Imbio

LUNG TEXTURE ANALYSIS™

v2.1

SOFTWARE USER MANUAL

Contents

1   Introduction

1.1   Scope of Manual

This user manual was written for the Imbio CT Lung Texture Analysis™ (LTA) Software.

Guidance for using the Imbio Core Computing Platform (CCP) is not included in this document. The Imbio CCP 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 Imbio. The Imbio CCP 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 CCP provides a system by which customers can still benefit from image processing job automation, while integrating with native DICOM tools and workflows. The Imbio CCP with cloud and enterprise options is a separate product developed by Imbio.

1.2   Product Overview

Imbio's CT Lung Texture Analysis™ Software is a set of image post-processing algorithms for the characterization and quantification of lung parenchymal patterns on CT scans. It segments and classifies the lung tissues and produces a report consisting of horizontal bar graphs and a 3D texture rendering. The graphs represent the percent volumes of each subsection within the left and right lung and color coded to represent the four parenchymal classifications. The LTA Software runs automatically on the input CT series, with no user input or intervention.

The purpose of the segmentation algorithm is to automatically identify and separate the two lungs from the rest of the body. The purpose of the classification algorithm is to identify each lung pixel as one of the four lung parenchymal pattern classifications.

The Imbio CT Lung Texture Analysis™ Software utilizes DICOM format high resolution CT lung inspiration series as input to the software. The specific requirements are given in the Scan Protocol section of this document (Section 2.2).

The DICOM outputs provided by the Imbio CT Lung Texture Analysis™ Software are three RGB overlay image series (Secondary Capture Image Storage SOP Class) and a summary report (Encapsulated PDF Storage SOP Class or Secondary Capture Image Storage SOP Class).

1.3   Contact Imbio

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Minneapolis, MN 55405, USA
United States
www.imbio.com

2 Indications for Use and Requirements

The Imbio CT LTA Software uses CT density values of pulmonary tissue to provide quantitation and visualization in support of diagnosis. The Imbio CT LTA Software performs three-dimensional segmentation and classifies the lung voxels into typical radiological categories. Automated reports and color overlays of the analysis are provided to support diagnosis when abnormal lung parenchymal densities are present.

2.1 Intended Users

The intended user base for the Imbio CT Lung Texture Analysis Software is Pulmonologists, Radiologists, and Radiology Technicians under the supervision of a Pulmonologist or Radiologist.

2.2 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. The DICOM data provides information on the basic acquisition parameters used and can be compared with Imbio's required parameters. The scan should also be visually assessed to ensure that there are no contraindications or missing information.

2.2.1 Imbio Acquisition Parameters

The Imbio CT Lung Texture Analysis™ Software will not generate outputs for scans with acquisition parameters that do not meet the requirements as outlined in the table below.

DICOM Tag	Name	Required Value
(0008,0060)	Modality	CT
(0028,0030)	Pixel Spacing	$\leq$ 2.0 x 2.0 mm^2
(0018,9305)	Revolution Time	$\leq$ 1.0 s (if present)
N/A	Slice Spacing	$\leq$ 2.0 mm
(0018,0050)	Slice Thickness	$\leq$ 2.0 mm
N/A	Field of View	$\geq$ 10.0 x 10.0 x 20.0 cm^3

2.2.2 Other DICOM Input Requirements

The Imbio CT Lung Texture Analysis™ Software utilizes specific DICOM data to generate its outputs. The following DICOM data tags are required in the input CT images.

DICOM Tag	Name	Required Value
(0028,1054)	Rescale Type	HU (if present)
(0020,0032)	Image Position Patient	(present and not empty)

2.2.3 Imbio Recommended Protocol

For the Imbio CT Lung Texture Analysis™ Software, Imbio recommends a 3D volumetric acquisition with pixel spacing less than 1 mm and slice thickness less than 2 mm for the input inspiration scan. Imbio also recommends that the patient lies in the supine position. Imbio does not recommend a contrast enhanced acquisition. Example protocols are listed in the table below. The protocols accepted by Imbio CT LTA Software are not limited to the scanners and protocols in the table, but the acquisition parameters should be similar. The Imbio CT LTA Software has not been characterized on iterative reconstruction methods. Failure to observe the recommended scan protocol could limit the software's ability to properly segment lungs.

Scanner Make	GE	SIEMENS	PHILIPS	TOSHIBA
Scanner Model	VCT 64	Sensation-64	64 Slice	Aq64
Scan Type	Helical	Spiral	Helical	Helical
Rotation Time (s)	0.5	0.5	0.5	0.5
Det. Configuration	64 x 0.625	64 x 0.6	64 x 0.625	64 x 0.5
Pitch	0.984	1.0	1.0	0.828
kVp	120	120	120	120
mA	200	200	200	150
Reconstruction				
Kernel	Standard†	B35f†	B†	FC13†
Thickness (mm)	0.625	0.75	0.67	1
Interval (mm)	0.5	0.5	0.5	0.5
DFOV(cm)	Lungs*	Lungs*	Lungs*	Lungs*

†More reconstruction kernels are considered acceptable than the kernels listed in this table. See table below listing all recommended and not recommended reconstruction kernels.
*Reconstruction field of view should encompass the widest diameter of the lung.

