



CT LVAS
Instructions for Use US



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1. Preface

These Instructions for Use (IFU) describe the operation of the CT LVAS Software, and CT LVAS Ventilation Report. 4DMedical recommends that the requesting physician takes note of all advice and precautionary statements included in this manual. Prior to use, please read this entire document.

2. Symbols

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



CAUTION

For information related to patient safety.



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



Consult Electronic Instructions for Use



Manufacturer



Date of Manufacture (YYYY-MM-DD)



Medical Device



Unique Device Identifier

3. Acronyms

CT	Computed Tomography
CT LVAS	Computed Tomography Lung Ventilation Analysis Software
DICOM	Digital Imaging and Communications in Medicine
FOV	Field of View
SaaS	Software as a Service

4. Product Overview

CT LVAS is a software-based image processing technology that analyzes two non-contrast CT images, reporting detailed ventilation information of pulmonary tissue, at regional locations of the lungs between inspiratory and expiratory volumes. Quantification and statistics are provided in the form of a CT LVAS Ventilation Report, including:

- The volume of ventilation, presented as three values;
- Visualization of lung ventilation with color-defined specific ventilation ranges overlaid on the CT slices;
- The heterogeneity of lung ventilation, presented as three values, which quantifies the regional variability of the ventilation; and
- Ventilation histogram of lung voxels' relative frequencies showing the frequency distribution of regional specific ventilation measured across the entire lung, including ventilation defect percentage which shows the volume of lung with low ventilation.

These regional measures are derived entirely from the lung tissue displacement and the lung volume change between the paired inspiration-expiration chest CT.

4.1 Indications for Use

CT LVAS software is a non-invasive image processing technology that measures volume changes from paired inspiration-expiration CTs to quantify and visualize regional and global ventilation. These regional measures are derived entirely from the lung tissue displacement and lung volume change between the paired inspiration-expiration chest CTs.

CT LVAS is for use in adult patients. Quantification and visualizations are provided in the form of a report.

CT LVAS may be used when physicians need a better understanding of a patient's lung function and/or respiratory condition.

4.2 Intended Use

The CT LVAS is intended to be used by referral from thoracic radiologists, pulmonologists or equivalent. The CT LVAS software can be used to provide these physicians with additional supporting clinical data regarding pulmonary ventilation for use in adult patients.

5. Safety and Regulatory

The CT LVAS Ventilation Report is intended to be interpreted by the requesting physician and they must ultimately use their clinical judgement in making decisions that concern patient management (See Section 6 for detailed information about acceptable datasets). Areas with artefacts and anomalies within the imaging may give unpredictable results, and therefore, the CT LVAS results should be interpreted with appropriate clinical judgement.

This software is designed to run on any input data that satisfies the criteria in Section 6. It is the responsibility of the medical professional who is acquiring the images (i.e., Radiologic Technologist) to ensure that the input data is of adequate quality. If the input data is not of adequate quality, the output CT LVAS Ventilation Report results will reflect the quality of the input data.

Read all safety information prior to prescribing acquisition of input data.

Acquisition of CT LVAS inputs involves exposure to radiation. A paired inspiration-expiration chest CT is required for the analysis. The requesting physician must use their judgement to assess the risk to the patient before proceeding with acquisition of images. For more information on the image acquisition protocol please refer to Section 7.

5.1 Information Relating to Input Data

Values presented in the Report are dependent on the correct information being supplied in the input data and associated metadata. The requesting physician is responsible for the suitability of the input images.

The Report output is dependent on the quality of input images. Images containing motion artifacts or the presence of foreign objects (e.g., metallic components) may impact the quality of the Report outputs.

6. Device Input Requirements

CT LVAS requires a pair of inspiratory and expiratory chest CT images, captured in a single study. If the input images do not meet the following criteria, the images will be rejected by the device, and no analysis will be undertaken.

