4DMedical™

PHA

Instructions for Use - US

Software Version 4.0.1 and onwards

PHA Instructions for Use

US

Contents

1 Introduction

1.1 Scope of Manual

This user manual was written for the 4DMedical PHA Software.

Guidance for using the 4DMedical Protected Platform (4DM-PP) is not included in this document. The 4DM-PP includes a cloud platform which is a subscription-based, scalable software-as-a-service product which allows customers to run computationally-intensive image algorithms in the cloud, on infrastructure maintained by 4DMedical. The 4DM-PP is also available as an on-premise hosted product, targeted at those organizations which desire to keep their image data in-house. This enterprise version of 4DM-PP provides a system by which customers can still benefit from image processing job automation, while integrating with native DICOM tools and workflows. The 4DM-PP with cloud and enterprise options is a separate product developed by 4DMedical.

1.2 Product Overview

4DMedical's PHA Software identifies the maximal diameters of the right and left ventricles, the main pulnonary artery, and aorta. The software also calculates the ratio of right ventricular diameter to left ventricular diameter (RV/LV) and the ratio of main pulmonary artery to aorta (PA/Ao).

The 4DMedical PHA Software utilizes non-gated, contrast-enhanced CT pulmonary angiogram images in DICOM format as input to the software.

The DICOM outputs provided by the PHA Software are a RGB image series (Secondary Capture Image Storage SOP Class) and a summary report (Encapsulated PDF Storage SOP Class and/or Secondary Capture Image Storage SOP Class).

2 Symbols

The meaning of the symbols shown on the labeling and/or instructions for use are as follows:


Consult Electronic Instructions for Use


Manufacturer


Date of Manufacture (YYYY-MM-DD)

Medical Device

Unique Device Identifier

Batch Code (Device Version)


Caution: Federal law restricts this Device to sale by or on the order of a physician.

3 Indications for Use and Requirements

3.1 Indications for Use

The PHA Software device is designed to measure the maximal diameters of the right and left ventricles of the heart, the main pulmonary artery, and the ascending aorta from a volumetric CTPA acquisition and report the RV/LV and PA/Ao ratios. PHA analyzes cases using an artificial intelligence algorithm to identify the location and measurements of the anatomy. The PHA software provides the user with annotated images showing measurements. Its results are not intended to be used on a stand-alone basis for clinical decision-making or otherwise preclude clinical assessment of CTPA cases.

3.2 Intended Use and Users

The intended use of this software application provides a calculation of the ratio of right ventricular diameter to left ventricular diameter and main pulmonary artery diameter to aorta diameter from contrast enhanced CT images of the chest acquired using a standard CT pulmonary angiogram acquisition.

This application is intended for use by Thoracic Radiologists, General Radiologists, Pulmonologists, Cardiologists, imaging technologists under the supervision of a physician, or researchers to aid in their assessment of right ventricular enlargement.

3.3 Cautions, Warnings, and Contraindications

There are no known contraindications. Known limitations and precautions related to image quality, anatomy, and artefacts are described in Sections 6 and 7.

3.4 Clinical Performance Validation

The PHA Software Clinical Performance Validation has shown that the tool is accurate in measuring the ratio of right ventricular diameter to left ventricular diameter and main pulmonary artery diameter to aorta diameter when compared with expert radiologists.

PHA Software was found to have a bias of 0.01 when RV/LV ratios were compared to ratios calculated by expert radiologists and the zero-line of equality was within the 95% confidence interval of the mean difference. Additionally, 97% of the RV/LV ratios were within the limits of agreement between PHA software and three expert radiologists.

The results of the PA, Ao and PA/Ao validation showed excellent agreement with the expert radiologists (ICC > 0.90). Furthermore, the biases of the PA, Ao and PA/Ao were not greater than the average biases of individual expert radiologists as shown in the table below.

