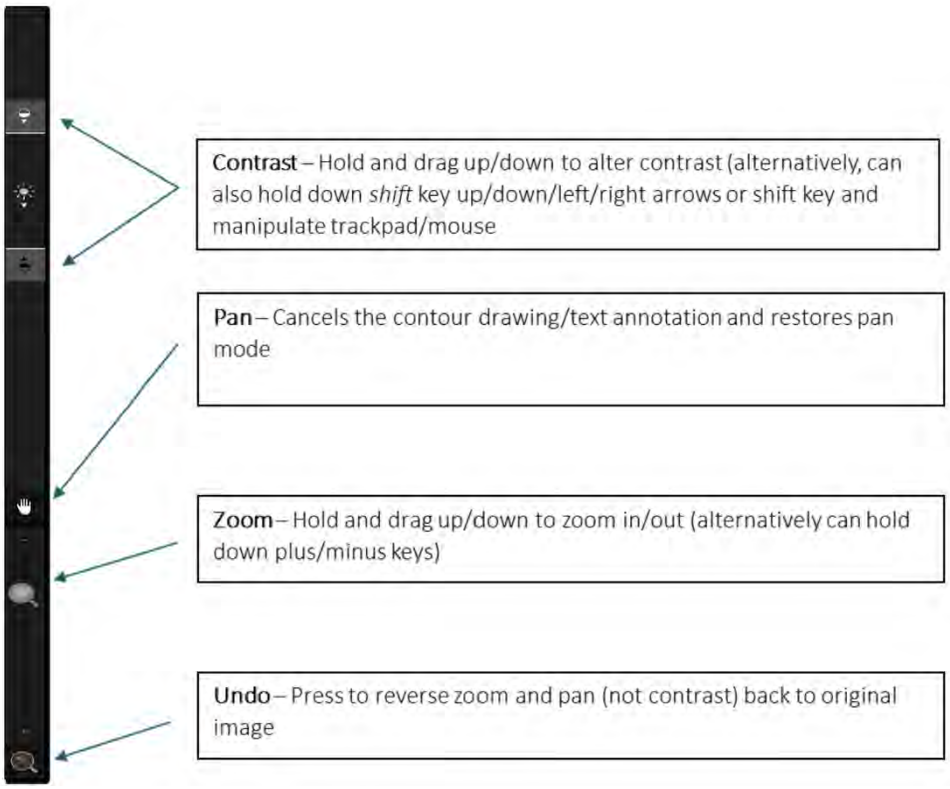
Save study as zip file
Save anonymised study as zip file
Software info (UDI/CE/FDA mark/UDI etc)
New window
Close study

Note: The instructions for use can also be accessed on the home screen central label. The end user license agreement is also accessed this way



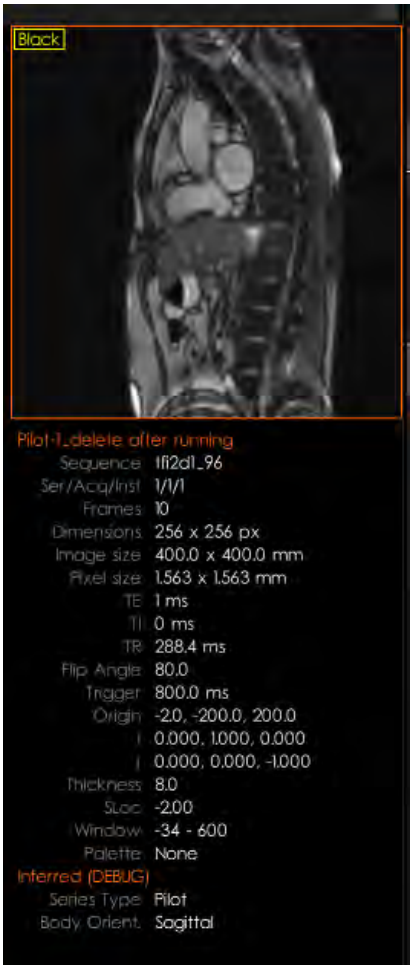
5.14.6 Control Banner

The *Control Banner* is displayed on the right-hand side of the screen. The functions are described below.