6.1 Image Requirements

6.1.1 CT: Resolution

To produce a CT LVAS Ventilation Report, the inspiration and expiration CT images must meet the following requirements:

Name	Required Value
Pixel Spacing	≤2.5mm
Slice Spacing (Interval/Increment)	≤2.5mm
Slice Thickness	≤2.5mm

6.1.2 Lung Volume Difference



CAUTION: The total lung volume difference between the inspiratory and expiratory CT images must be more than 0.5 liters (or more than 10% of the expiration CT volume). If the measured volume is less than 0.5 liters or 10% of the expiration CT volume, then no Report will be generated.

NOTICE: If the expiratory to inspiratory volume change is less than 0.8 liters and 20% of expiratory volume, the low values may be related to the image acquisition process and may not be representative of the patient's actual lung function.

If the notice is present on the Report and is not believed to be due to an error in the image acquisition, please contact 4DMedical using the information in Section 10.

6.1.3 CT: Filetype

The CT images must be in DICOM (Digital Imaging and Communications in Medicine) format. An uncompressed DICOM format is preferred, however, a lossless compression algorithm is acceptable.

6.1.4 Testing of the Quantitative Measurements

4DMedical has conducted performance testing in the form of verification across a wide range of pixel and slice spacings and Signal to Noise Ratios (SNRs). Testing of the quantitative measurements included a combination of synthetically generated phantom image data and clinically acquired data. The clinically acquired data included a range of models, manufacturers and institutions, a range of volume changes between the inspiration and expiration CTs, and a diverse range of patients. The primary sources of variability affecting the quantitative measurements are voxel size and signal-to-noise-ratio (SNR). The Device requires a maximum pixel spacing of 2.5mm x 2.5mm, and a slice spacing/slice thickness of 2.5mm. The verification testing demonstrated that the device was robust within acceptable performance limits across the entire range of these inputs.

7. Imaging Protocol

The imaging protocol for a CT LVAS is documented in *DOC-4554 CT LVAS Imaging Protocol*.

7.1 Image Transfer and CT LVAS Ventilation Report Delivery

4DMedical utilizes a DICOM routing system to facilitate the transfer of the CT series from healthcare facilities to 4DMedical's SaaS platform for processing. To order a CT LVAS report, starting from the institution's RIS (Radiological Imaging System)/PACS (Picture Archiving and Communication System), enter the relevant CT LVAS exam code, or search for the relevant code, select the code and continue. Once the images have been acquired, the exam code is marked as complete, which will automatically trigger a workflow to send the files to 4DMedical. The automated workflow is initiated in the DICOM routing system hosted at the facility to de-identify (anonymize) the study prior to sending the data to 4DMedical's SaaS platform via a secure channel established between the parties. Upon completion of analysis by the device, the CT LVAS ventilation report is returned via the secure channel, where it is re-identified by the DICOM routing system and saved back into the RIS/PACS.

If your institution requires assistance establishing a connection from its RIS/PACS to 4DMedical's SaaS platform, please contact your local 4DMedical representative.

8. Performance Testing

The CT LVAS Software was designed, developed, and tested in accordance with the ISO 62304 standard. Known hazards were identified and mitigated in accordance with the ISO 14971 standard. Unit level, performance, and integrated system testing were performed. The results of testing demonstrate that the device is effective and meets the manufacturer's intended performance criteria. Clinical and non-clinical studies were also conducted.

8.1 Verification

4DMedical has conducted performance testing in the form of verification across a wide range of pixel and slice spacings and Signal to Noise Ratios (SNRs). Testing of the quantitative measurements included a combination of synthetically generated phantom image data and clinically acquired data. The clinically acquired data included a range of models, manufacturers and institutions, a range of volume changes between the inspiration and expiration CTs, and a diverse range of patients. The primary sources of variability affecting the quantitative measurements are voxel size and signal-to-noise-ratio (SNR). The Device requires a minimum pixel spacing of 2.5mm x 2.5mm, and a slice spacing/slice thickness of 2.5mm. The verification testing demonstrated that the Device was robust within acceptable performance limits across the entire range of these inputs.