	Pulmonary Artery	Aorta	PA/Ao
Average Annotator	1.60 mm	0.37 mm	0.035
Algorithm	1.24 mm	0.03 mm	0.035

3.5 Clinical Benefit

The PHA Software provides measurements of clinically relevant cardiovascular structures and the raio of those measurements. The RV/LV and PA/Ao ratios are well-accepted biomarker of acute pulmonary embolism severity [1] and pulmonary artery pressure [2].

3.6 Scan Protocol Requirements

The ability to segment a scan is dependent on the resolution; therefore, it is important to analyze the scan resolution. The resolution can be determined by assessing the acquisition protocols from the DICOM data as well as visually assessing the images themselves. Additionally, adequate contrast between the ventricular cavity and the surrounding myocardium is a prerequisite for optimal performance. For RV/LV measurements, the LV attenuation should be > 100 HU. The scan should also be visually assessed to ensure that there are no artifacts or missing information.

3.6.1 Acquisition Parameters

The PHA Software will not generate outputs for scans with acquisition parameters that do not meet the requirements as outlined in the table below. In addition, 4DMedical PHA Software will not generate outputs unless DICOM Patient Image Orientation (DICOM tag 0020,0037) can be rounded to [+1,0,0,0,+1,0].

DICOM Tag	Name	Required Value
(0018,0050)	Slice Thickness	≤ 4.0 mm (for ventricle analysis)
(0018,0050)	Slice Thickness	≤ 2.0 mm (for arterial analysis)
(0008,0060)	Modality	CT
(0028,0030)	Pixel Spacing	≤ 2.0 x 2.0 mm²

3.6.2 Recommended Protocol

For the PHA Software, it is recommended that a contrast enhanced 3D volumetric acquisition with pixel spacing less than 2 mm and slice thickness less than 2 mm for the input scan. Example protocols are listed in the table below. Failure to observe the recommended scan protocol could limit the software's ability to properly segment the left and right ventricles.

Additionally, adequate contrast between the cardiovascular structures and the surrounding tissue is a prerequisite for optimal performance. For RV/LV measurements, the LV attenuation should be > 100 HU.

Acquisition Parameters	
Scan Type	AXIAL
kVp	80-120
mA	200
Contrast Volume (mL)	75-100
Contrast Concentration (mg/mL)	370
Contrast Injection Rate (mL/s)	3
Threshold Attenuation (HU)	80
Reconstruction Parameters	
Kernel	Standard, non-edge enhancing
Thickness (mm)	1.0

3.7 Hardware Requirements

Hardware requirements for running PHA are as follows:

- 4 CPU Cores
- 8 GB Ram
- 50 GB Storage

3.8 Product Lifecycle

The software is supported and maintained throughout its active lifecycle. Users will be notified in advance of end-of-support or end-of-life milestones. Use beyond end-of-support is not recommended as performance and cybersecurity cannot be assured.

4 Quality Assessment

The scan quality and possible artifacts must be assessed before utilizing the results produced by the PHA Software.

This software is designed to run on any input data that satisfies the criteria in Section 3.6.1 and it does not perform any additional quality checking. **It is the responsibility of the medical professional who is using the application to ensure that the input data is of adequate quality.** If the input data is not of adequate quality, the application's results should be disregarded. PHA Software is not intended for use as a primary tool for disease detection and/or diagnosis.

Areas of the image where comorbidities or anomalous pathologies are present may give unpredictable results, and the RV/LV results should be interpreted with a knowledge of the location and extent of any comorbidities or anomalous pathologies.

PHA was designed and validated on adult hearts and has not been validated on children.

4.1 Algorithm Malfunction or Performance Changes

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. In the case of an algorithm malfunction or performance change of the PHA Software, submit an email with details to support@4dmedical.com.

5 PHA Software

5.1 Input

The PHA Software requires one DICOM format contrast-enhanced CT pulmonary angiogram acquisition as input.

5.2 Outputs

When run with appropirate input data, the PHA Software generates two DICOM outputs; the PHA Annotated Image Series and the PHA Summary Report. More information about these outputs is given below. In the event that the provided data fails the input check process, and Input Check Failure Report will be generated.