5.15 *Meta*data

Within the *All and Unseen* tabs, to the right of the displayed images, data acquisition metadata from the DICOM header is displayed beneath the highlighted series. Under the title 'inferred' is the type of image the software thinks the series is based on the applied heuristic labels. If the user observes values in the metadata that seem unlikely to be accurate, it is possible that the DICOM study has become corrupted. In this situation, the user should not analyse the DICOM study with this software.



6 Help

- Hit the '*i*' button top right to display these instructions for use.

7 RENEWAL AND DISPOSAL

7.1 Expired License

To be able to continue using the ***1CMR Pro*** application, you should re-activate the License following the instructions in section 4 of this IFU.

7.2 Terminate your License

For information about early termination of your 1CMR Pro Licence, please consult our terms of Use. For additional support please contact support@mycardium.com

7.3 Delete 1CMR Pro account

To delete your ***1CMR Pro*** account, please request our team with reason for wishing to cancel 1CMR Pro account at support@mycardium.com

8 PERFORMANCE (ACCURACY and PRECISION)

1CMR Pro uses AI developed at University College London. The basic models have all been published, and have, in some cases won awards. The key publication is Davies et al, 2022[1] which won the SCMR 2022 best paper of the year.

The AI has been designed to be generalizable - any scanner, any disease, anywhere. It is also explainable – that is it displays contours to the user. These can be edited. The AI uses computer vision and specifically CNNs (convolutional neural networks).

The AI in 1CMR pro is fixed and does not "learn" from presented data during use.

It should be noted that these algorithms are not independent but have a "human in the loop" and all contours are visible and editable.

Training data: The training dataset was composed of a total of approximately 700,000 cine images, 60,000 segmentations from 1923 patients [9 diseases and health]. These patients had high rates of co-morbidity (hypertension, diabetes) and are representative of clinical practice. Images were taken from three CMR vendors including 10 different models:

Siemens: *Aera, Prisma, Avanto, Trio, Skyra, Biograph mMR, Verio*
Philips: *Achieva, Intera*
GE: *Signa Explorer*

The ratio of scanner types reflected clinical practice (and was weighted therefor to Siemens). Some patients had devices. No validation was done on 0.5T acquired data.

The overall demographics of the training dataset are published (supplementary data to Davies et al) and reproduced below:

Age (Median, IQR), years	57 [45-66]
Male (%)	58%
BMI median, [IQR] (kg/m2)	28.7 [24.9-34.0]
Heart failure	31%

[1] Rhodri H. Davies, JoÃ£o B. Augusto, Anish Bhuva, Hui Xue, Thomas A. Treibel, Yang Ye, Rebecca K. Hughes, Wenjia Bai, Clement Lau, Hunain Shiwani, Marianna Fontana, Rebecca Kozor, Anna Herrey, Luis R. Lopes, Viviana Maestrini, Stefania Rosmini, Steffen E. Petersen, Peter Kellman, Daniel Rueckert, John P. Greenwood, Gabriella Captur, Charlotte Manisty, Erik Schelbert, James C. Moon,
Precision measurement of cardiac structure and function in cardiovascular magnetic resonance using machine learning,
Journal of Cardiovascular Magnetic Resonance,
Volume 24, Issue 1, 2022, 16, ISSN 1097-6647,
https://doi.org/10.1186/s12968-022-00846-4

Hypertension	51%
Diabetes	22%
LVEDV median, [IQR] (ml)	166 [132-211]
LVESV median, [IQR] (ml)	69 [47-113]
LVEF median, [IQR] (%)	57 [44-66]
LVM median, [IQR] (g)	129 [99-162]
Infarct pattern on LGE	21%
Non-infarct pattern on LGE	22%

The diseases – reflecting clinical subgroups and also including comorbidities are listed below.