The software verification was completed to assure that the software fully satisfies all expected system requirements and features. Test cases were executed against the system features and requirements.

8.2 Analytical Validation

The software analytical validation was completed to assure the software conforms to user needs and intended use. Workflow testing was conducted to provide evidence that the system requirements and features were implemented, reviewed and met.

8.3 Summary of Non-Clinical Tests

Benchtop Verification and Validation Testing was conducted on CT LVAS. This included generation of synthetic CT images that simulated breath-hold CT pair images of a human. A range of input parameters covering a spectrum of patient anatomies and breathing physiologies was used. These synthetic CT pairs, with known simulated lung physiologies and ventilation volumes (the 'ground truth') were then analysed using the CT LVAS Software. The ventilation measurements derived by CT LVAS were then compared to the 'ground truth' values.

8.4 Summary of Clinical Studies

The performance of CT LVAS was assessed across a diverse patient population in two clinical studies. These studies were conducted to demonstrate the safety and effectiveness of the Device and included patients presenting with symptoms including shortness of breath, frequent coughing, excessive phlegm (mucus) production and frequent chest tightness. The studies included patients across the spectrum of lung health and included healthy subjects and subjects with Asthma, Chronic Obstructive Pulmonary Disease and Lung Cancer.

The studies compared the regional ventilation measurements output by CT LVAS with gold-standard and best practice measures for respiratory diagnosis. The performance of the Device was assessed both quantitatively and qualitatively to determine consistency of the Device's outputs with the gold-standard measures including Pulmonary function testing (PFT) and Nuclear Medicine Imaging (SPECT and PET).

Clinical Study 1

The first clinical study was an observational comparison study conducted using data acquired in the USA with the objective of demonstrating agreement between CT LVAS and SPECT ventilation. This study consisted of quantitative, statistical analysis demonstrating the correlation between PFT and CT LVAS metrics, as well as qualitative analysis of five case studies which compared CT LVAS outputs with SPECT ventilation image data. The target population consisted healthy participants as well as participants with previously diagnosed lung diseases.

A total of 32 participants were included in the study. There were 19 male and 13 female study participants, and their ages ranged from 26 to 78 years of age. The body mass index of the subjects varied between 17.9 and 44.8 kg/m². The participants' mean height was 67 inches, and their mean weight was 163 pounds. Fifteen (15) patients had received a previous diagnosis of COPD and the remainder were categorized as healthy. The participant cohort included patients presenting with symptoms including shortness of breath, frequent coughing, excessive phlegm production and frequent chest tightness. The study included participants from diverse racial demographic groups representative of the USA's population, with participants self-describing as: Asian or Pacific Islander 3% (n=1); Black or African American 6% (n=2); Hispanic or Latino 22% (n=7); Multiracial or Biracial 3(n=1); and White or Caucasian 63% (n=20).

The study demonstrated the following:

- CT LVAS metrics correlated with PFT metrics. In particular, CT LVAS Inspiratory Volume, Expiratory Volume and Volume Change correlated with Total Lung Capacity (TLC), Functional Residual Capacity (FRC), and Vital Capacity (VC), respectively. Functional metrics ventilation heterogeneity (VH), ventilation heterogeneity small scale (VHSS), ventilation heterogeneity large scale (VHLS) and ventilation defect percentage (VDP) correlated with FEV1 (% predicted) and FEV1/FVC;
- CT LVAS provided information regarding regional ventilation that was complementary to global ventilation metrics provided by PFT; and
- CT LVAS visualizations were consistent overall with SPECT ventilation images, however provided additional clarity for assessment of regional distribution of ventilation.