5.2.1 PHA Annotated Image Series

The PHA Annotated Image Series is a Secondary Capture DICOM Image showing the input image series with an RGB overlay. The detected interventricular septum in each slice is represented as a green line. There are two solid red lines in each Annotated Image Series. These solid red lines represent the largest ventricular diameter detected by the algorithm. The ventricular diameters in all other slices are marked with dashed lines, either blue or red. The dashed red lines simply indicate that that slice is within 10 slices of the global maximum ventricular diameter. They should be used to assist the user in finding the slice that contains the maximum ventricle measurement.

Additionally, at the slice where the main pulmonary artery bifurcation is detected, there are solid cyan and solid orange lines, representing the reported diameters of the main pulmonary artery and aorta, respectively.

Below are example slices from the PHA Annotated Image Series.

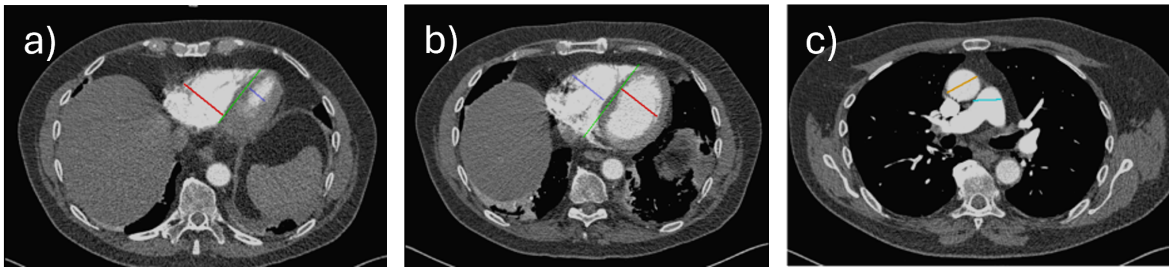


Figure 1: (a) Axial slice of PHA Annotated Image Series displaying the largest ventricular diameter of the right ventricle and the detected interventricular septum. (b) Axial slice of PHA Annotated Image Series displaying the largest ventricular diameter of the right ventricle and the detected interventricular septum. (c) Axial slice of PHA Annotated Image Series showing themain pulmonary artery and the aorta mesurements.

5.2.2 PHA Summary Report

The PHA Summary Report is a DICOM compatible format file containing results from the PHA Software. The SOP Class of the report is either Secondary Capture or Encapsulated PDF Storage. The report summarizes the results of the PHA Analysis. It contains patient information, images showing the slices where the measurements were taken, the RV/LV and PA/Ao ratios, and the individual structure measurements if available. An example report is shown below in Figure 2. Note the maximum ventriucular diameters of the right and left ventricle are determined independently and may occur on different slices, whereas the diameters of the main pulmonary artery and the aorta are both taken on the slice containing the main pulmonary artery bifurcation.