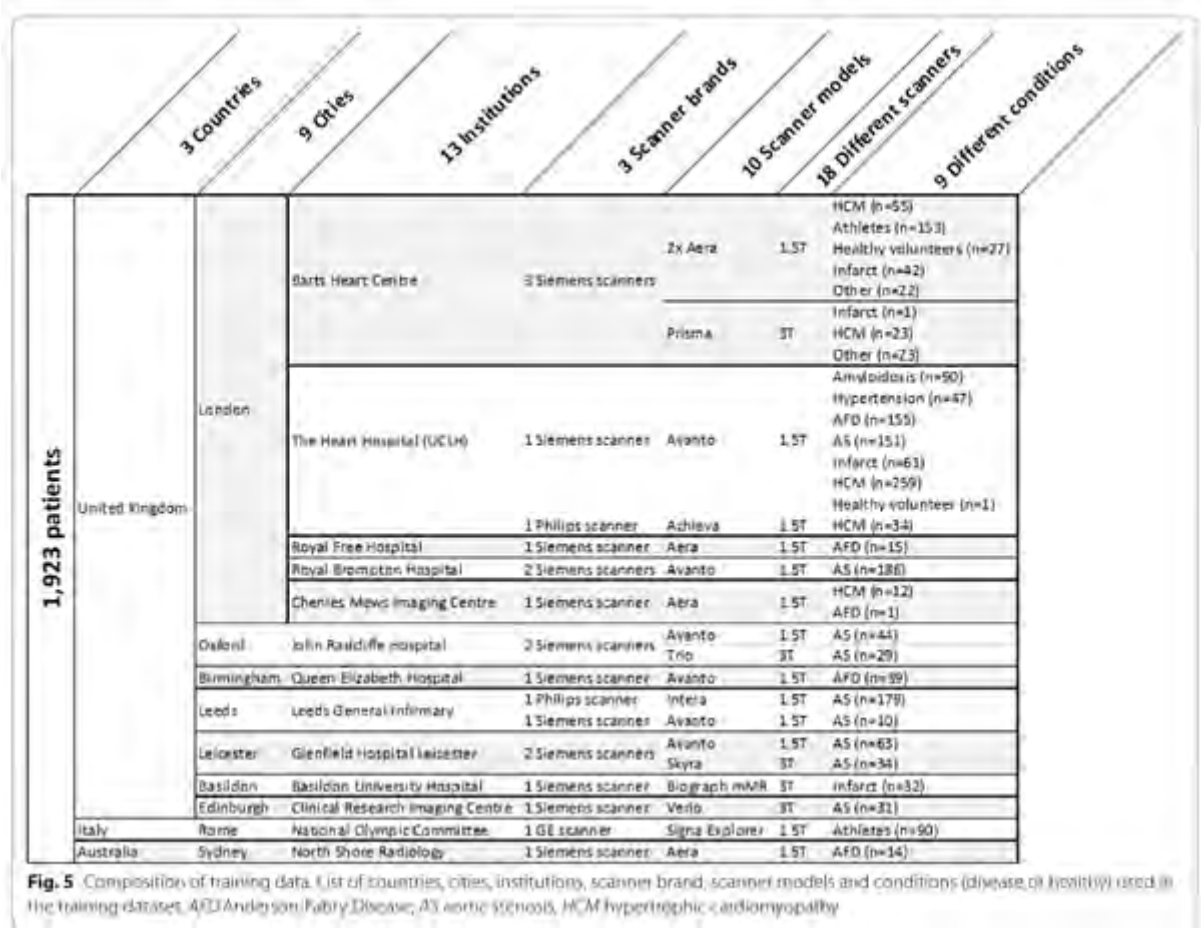


Fig. 5 Composition of training data. List of countries, cities, institutions, scanner brand, scanner models and conditions (disease or healthy) used in the training dataset. AFD Anderson Fabry Disease; AS aortic stenosis, HCM hypertrophic cardiomyopathy

Regarding ethnicity, whist ethnicity was specifically curated and enriched for the US population in the validation dataset, individual ethnicities were not recorded in the training dataset. These patients were 50% recruited in East London, England, where Barts Heart hospital is. East London has perhaps the highest ethnic diversity in Europe. Additional recruitment was from other UK towns of Leeds, Leicester Glenfield, Basildon, with some recruitment in Sydney (Australia) Rome (Italy) and Edinburgh (Scotland, UK).