The Computed Tomography Ventilation (CT LVAS) metrics and ventilation visualizations as tools for lung assessment were further assessed through the evaluation of five individuals, each characterized by different degrees of lung disease, inclusive of a healthy subject. The effectiveness of CT LVAS in providing visualization and quantifiable data pertaining to regional ventilation variability was demonstrated.

Clinical Study 1 showed the consistency of CT LVAS outputs with those of gold-standard measures. Specifically, the study supported the conclusion that there is substantial equivalence between CT LVAS and SPECT in the assessment of regional distribution of ventilation, with both modalities also shown to render functional and pathological details of the lungs. The study also demonstrated a statistically significant correlation between the CT LVAS and PFT outputs.

Clinical Study 2

The second study was performed using a publicly available dataset that was collected from a single institution, in Australia. The study comprised of seventeen (17) lung cancer patients undergoing radiotherapy, each of which had varying lung function. The participants were between 54 and 73 years of age.

This study quantitatively compared the CT LVAS outputs PET (positron emission tomography) using statistical analysis. Like CT LVAS and SPECT, PET outputs three-dimensional ventilation fields. The distribution of lung ventilation for individual lung lobes was reported as a proportion of the ventilation of the entire lung for both CT LVAS and PET.

The study demonstrated consistency between CT LVAS and Nuclear Medicine Imaging in the assessment of spatial ventilation distribution at both lobar and voxel levels. There were no systematic differences in the lobar ventilation between CT LVAS and PET. Furthermore, the absence of mean difference, systematic bias or heteroscedasticity demonstrated that the measurements from CT LVAS and PET detect similarly at the high or low range of lung ventilation. Similarly, voxel-wise analysis via Spearman correlations demonstrated strong association between CT LVAS and Nuclear Medicine Imaging spatial ventilation data.

Given the agreement between PET ventilation scanning and CT LVAS, it was concluded that the methods are substantially equivalent for the purpose of examining the regional distribution of ventilation.

Clinical Studies Conclusion

Overall, the clinical studies conducted for the Device successfully demonstrated the feasibility of generating valid data that is reliable and consistent with Nuclear Medicine Ventilation imaging results.

Clinical Study 1 demonstrated the equivalence between CT LVAS and SPECT in the assessment of regional distribution of ventilation and that there was a statistically significant correlation between the CT LVAS and PFT outputs.

Based on the clinical performance documented in the clinical studies, CT LVAS Software was found to have a safety and effectiveness profile that is similar to the predicate device. Further, it demonstrated the capability of the Device to provide this information without the use of contrast agents utilized by alternative methods.

Performance Testing Conclusion: The performance testing (verification, analytical validation, non-clinical tests and clinical studies) demonstrated that the CT VLAS Software was found to have a safety and effectiveness profile that is similar to the predicate device but without the need for contrast agents.

9. Information Security Statement

CT LVAS and the resulting CT LVAS Ventilation Report are delivered using a Software as a Service (SaaS) model, with one main component, commonly referred to as a DICOM Router, which needs to be managed by your local institution's IT support. Information security is a shared responsibility, please follow your institutions information security protocols. 4DMedical will follow the appropriate jurisdictional requirements in communicating with your institution regarding information security, as required.

10.Support and Notice

10.1 Support

To contact 4DMedical please use the details below. Support will be available during 4DMedical’s standard business hours.

Contact 4DMedical

U.S.

Phone: +1-833-XV-SCANS (1 833 98 72267)

Address: 21255 Burbank Blvd. Suite 120
Woodland Hills, California
91367
USA

Email: support@4DMedical.com | 4DMedical.com/ventilation-support

10.2 Labelling

Labelling is applied to the Report (example shown in Figure 1).