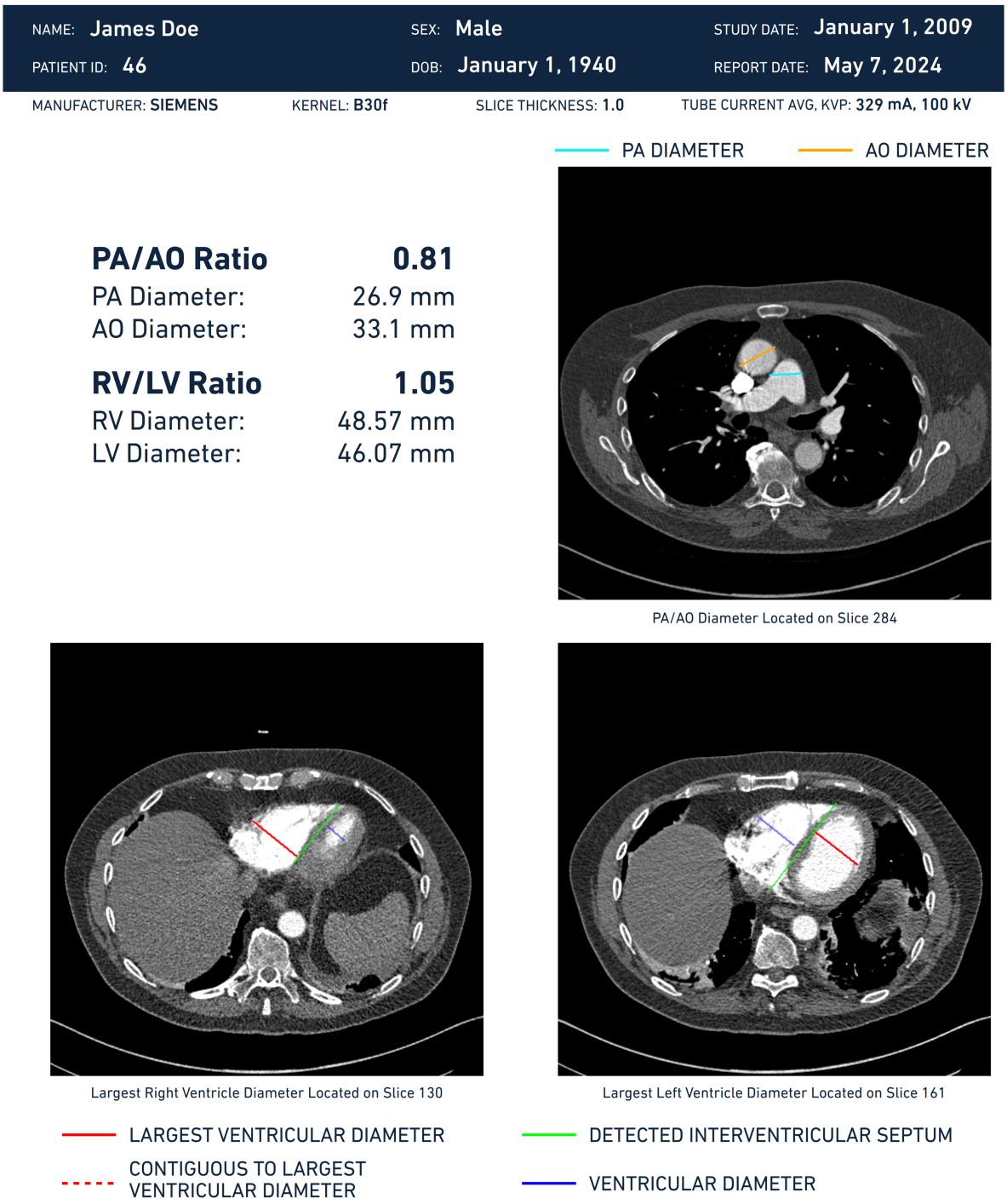


Figure 2: Example PHA Summary Report

5.2.3 Input Check Failure Report

The PHA Input Check Failure Report is a DICOM compatible format file containing results of the Input Check process. This report is only produced if the input check process fails. The SOP Class of the report is either Secondary Capture or Encapsulated PDF Storage. The Input Check Failure Report is also available as a PDF file. The report contains patient information, and summarizes whether each input requirement was met. An example report is shown below in Figure 3. In this example, the slice thickness was

outside of the specifications.