Combined this provides wide ethnic and geographical diversity. All these patients are from published peer reviewed studies (more than 50) from one of the world's leading CMR research groups. Examples of published studies are below:

Health: The Effect of Blood Composition on T1 Mapping. Rosmini S, Bulluck H, Abdel-Gadir A, Treibel TA, Culotta V, Thompson R, Piechnik SK, Kellman P, Manisty C, Moon JC. JACC Cardiovasc Imaging. 2019 Sep;12(9):1888-1890. doi: 10.1016/j.jcmg.2019.03.018. Epub 2019 May 15.

Athletes: Prevalence of Subclinical Coronary Artery Disease in Masters Endurance Athletes With a Low Atherosclerotic Risk Profile. Merghani A, Maestrini V, Rosmini S, Cox AT, Dhutia H, Bastiaenan R, David S, Yeo TJ, Narain R, Malhotra A, Papadakis M, Wilson MG, Tome M, AlFakih K, Moon JC, Sharma S. Circulation. 2017 Jul 11;136(2)

Aortic Stenosis: Myocardial Scar and Mortality in Severe Aortic Stenosis. Musa TA, Treibel TA, Vassiliou VS, Captur G, Singh A, Chin C, Dobson LE, Pica S, Loudon M, Malley T, Rigolli M, Foley JRJ, Bijsterveld P, Law GR, Dweck MR, Myerson SG, McCann GP, Prasad SK, Moon JC, Greenwood JP. Circulation. 2018 Oct 30;138(18):1935-1947

Hypertrophic Cardiomyopathy: Insight into hypertrophied hearts: a cardiovascular magnetic resonance study of papillary muscle mass and T1 mapping. Kozor R, Nordin S, Treibel TA, Rosmini S, Castelletti S, Fontana M, Captur G, Baig S, Steeds RP, Hughes D, Manisty C, Grieve SM, Figtree GA, Moon JC. Eur Heart J Cardiovasc Imaging. 2017 Sep

Fabry: Proposed Stages of Myocardial Phenotype Development in Fabry Disease. Nordin S, Kozor R, Medina-Menacho K, Abdel-Gadir A, Baig S, Sado DM, Lobascio I, Murphy E, Lachmann RH, Mehta A, Edwards NC, Ramaswami U, Steeds RP, Hughes D, Moon JC. JACC Cardiovasc Imaging. 2019 Aug;12(8 Pt 2):1673-1683.

Amyloidosis: Native T1 and Extracellular Volume in Transthyretin Amyloidosis. Martinez-Naharro A, Kotecha T, Norrington K, Boldrini M, Rezk T, Quarta C, Treibel TA, Whelan CJ, Knight DS, Kellman P, Ruberg FL, Gillmore JD, Moon JC, Hawkins PN, Fontana M. JACC Cardiovasc Imaging. 2019 May;12(5):810-819

Hypertension: Extracellular volume quantification in isolated hypertension - changes at the detectable limits? Tr eibel TA, Zemrak F, Sado DM, Banypersad SM, White SK, Maestrini V, Barison A, Patel V, Herrey AS, Davies C, Caulfield MJ, Petersen SE, Moon JC.J Cardiovasc Magn Reson. 2015 Aug 12;17(1):74

Please note: not all patients were included to not skew the training data too far towards specific pathologies (e.g. not all healthy volunteers/athletes).

