MYCARDIUM
PRECISION CARDIAC DIAGNOSTICS

1CMR Pro

Table of Contents

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 has the following functions:

- Presentation of CMR image slices by cardiac chambers for concurrent viewing in separate windows
- The ability to play cine images
    - One at a time or as a group in sync across different viewing windows
    - User-selected playback speed.
- Simple linear image interpolation for viewing
- User controlled zoom, pan, and image-level contrast change
- The ability for users to put images into or out of an array, including cascading images
- *1CMR Pro* has inbuilt AI-based algorithms for contouring structures including the LV endocardium and epicardium, RV endocardium, long axis function and both atria. This enables quantification of LV mass, end-diastolic and end-systolic volumes for calculation of stroke volume and ejection fraction, long axis function and RV volumetric assessment

1.3 Contraindications and Warnings

- *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 <16), patients with congenital cardiac abnormalities.
- *1CMR Pro* must be used by experienced clinicians as described in section 2.2
- *1CMR Pro* users must read Instructions for Use and click to accept the End User License Agreement (EULA) prior to use.
- *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

2 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 all, 2022 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 therefore to Siemens). Some patients had devices. No validation was done on 0.5T acquired data.

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 1CMRpro and Circle – but with Circle improving more (as there are more obviously incorrect contours in Circle).

3 CYBERSECURITY

1CMR Pro application uses industry-standard encryption protocols to secure all data in transfer and at rest. MyCardium AI uses industry best practices compliant with and certified to international information security standard ISO 27001.

4 MANUFACTURER

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

Website: www.mycardiumai.com

Tel: (44)151 230 2116

Email: enquiries@mycardium.com