Recommended Reconstruction Kernels

Imbio does not provide an exhaustive list of acceptable reconstruction kernels due to the large number of reconstruction kernels available and the implementation of new kernels. However, Imbio recommends using the table below as a guide to the choice of reconstruction kernel. If an image with a higher degree of edge enhancement is desired for a human reader, then Imbio recommends performing two reconstructions: one reconstruction for a human reader and a second reconstruction with one of the recommended kernels for LTA analysis.

Scanner Manufacturer	Recommended 1st Preference	Recommended 2nd Preference	Not Recommended
GE	Bone, Standard	Soft	Bone+, Lung
SIEMENS	B31f, B35f, B45f, B46f	B20, B40	B18, B19, B25, B30, B50, B60, B70, B75, B80
PHILIPS	B, C	L	A, D
TOSHIBA	FC01, FC13, FC14, FC19	FC05, FC18	FC35, FC50, FC51, FC52, FC56, FC85

2.2.4 Breathing Instructions

The patient should be coached to achieve and hold full inspiration, with several practice attempts prior to scan acquisition. If the patient is unable to hold their breath for the scan period, such as the case for a severely ill patient, a faster scanner needs to be utilized. Below is a suggested script of how to coach a patient for the inspiratory scan.

Breathing Instructions Script
Inspiratory CT
For the first part of this scan, I am going to ask you to take a deep breath in and hold it
First let's practice:
    Take a deep breath in
    Hold it - do not breathe
    Breathe and relax
Take a deep breath in
    Let it out
Take a deep breath in
    Let it out
Breath all the way IN...IN...IN...
    Keep holding your breath - DO NOT BREATHE!
    At end of scan: *Breathe and relax*
Start scan at bottom of lungs; end at top of lungs

3   Quality Assessment

The scan quality and possible contraindications must be assessed before executing the Imbio CT Lung Texture Analysis™ Software.

3.1   Scan Quality

Lung density values from a CT scan may vary due to different acquisition parameters thus causing variation in LTA results. Sources of variation include but not limited to dose, reconstruction kernel, slice thickness, scanner calibration and respiratory cycle. Users should not compare LTA results across acquisitions with different acquisition parameters.

Imbio may generate errors in the following instances:

Scan Quality Component	Result
Noise	The airway segmentation in a noisy scan may fail if the lung tissue is not distinguishable from other tissue.
Missing slices	If slices within the tissue containing lung are missing, the resultant Lung Texture Analysis™ map and summary report could be inaccurate.
Entire lung not included	If scan does not fully contain the lungs, segmentation of the lungs will fail.
Intubation	If the patient is intubated during the scan, the lung segmentation will fail.

3.2   Contraindications

This software is designed to run on any input data that satisfies the criteria in Section 2.2.2 and it does not perform any additional quality checking. **It is the responsibility of the medical professional who is using the application (i.e., the Radiologist, Pulmonologist or Radiology Technologist) 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. Imbio's CT Lung Texture Analysis™ Software is not intended for use as a primary tool for disease detection and/or diagnosis.

Areas of the lung where comorbidities or anomalous pathologies are present may give unpredictable results, and the Lung Texture Analysis™ results should be interpreted with a knowledge of the location and extent of any comorbidities or anomalous pathologies.

Lung Texture Analysis™ was designed and validated on adult lungs and has not been validated on children. Lung Texture Analysis™ should not be used on patients with only one lung.

4 Lung Texture Analysis

4.1 Input

The Lung Texture Analysis™ Software takes an inspiration scan as input.

4.2 Outputs

The LTA Software generates four outputs: the LTA Map, the LTA Summary Report, the LTA Lung Labels, and the LTA Pulmonary Vasculature Labels.

LTA Output	DICOM Series Description
LTA Map	LTA RGB v2.1
LTA Summary Report	LTA Report v2.1
LTA Lung Labels	LTA Lung Labels v2.1
LTA Pulmonary Vessels Labels	LTA Pulmonary Vessels Labels v2.1

The outputs from LTA Software have DICOM tags populated according to the Co-ordinated Universal Time (UTC) for the following tags:

DICOM Tag	Name
(0008,0021)	Series Date
(0008,0023)	Content Date
(0008,0031)	Series Time
(0008,0033)	Content Time
(0040,a032)	Observation Date Time

4.2.1 Lung Texture Analysis Map

The LTA Map is a DICOM Secondary Capture Image with voxel data that is the original inspiration image with an RGB overlay. The RGB overlay colors each lung tissue voxel as one of four colors which correspond to the lung parenchyma pattern classifications.

Below is the list of the default colors for each lung parenchyma pattern classification. The colors can be customized upon installation of the software.