Validation (algorithms): The validation of the underlying algorithms has been peer reviewed and published. Whilst *accuracy* was confirmed, *precision* (test:retest repeatability in health and disease) was also assessed and proven to exceed human performance with a 40% increase in precision. This means that the algorithms have a smaller "detectable difference" and, if used in research, increase the power of research studies.

However, the algorithms have been platformed in 1CMR pro and therefore formal testing in this platform has been undertaken. Full results have been reviewed and lodged with the relevant international bodies as part of regulatory approval.

Validation (1CMR pro) hold out data: This platform validation used "hold out" data – that is data that had not been used for training. This was:
- 65 scans (86% US, 39% female, 47% non-white, 70% disease (14% HCM, 19% DCM, 23% MI, 14% LVH)
- the Sunnybrook dataset
- 110 subjects (health and disease) scanned twice.

Validation (1CMR pro). This comprised 3 types of assessment: DICE scores, Accuracy and Precision. This was done by 3 independent truthers, all with >5 years experience.

Results: DICE scores: Dice scores were used for the LV short axis contours. The AI passed and was superior to truthers (In brief, AI vs. Truther overall Dice scores averaged 0.90 compared to Truther vs. Truther Dice scores average 0.89). Both humans and AI were more variable at the base of the heart.

Results: Accuracy: Accuracy was assessed for 14 variables: volumes (LV and RV: EDV, ESV, SV; LA, RA), LV mass, function (LVEF, RVEF, TAPSE, MAPSE, GLS). The AI passed all assessments and the majority of analyses showed that the AI exceeded that of the truthers. There was some variability in truthing: some truthers drew contours "larger" than others, but ratios (eg EF) were more consistent. There were variations in the performance: the LV was more accurate than the RV, analysis in health more accurate than in disease. There were no differences by age or ethnicity. Performance was higher for Siemens vs non Siemens scanners – but the sample size was smaller for non-Siemens scanners.

Results: Precision: Precision was performed for LV variables. The AI passed was superior to humans for all measurements and prior FDA approved software. Example results are:

AI vs Clinician coefficient of variation (CoV) for LVEF: 4.3±0.3% vs 7.0±0.6%, p<0.001
AI vs Clinician CoV for LVmass: 3.8±0.3% vs 4.6±0.3%, p<0.001
AI vs Clinician CoV for LVEDV: 4.9±0.4% vs 6.2±0.5% p=0<0.001
AI vs Clinician CoV for LVESV: (5.4 (4.3-6.4%) vs 11.4 (6.5-15.6%, p=0.008)

In addition, ***1CMR Pro*** was assessed against other approved software (Circle CVI v 5.13). The testing here used no human editing. ***1CMR Pro*** exceeded the performance in every measured variable. (LVEF 4.2% (95% CI: 3.5-5.0%) vs 10.4% (6.8-14.0%), p<0.001); mass (4.2% (95% CI: 3.5-5.0%) vs 10.4% (6.8-14.0%), p<0.001); LVEDV (5.4 (4.3-6.4%) vs 11.4 (6.5-15.6%, p=0.008). Note: in the real world with "human in the loop", we expect performance with

human editing would improve for both 1CMR Pro and Circle – but with Circle improving more (as there are more obviously incorrect contours in Circle).

9 HYGIENIC MAINTENANCE

There are no cleaning measures required for ***1CMR Pro***, as the device is SaMD (Software as a Medical Device) and will not directly be applied or interact with any part of the human body or tissue type.

10 CYBERSECURITY

1CMR Pro application does not transfer data from your computer. MyCardium AI uses industry best practices compliant with and certified to international information security standard ISO 27001.