ACCESSION NUMBER: **Unknown**	MANUFACTURER: **SIEMENS**	KERNEL: **B20f**
STATION NAME: **BWCTED**	MODEL: **Definition AS+**	TUBE CURRENT AVG, KVP: **411 mA, 120 kV**

	Requirement	Value	Result
Series Instance UID	Valid UID 1.2.840.113747.1333543965.5772.3240.2819322250408.6866		✓
Modality	CT	CT	✓
Pixel Spacing	<= [2.0, 2.0]	[0.65, 0.65]	✓
FOV/ImagePositionPatient	>= (200, 100, 100)	(333, 333, 251)	✓
Image Orientation	(1,0,0,0,1,0)	(1.0, 0.0, 0.0, 0.0, 1.0, 0.0)	✓
Slice Thickness	<= 4.0	5.0	✗
Patient Age	>= 22	68	✓
Patient Position	Supine	HFS	✓
Rows	Present	Present	✓
Columns	Present	Present	✓

Figure 3: Example PHA Input Check Failure Report

6 Possible Encountered Exceptions

The 4DMedical PHA Software produces notifications and errors when an exception is encountered within the algorithm. Below are possible errors generated by the software with further descriptions and probable causes of the exceptions.

6.0.1 Input Errors

`ERROR: Unacceptable input data`

This error occurs if one or more acquisition parameters do not meet 4DMedical's requirements. For the details on each required parameter, see Section 3.6.1.

6.1 General Errors

`ERROR: "Cannot compute septums"`

This error indicates the interventricular septum could not be detected. Possible causes include the input image does not contain the heart, the input image is noisy, or there is not adequante contrast between the ventricle chambers and the septum/myocardium.

7 Considerations to Reduce Risk

7.1 Protocol

For optimal results, users should follow the CT protocol as outlined in Section 3.6.2.

7.2 Algorithm Limitations

The PHA Software checks input parameters and notifies users with warnings or error messages. Even so, there are a small number of cases where no warning or error is given and the output report is generated with potentially misleading results. Below are examples of possible cases. Users of the software should look for this type of output. If present, the results should not be used. The PHA Software should only be used by intended users as specified in Section 3.2.

1. Poor Diameter Measurements: This error can be identified by viewing the PHA Annotated Image Series or the Report. Figure 4 shows that the red lines, indicating where the diameter measurement is taken, do not extend to the edge of the ventricular cavity.

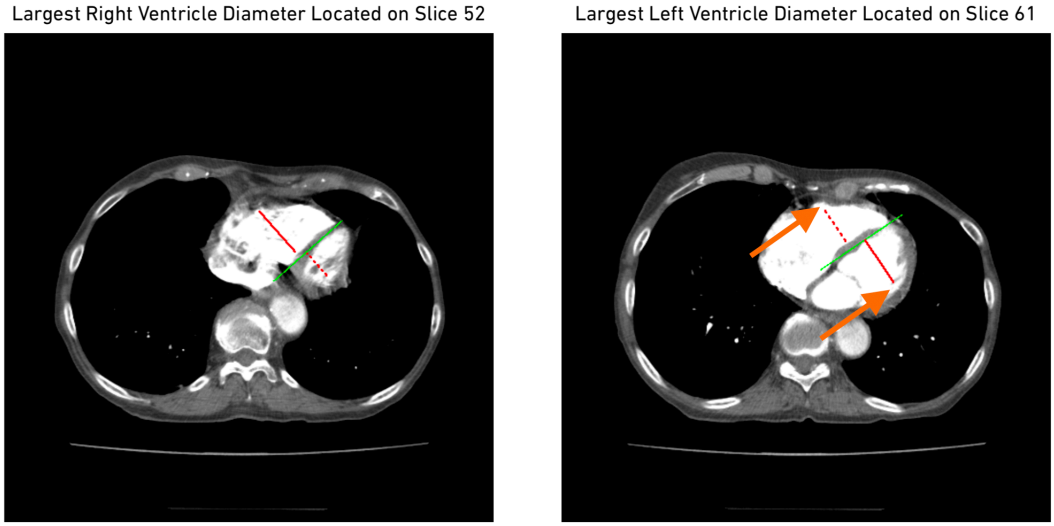


Figure 4: The measurements, indicated by the solid red lines, do not measure the entire distance of the cavity.

2. Poor Image Contrast: This error can be identified by viewing the PHA Annotated Image Series or the Report. In Figure 5 below, there is minimal contrast between the cavity and the surrounding myocardium of the left ventricle. This is caused by a poorly timed CTPA acquisition and can impact both the automated algorithm and the visual QA process.