■ HYPERLUCENT

■ GROUND GLASS

■ RETICULAR

■ HONEYCOMB

Example axial slices from the Lung Texture Analysis Map is shown below in Figure 1.
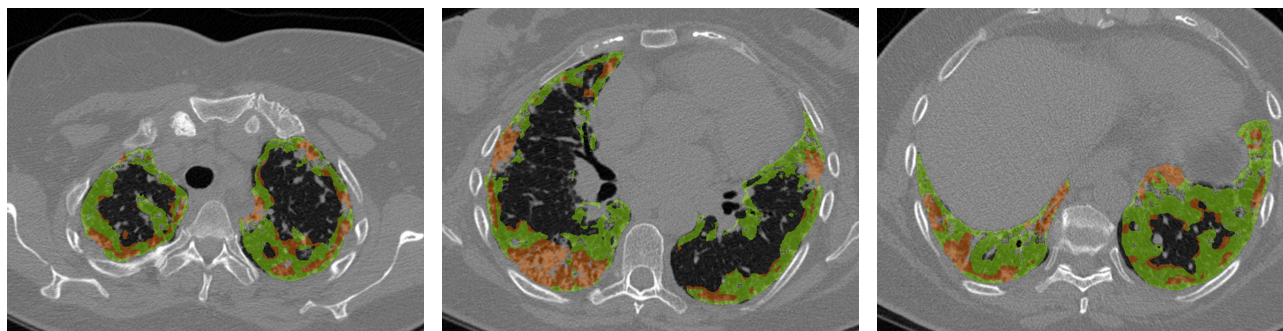
Figure 1: Axial slices of Lung Texture Analysis Map

4.2.2   Lung Texture Analysis Summary Report

The LTA Summary Report is a DICOM compatible format file containing results from the Lung Texture Analysis™ Software. The SOP Class can be Encapsulated PDF Storage or Secondary Capture Image Storage. The report summarizes the results of the Lung Texture Analysis Map. It contains patient information, a 3D lung texture rendering, bar graphs and a table displaying percentages of each lung parenchyma pattern classification. An example report is shown below in Figure 2.

LUNG TEXTURE ANALYSIS
version 2.1

NAME:	**Jane Doe**	SEX: **Female**		STUDY DATE:	**October 10, 2006**
PATIENT ID:	**JD1234**	DOB: **July 1, 1951**		REPORT DATE:	**May 4, 2021**

MANUFACTURER: **SIEMENS**   KERNEL: **B46f**   SLICE THICKNESS: **1.0**   TUBE CURRENT AVG KVP: **319 mA, 120 kV**

3D Texture Rendering
(Not to be solely used for clinical decision)

Lung Rind (Peripheral)

Lung Core (Central)

TEXTURES

- HYPERLUCENT (blue)
- RETICULAR (orange)
- GROUND GLASS (green)
- HONEYCOMB (purple)

SUMMARY		Vol. (L)	Hyperlucent	Ground Glass	Reticular	Honeycombing	PVV (cm^3)
TOTAL LUNG:		1.9 L	0 %	39 %	17 %	0 %	192
Left Lung:		1.0 L	0 %	44 %	13 %	0 %	90
Left Upper	LU		0 %	41 %	16 %	0 %	34
Left Middle	LM		0 %	42 %	10 %	0 %	32
Left Lower	LL		0 %	51 %	14 %	0 %	23
Right Lung:		0.9 L	0 %	34 %	21 %	0 %	101
Right Upper	RU		0 %	37 %	16 %	0 %	31
Right Middle	RM		0 %	29 %	20 %	0 %	46
Right Lower	RL		0 %	44 %	28 %	0 %	23

ADDITIONAL INFORMATION

ⓘ Total lung capacity predicted using Crapo et al. Bull. Europ. Physiopathol. Respir. 1982; 18:419-425. **TLC = 82% predicted.**
ⓘ Rind = Peripheral 50% of lung volume. Core = Central 50% of lung volume. PVV = Pulmonary Vessel Volume.