The software is downloaded to your computer in the form of a regular webpage (that uses JavaScript, WebGL, WebGPU, Web Assembly, HTML, and CSS) using the HTTPS protocol. No other communications protocol is used by the software. The software does not enable or disable any communications protocols. An SSH certificate is used to help provide secure communication of the software. The software does not require installation. No data is transmitted from your computer. No communications protocol or interface is used to transmit data from your computer. All output files from the software are saved to your Downloads folder. The following types of files are output from the software:

- Dicom Files (.dcm file) – The export study and anonymise study features output DICOM files.
- Spreadsheet Files (.csv, .xlsx files) – The save spreadsheet and generate report features output spreadsheet files.
  Image Files (.png file) – The export image button generates PNG files.
- Movie Files (.mp4 file) – The export movie button generates mp4 files.

At the time of writing, there are no known cybersecurity vulnerabilities that affect the safe use of the software (including the HTTPS transmission of the software to your computer and the exported file types listed above). A post market surveillance process is used by the Company to proactively identify and address cybersecurity vulnerabilities.

1CMR Pro uses internet connectivity to download the software from the Mycardium Server (hosted by Amazon Web Services (AWS)). If the internet is not available on the user's computer, or if the Mycardium Server stops working, then the software will not be accessible. In these scenarios, the user will typically be presented with a '404 Not found' message when they attempt to visit their 1CMR URL. First of all, the user should contact their technical team to ensure that their internet connection is working correctly. If the internet is working, but the URL is not working correctly, they should send an email to support@mycardium.com. The Company will endeavour to reinstate access accordingly.

Whilst ***1CMR Pro*** does not specifically require additional security software to function securely, it is recommended that the user's computer is configured by their institution's IT

team in a secure manner with a firewall and anti-virus software.

For you as a ***1CMR Pro*** user, it is very important to keep in mind the following recommendations:

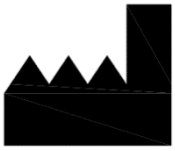
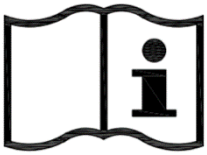
- Never share your ***1CMR Pro*** credentials;
- Use a secured Internet connection;
- Only use compatible devices;
- Do not use emulators.
- In the event of any cybersecurity incidents or concerns involving ***1CMR Pro*** please contact support@mycardium.com, marking the email as 'Urgent'
- In the event of any data breach resulting from the use of ***1CMR Pro*** contact support@mycardium.com, marking the email 'Urgent FAO DPO'

11 PATIENT SAFETY

It is unlikely that any authorized use of ***1CMR Pro*** will result in patient safety issue, however in the event that an issue does arise, suspend all use of ***1CMR Pro*** and report the matter immediately to support@mycardium.com, marking the email as 'Urgent'.

12 APPLICABLE SYMBOLS found on the software label

MYCARDIUM PRECISION CARDIAC DIAGNOSTICS	1CMR Pro
MD	This software is a medical device
REF	Ver 1.01.01 *(example version number – the version is shown on the label)*
UDI	Universal Device Identifier (UDI)– for example: - (01)5061038730029(8012)010101 Quote the UDI actually seen in the software user interface when submitting feedback or complaints.
	Release date: 2023-01-19 *(example date – the actual date is shown on the label)*

	Mycardium AI Limited The Spine Building, 2 Paddington Village, Liverpool, L7 3FA, United Kingdom
	Name, address and contact email for EU Authorized Representative - *this symbol is shown in the software only when it is released for use in the EU.*
 	Consult instructions for Use in the app. Users have access to IFU, accessible on our webpage: www.mycardium.com
	Prescription-only – *this symbol is shown in the software only when it is released for use in the USA.*
 2797	CE-marked medical device – *this symbol is shown in the software when it is released for use in the EU and UK.*

13 CONTACT DETAILS

For more information or questions, please contact us at support@mycardiumai.com

Serious incidents that have occurred in relation to the device shall be reported to:

(1) the legal manufacturer via support@mycardium.com

(2) the local competent authority (the Food and Drug Administration in the USA)

14 MANUFACTURER

Mycardium AI Limited
The Spine Building, 2 Paddington Village, Liverpool, L7 3FA, United Kingdom