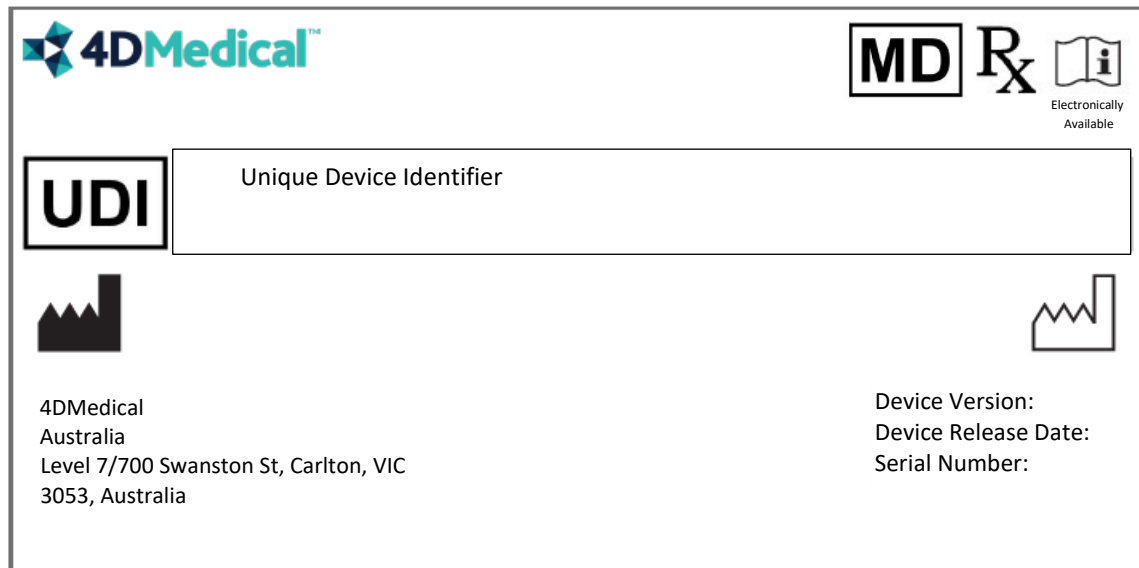


Figure 1 Device label

10.3 Notice

The information provided in the CT LVAS Ventilation Report is intended to support physicians with their assessment of patients with lung diseases. CT LVAS and the resulting CT LVAS Ventilation Report does not, in itself, provide a diagnosis of lung health. 4DMedical assumes no responsibility for the improper use of, or self-diagnosis using, CT LVAS and the resulting CT LVAS Ventilation Report.

11. Glossary

See below for more information regarding terms found in the CT LVAS Ventilation Report. For a more detailed explanation of these terms, refer to the how-to-read section of the CT LVAS Ventilation Report.

Term	Definition
Expiration Volume	The total volume (L) of lung tissue at deep expiration.
Inspiration Volume	The total volume (L) of lung tissue at deep inspiration.
Specific ventilation	Defined as the ratio of the change in volume of a region of the lung (ΔV) following an inspiration, divided by the end-expiratory volume (V_0) of that same lung region. Presented values are normalized by mean specific ventilation (i.e. normalized by the average of the specific ventilation values).
Ventilation defect percentage	The percentage of ventilation volume below 60% of the mean specific ventilation.
Ventilation Heterogeneity	The regional variability of the ventilation. This is the ratio of the interquartile range to the mean of the specific ventilation. Low Ventilation Heterogeneity values are associated with uniform ventilation throughout the lung, while high Ventilation Heterogeneity values represent significant variability in the lung.
Ventilation heterogeneity: large scale	The degree of heterogeneity within larger regions of the lung (e.g. lobar and larger), calculated after first filtering out small scale variations (i.e. scales smaller than 64 mm / 2.5").
Ventilation heterogeneity: small scale	The degree of heterogeneity within local regions of the lung (e.g. alveolar to lobar size), calculated after first filtering out large scale variations (i.e. scales larger than 64 mm / 2.5").
Ventilation heterogeneity: total	The overall value of heterogeneity, calculated using all regional specific ventilation data (as displayed in the Ventilation Report Regional Ventilation Visualizations)
Change in Volume	The difference in the volume (L) between deep inspiration and deep expiration.