ⓘ User manual for Lung Texture Analysis 2.1 can be found at https://www.imbio.com/support-documentation.
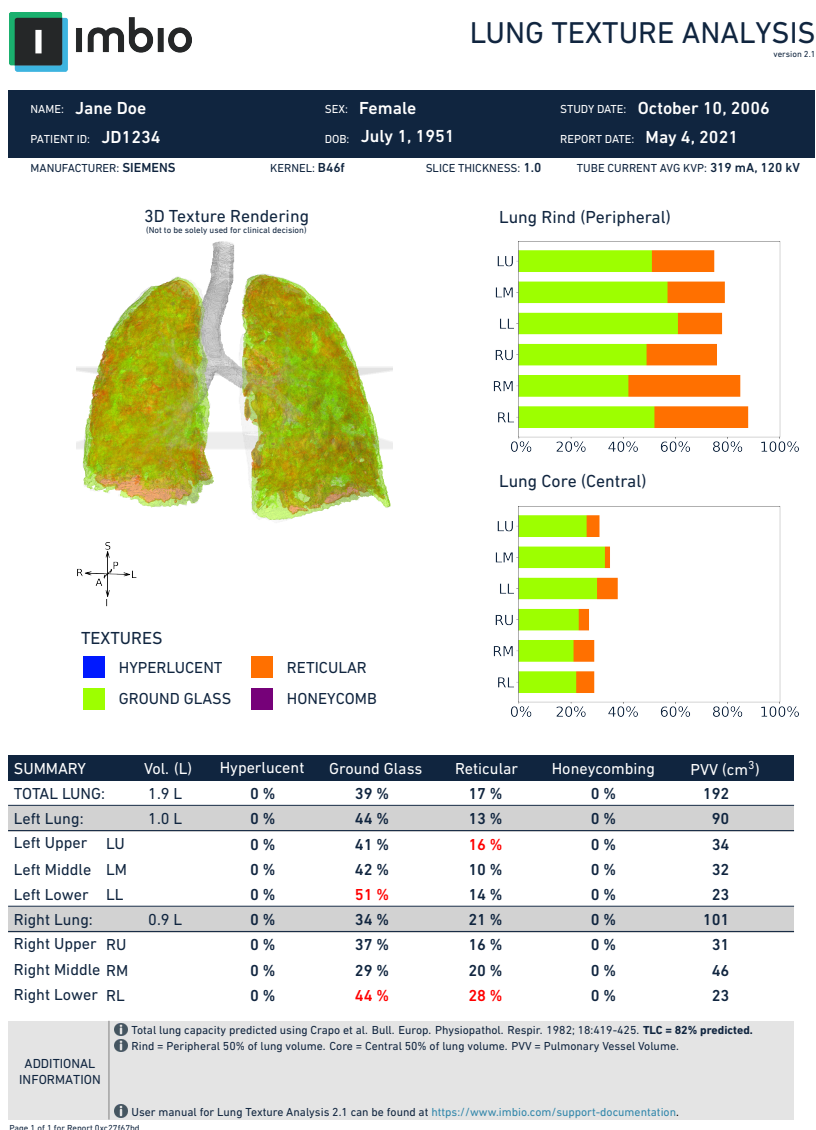
Page 1 of 1 for Report 0xc27f67bd

Figure 2: Example LTA Summary Report

Report Statistics

The statistics reported in the LTA Summary Report are lung volumes and percentages of lung tissue in each lung parenchyma pattern classification.

The percentages for each lung parenchyma pattern classification are given for the right, left and total lungs. Percentages are also broken down for upper, middle and lower thirds for the right and the left lung.

The total lung, left lung and right lung volumes of the segmented inspiration lungs is reported. Also, if the following DICOM attributes are present and filled, a total

lung capacity is predicted using Crapo's method.[1]

DICOM Tag	Name
(0010,0040)	Patient Sex
(0010,1020)	Patient Size
(0010,0030)	Patient Birth Date*

*Patient Birth Date is needed for Crapo's methods only if Patient Sex is Male.

Report Graphics
The report displays a 3-dimensional (3D) rendering image of the lung textures from the Lung Texture Analysis Map. Below is an example of the 3D lung texture rendering found in the report. Note that the rendering is not to be solely used for clinical decision-making
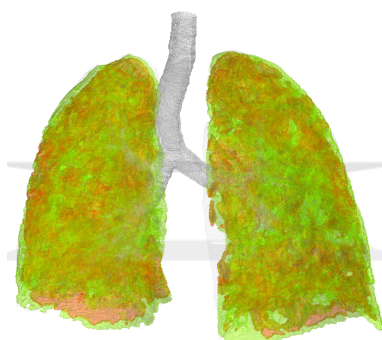
Figure 3: Example of the 3D lung texture rendering in LTA Summary Report

The other graphics in the report are a horizontal bar graphs. Each graph is divided into 6 sections corresponding to the thirds of the lungs (RU = Right Upper, RM = Right Middle, RL = Right Lower, LL = Left Lower, etc.). The bar for each third is filled with the colors corresponding to the lung parenchyma pattern classification, where the length of each color bar is proportional to the percentage of the lung parenchyma pattern classification.

The report contains two different graphs: Lung Rind (Peripheral) Graph and Lung Core (Central) Graph. The Lung Rind (Peripheral) Graph summarizes the lung rind which is defined as the region of lung parenchyma of the exterior or peripheral portion of the lung that is comprised of about half of the lung volume. The Lung Core Glyph summarizes the lung parenchyma of the lung core which is defined as the region of lung parenchyma centered around the centroid of the lung that is

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[1]Crapo RO, Morris AH, Clayton PD, and Nixon CR. Lung Volumes in Healthy Nonsmoking Adults. Bull. Europ. Physiopathol. Respir. 1982; 18:419-425.

comprised of about half of the lung volume.

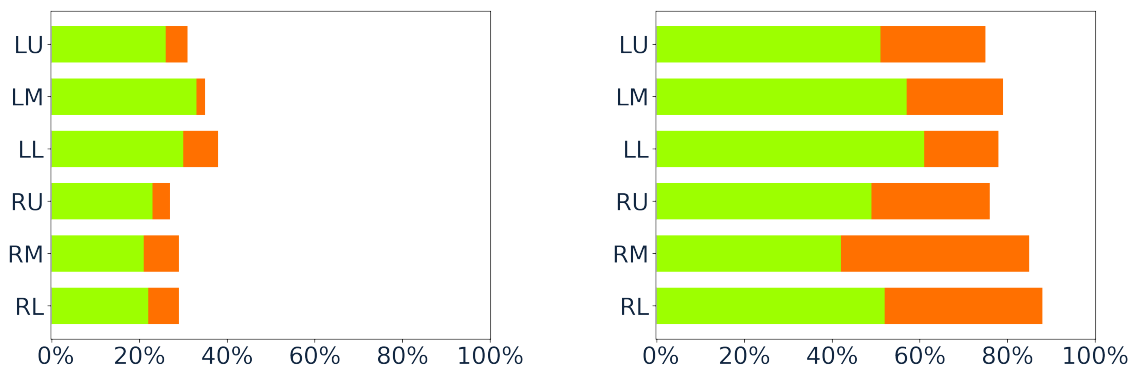Below is an example of the two graphs found in the report.