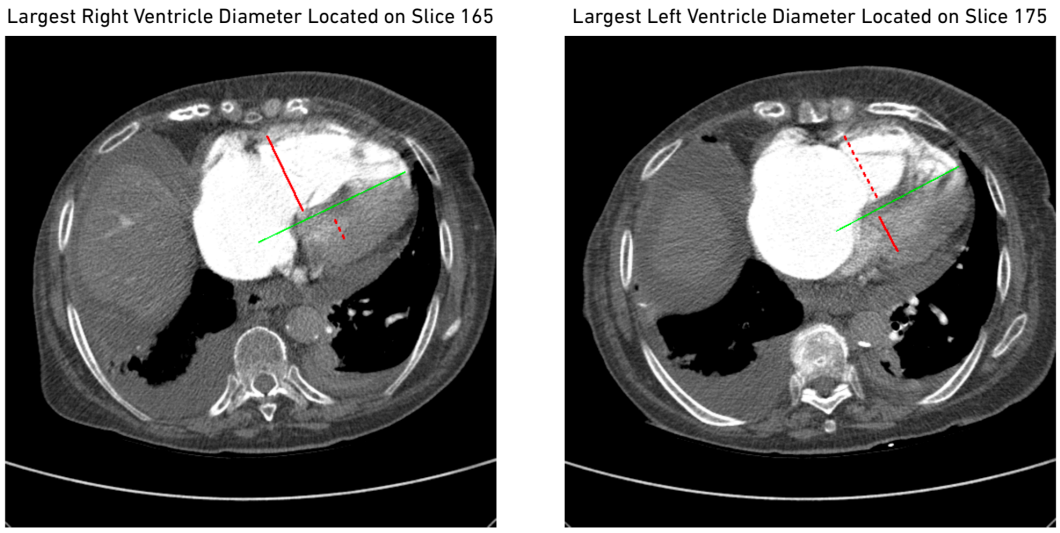


Figure 5: Poor contrast between the cavity and the myocardium can complicate the analysis.

3. Poor Septum Detection: This error can be identified by viewing the PHA Annotated Image Series or the Report. In Figure 6 below, the interventricular septum (green line) is poorly detected. The ventricular measurements are made perpendicular to the detected septum, so a poor septum detection can impact the final ventricular measurements and ratio.

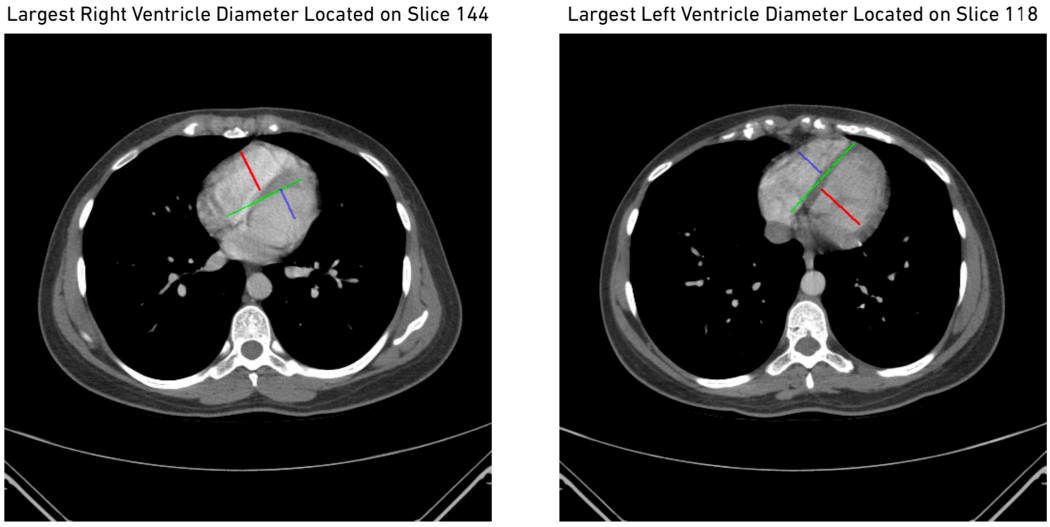


Figure 6: The interventricular septum has been identified incorrectly, leading to a poor segmentation.