Figure 4: Example of the Lung Rind (left) and Lung Core (right) Graphs in LTA Summary Report

### 4.2.3   Lung Texture Analysis Lung Labels

The LTA Lung Labels image series is a DICOM Secondary Capture Image with voxel data that is the original inspiration image with an RGB overlay. The RGB overlay shows the results of LTA's segmentation algorithm in accordance with the list of colors below:

██ Right Lung

██ Left Lung
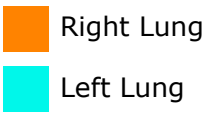
Example axial slices from the LTA Lung Labels image series is shown below in Figure 5.

4.2.4   Lung Texture Analysis Pulmonary Vessel Labels

The LTA Pulmonary Vessel Labels image series is a DICOM Secondary Capture Image with voxel data that is the original inspiration image with an RGB overlay. The RGB overlay shows the results of LTA's pulmonary vasculature segmentation algorithm in accordance with the list of colors below:
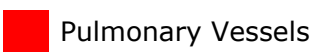
██ Pulmonary Vessels

Example axial slices from the LTA Pulmonary Vessel Labels image series are shown below in Figure 6.

Figure 5: Axial slices of LTA Lung Labels image series

Figure 6: Axial slices of LTA Pulmonary Vessel Labels image series

5   Possible Encountered Exceptions

The Imbio CT Lung Texture Analysis™ 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.

5.1   Input Errors

`ERROR: Input data invalid:: [EXPLANATION]`

This error occurs if one or more acquisition parameters do not meet Imbio's requirements, as listed in the EXPLANATION. For the details on each required parameter, see Section 2.2.2.

In the event that this error occurs, the algorithm will output an Input Check Report

indicating the reason why the input data was deemed unacceptable. An example Input Check Report for LTA is shown in Figure 7.

LTA INPUT CHECK REPORT
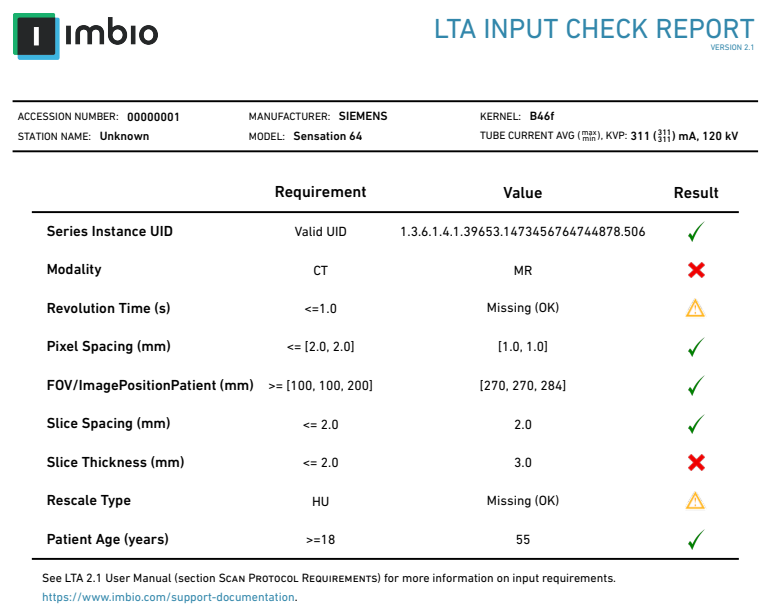VERSION 2.1

| ACCESSION NUMBER: | 00000001 | MANUFACTURER: | SIEMENS | KERNEL: | B46f |
| STATION NAME: | Unknown | MODEL: | Sensation 64 | TUBE CURRENT AVG ($\frac{max}{min}$), KVP: 311 ($\frac{311}{311}$) mA, 120 kV |

	Requirement	Value	Result
Series Instance UID	Valid UID	1.3.6.1.4.1.39653.1473456764744878.506	✓
Modality	CT	MR	✗
Revolution Time (s)	<=1.0	Missing (OK)	⚠
Pixel Spacing (mm)	<= [2.0, 2.0]	[1.0, 1.0]	✓
FOV/ImagePositionPatient (mm)	>= [100, 100, 200]	[270, 270, 284]	✓
Slice Spacing (mm)	<= 2.0	2.0	✓
Slice Thickness (mm)	<= 2.0	3.0	✗
Rescale Type	HU	Missing (OK)	⚠
Patient Age (years)	>=18	55	✓

See LTA 2.1 User Manual (section SCAN PROTOCOL REQUIREMENTS) for more information on input requirements.
https://www.imbio.com/support-documentation.

Figure 7: Example of an Input Check Report

The cause(s) of the input check failure can be identified by the red 'X' mark in the Result column. In Figure 7, the offending parameters are the modality and slice thickness. Note the yellow triangle warning signs indicate sub-optimal parameters or parameters that are missing from the input meta data (Revolution Time or Rescale Type). These warnings will not result in an input check failure, but should be noted nonetheless.

`ERROR: [DIRECTORY] contains more than one series`

This error occurs if the input directory contains more than one images series.

`ERROR: User-supplied mask data invalid: [EXPLANATION]`

This error occurs if the user-supplied segmentation mask fails to meet one of the following requirements, which would be written in the EXPLANATION of the error:

1. Mask data must be either signed or unsigned integer data type.

2. Mask values must be 0, 1, 2 or 3.

3. Mask must have the same shape as input data.

5.2 Segmentation and Classification Errors

`ERROR: LTA executable failed`

This error indicates an exception has occurred during the segmentation or classification algorithm. Possible causes include the input image does not contain lungs, the input image is noisy or the image only has one lung present.

`ERROR: Lung rind volume percentage [VALUE] not in expected range`
`ERROR: Lung core volume percentage [VALUE] not in expected range`

Theses errors indicate a failure of the segmentation produced by Imbio CT Lung Texture Analysis™ to pass an internal Quality Assurance check. This check expects that segmented lung rind and core be between 30% and 70% of the total lung volume.

6   Considerations to Reduce Risk

6.1   Protocol

Users must follow CT protocol as outlined in Section 2.2.

6.2   Algorithm Limitations

6.2.1   Segmentation Errors

The Imbio CT Lung Texture Analysis™ Software uses advanced image processing techniques to segment the lungs from thoracic CT images so that texture analysis can be performed. The software checks input parameters and notifies users with warnings or error messages when there is a suspected issue. 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 inspect outputs of the software for these or similar issues. If present, users should proceed with caution. The Imbio CT Lung Texture Analysis™ Software should only be used by intended users as specified in Section 2.1.

- Over-segmentation of the lung. This includes but is not limited to the following:
    - Air outside of the body is categorized as lung.
    - Air in the gut is categorized as lung.
    - Peripheral non-lung tissue categorized as lung

- Under-segmentation of the lung. This includes but is not limited to the following:
    - Part of the lung is categorized as belonging to the airway tree, removing that part of the lung from the analysis.
    - High-density areas of the lung parenchyma being excluded from the segmentation. This is usually caused by the presence of dependent atelectasis or lung nodules.

- Left/right lung labeling error.
    - Part of the left lung is incorrectly classified as belonging to the right lung, or vice versa.

6.2.2 Examples of Segmentation Errors

Outside air classified as lung. During segmentation, the air outside of the body may be misidentified as lung parenchyma. This will lead to a portion of non-lung tissue to be included in the statistical analysis. This error can be identified by viewing either the LTA Map or the Lung Label series. Figure 8 shows Lung Label (left) and LTA Map (right) images for a case that exhibits this type of error. The red arrows highlight the area of outside air that is included in the lung.
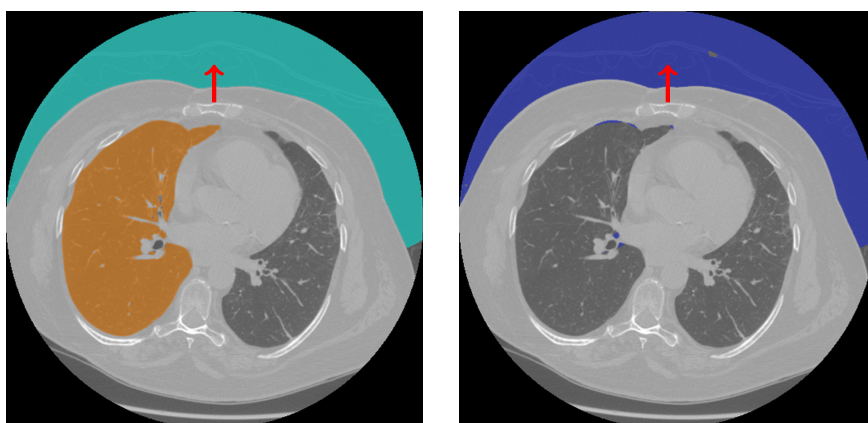
Figure 8