7.3 Cybersecurity Recommendations

When deploying systems on which this application will run, please consider the following technical security guidelines:

- Ensure only permitted users are able to sign into the system, using at minimum, a username and strong password.
- Ensure that system firewalls are configured in such a way as to only allow needed traffic to ingress the system.
- Ensure that operating system patches are kept up-to-date, and monitor operating system vendor communications for security and patching-related announcements.

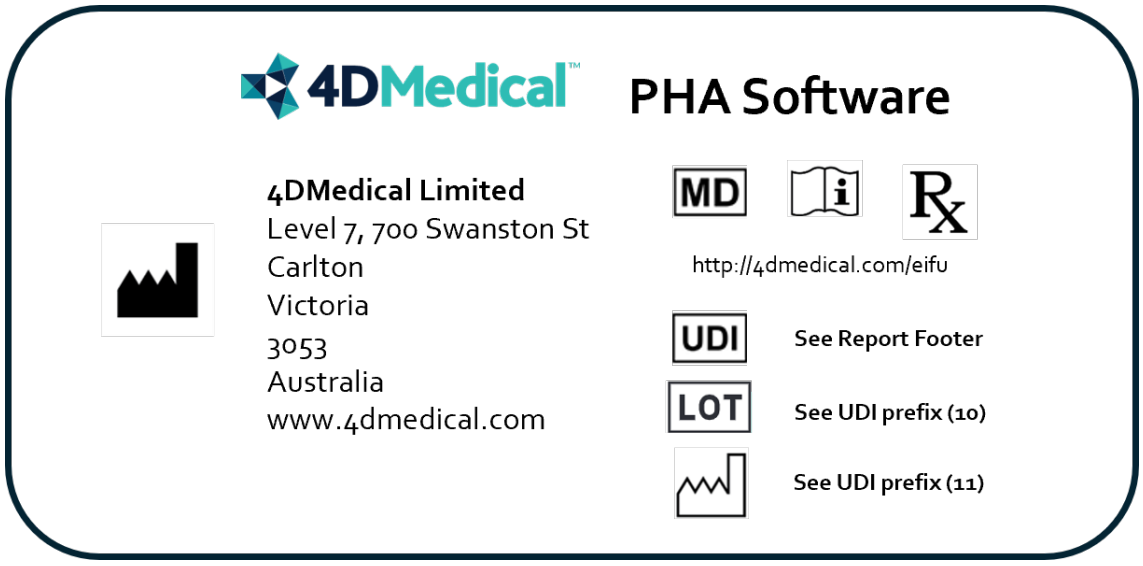
8 Regulatory Information

8.1 Contact 4DMedical

For support, contact 4DMedical using the details below during standard business hours.

Phone: +1 833 877 2267
Address: 21255 Burbank Blvd. Suite 120
Woodland Hills, California
91367
U.S.A
Email: support@4DMedical.com | 4DMedical.com/support

8.2 Software Label



Disclaimer

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References

[1] D. Collomb, P. J. Paramelle, O. Calaque, J. L. Bosson, G. Vanzetto, D. Barnoud, C. Pison, M. Coulomb, and G. Ferretti. Severity assessment of acute pulmonary embolism: evaluation using helical CT. *European Radiology*, 13(7):1508–1514, July 2003.

[2] Pei-Ni Jone, Julie Hinzman, Brandie D. Wagner, David Dunbar Ivy, and Adel Younoszai. Right Ventricular to Left Ventricular Diameter Ratio at End-Systole in Evaluating Outcomes in Children with Pulmonary Hypertension. *Journal of the American Society of Echocardiography*, 27(2):172–178, 2014.