Air in the bowel is classified as lung. The segmentation algorithm may misidentify air in the bowel as lung parenchyma. This will cause non-lung tissue to be included in the statistical analysis. This error can be identified by viewing either the LTA Map or the Lung Label series. Figure 9 shows Lung Label (left) and LTA Map (right) images for a case that exhibits this type of error. The red arrows highlight the area of bowel inclusion.
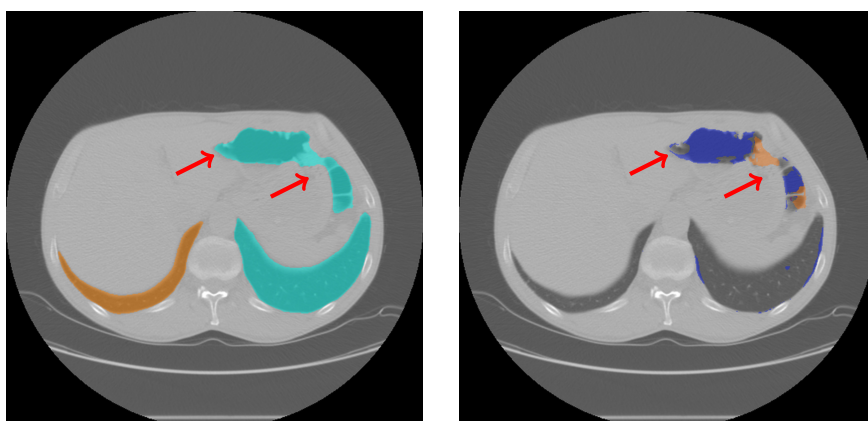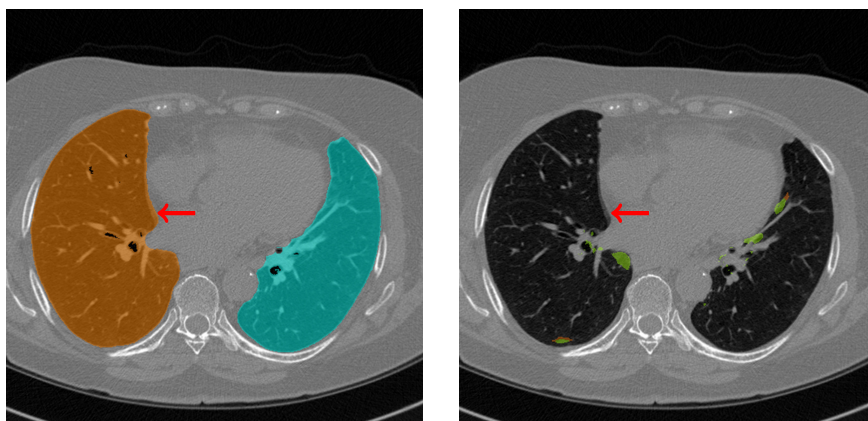

Figure 9

Peripheral non-lung tissue included as lung. The segmentation algorithm may result in a slight overestimation of the lung region by including a small amount of non-lung tissue around the periphery. This over segmentation error is estimated to be about 1 to 2 voxels thick. This non-lung tissue is typically identified as one of the four textures thus affecting the texture percentages. This error can be identified by viewing either the LTA Map or the Lung Label series. Figure 10 shows Lung Label (left) and LTA Map (right) images for a case that exhibits this type of error. The red arrows highlight the area of non-lung inclusion.

Figure 10

Airway segmentation leak into the lung parenchyma. The segmentation of the airways may leak into the lung parenchyma. This error will result in patches of lung parenchyma being excluded from the analysis. Figure 11 shows Lung Label (left) and LTA Map (right) images for a case exhibiting this error. The red arrows highlight the area of airway leakage.
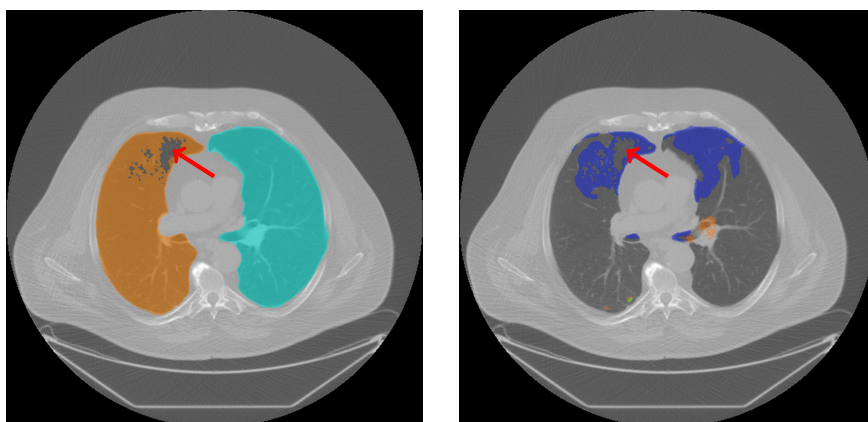

Figure 11

Exclusion of the lung due to high density parenchyma. The segmentation

step of LTA may not identify all lung tissue. This may be due to highly fibrotic tissue or anomalous anatomy. This error may cause a portion of the lung to be excluded from statistical analysis. This error can be identified by viewing either the LTA Map or the Lung Label series. Figure 12 shows Lung Label (left) and LTA Map (right) images for a case that exhibits this type of error. The red arrows highlight the area of lung exclusion.
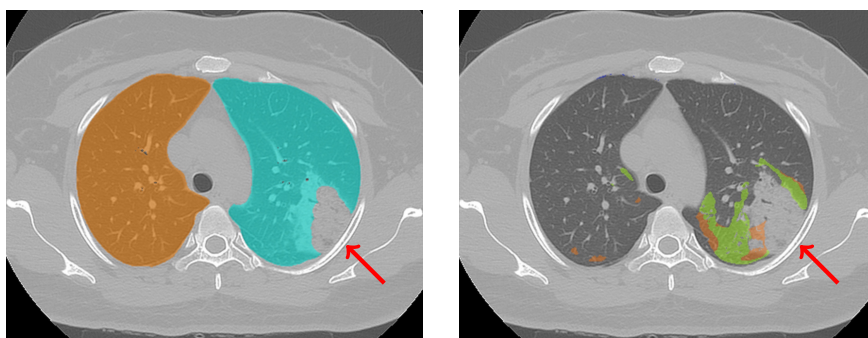

Figure 12

Left/right lung labeling error. The segmentation step of LTA may misidentify the boundaries between right and left lung. This error will cause the statistical analysis to be inaccurate. *This error can be identified only by viewing the Lung Label series.* Figure 13 shows Lung Label (left) and LTA Map (right) images for a case that exhibits this error. The red ellipse highlights the area of error.
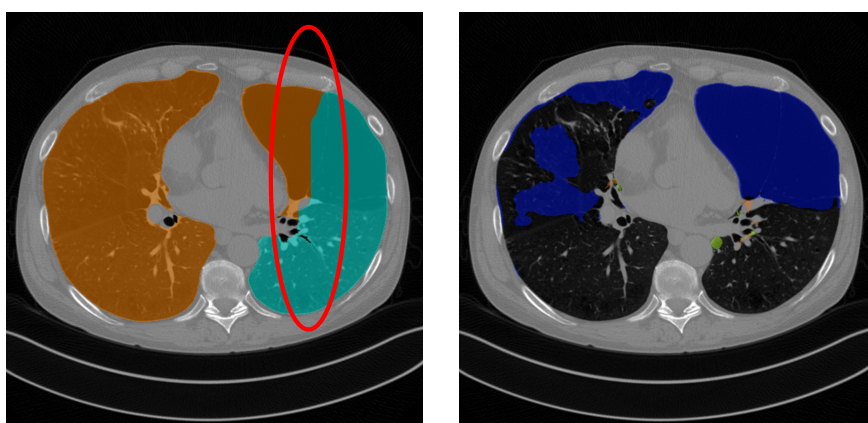

Figure 13

6.2.3   Classification Errors

Misidentified textures due to atelectasis. If atelectasis is present in the CT lung scan, the algorithm may misclassify the lung tissue as a texture that is not normal. This error can be identified by viewing the LTA Map in addition to the original CT scan for the presence of atelectasis. Figure 14 gives an example of this type of error.
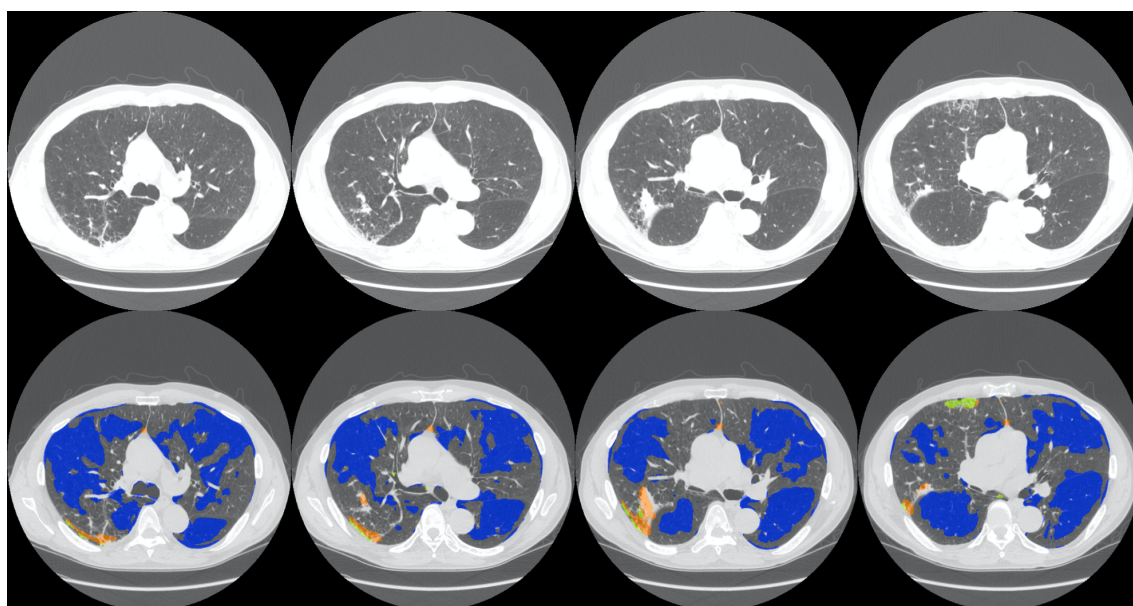

Figure 14: Slices of LTA Map displaying misidentified texture due to atelectasis. First row displays the original CT lung image and second row displays LTA Map of corresponding slices.

7   Command Line Commands

If Imbio CT Lung Texture Analysis™ Software is installed without the Imbio Core Computing Platform (cloud or enterprise options), the Imbio LTA software is executed using the command line. The command line commands needed to run Imbio LTA are found in the Imbio LTA Installation and Quick Start Guide (Document Number: QSG-3).

8   Software Label

CT Lung Texture Analysis Software
Version 2.1

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