Imbio

LUNG DENSITY ANALYSIS™

SOFTWARE USER MANUAL

Contents

IMBIO CT LUNG DENSITY ANALYSIS™ USER MANUAL

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1   Introduction

1.1   Prescription Use Statement

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

1.2   Scope of Manual

This user manual was written for the Imbio CT Lung Density Analysis™ (LDA) 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.

1.3   Product Overview

Imbio's CT Lung Density Analysis™ Software is a set of image post-processing algorithms designed to help radiologists and pulmonologists determine the location and extent of tissue damage in patients with COPD, by providing visualization and quantification of areas with abnormal CT tissue density. The LDA Software runs automatically on the input CT series, with no user input or intervention. The LDA Software consists of the Functional Assessment and the Inspiration Assessment.

The Imbio CT Lung Density Analysis™ Functional Assessment performs image segmentation, registration, thresholding, and classification on CT images of human lungs. The Functional Assessment performs the four algorithms sequentially on two CT scans (inspiration and expiration lung datasets).

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 registration algorithm is to map one lung image onto another, so that a pairwise mapping comparison between lung images can be done. The purpose of the thresholding algorithm is to identify voxels above and below a given threshold for the inspiration series and to identify voxels above and below a given threshold for the expiration series. The purpose of the classification algorithm is to compare inspiration and expiration lung images that have been registered and have gone

through thresholding. Further description of this component is in the Functional Assessment section of the document (Section 4.1).

The Imbio CT Lung Density Analysis™ Inspiration Assessment is a component for users who only acquire inspiration datasets. The Inspiration Assessment performs image segmentation and thresholding on an inspiration CT scan. Volumetric percentages of the lung tissue below the user configurable threshold are calculated. Further description of this component is in the Inspiration Assessment section of the document (Section 4.2).

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

The output provided by the Imbio CT Lung Density Analysis™ Software is a RGB lung image series in DICOM format and a DICOM summary report (Encapsulated-PDF SOPClass or Secondary Capture Image Storage SOPClass).

1.4   Contact Imbio

Imbio LLC
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United States
www.imbio.com

1.5   EU Declaration of Conformity

Imbio declares that this product conforms to the following Standard:

The product complies with the Essential Requirements laid down in Annex I and is CE marked in accordance with Annex II of the European Medical Devices Directive 93/42/EEC as modified by 2007/47/EC.

0086

1.6   Language Translation

Imbio typically creates labeling, including user manuals, in English to satisfy regulatory requirements. If requested by purchasers, the user manual shall be made available in French to the requesters as early as possible.

2   Indications for Use and Requirements

The Imbio CT Lung Density Analysis™ Software provides reproducible CT values for pulmonary tissue, which is essential for providing quantitative support for diagnosis and follow up examinations. The Imbio CT Lung Density Analysis™ Software can be used to support the physician in the diagnosis and documentation of pulmonary tissue images (e.g., abnormalities) from CT thoracic datasets. Three-D segmentation and isolation of sub-compartments, volumetric analysis, density evaluations, and reporting tools are provided.

2.1   Intended Users

The intended user base for the Imbio CT Lung Density 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 and register the scans is dependent on the resolution of the scan; 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 not contraindications or missing information.

2.2.1   Imbio Acquisition Parameters

The Imbio CT Lung Density Analysis™ Software will not generate outputs for scans with acquisition parameters that do not meet the requirements as outlined in the table below. In addition, Imbio CT Lung Density Analysis™ Software **will not generate outputs unless the scan is performed with the patient in a supine position**. This is confirmed by checking the DICOM Patient Image Orientation (DICOM tag 0020,0037). If it is not equal to [1,0,0,0,1,0], then the software will not produce outputs.

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	$\leq$ 4.0 mm
(0018,0050)	Slice Thickness	$\leq$ 4.0 mm
N/A	Field of View	$\geq$ 10.0 x 10.0 x 20.0 cm^3
(0018,1210)	Convolution Kernel	Not an edge enhancing kernel*

*Imbio limits the inputs to images reconstructed with non-edge enhancing kernels. Sharp kernels are not appropriate for Lung Density Analysis. For an exhaustive list of prohibited kernels, see list below.

Unacceptable Kernels
Below is a list of kernels that are not acceptable for Imbio CT Lung Density Analysis™ Software. If an image with one of the following kernels is passed to the software, an error will be raised and the analysis will not run.

    GE: bone+, edge, lung
    PHILIPS: D
    TOSHIBA: FC30, FC31, FC80, FC81, FC82
    SIEMENS:[B/S/U][6-8][0-5][s/f/h], [C/D/H/T][2-8][0-5][s/f/h]*

*This notation is meant to simplify the combination of kernel names. This notation expanded would be the following: B60s, B60f, B60h, B61s, B61f, B61h, B62s, B62f, B62h, B63s, B63f, B63h, B64s, B64f, B64h, B65s, B65f, B65h, B70s, B70f, B70h, B71s, B71f, B71h,...,B80s, B80f, B80h, B81s, B81f, B81h,...,S60s, S60f, S60h, S61s, S61f, S61h... etc.

2.2.2 Imbio Recommended Protocol

For the Imbio CT Lung Density Analysis™ Software, Imbio recommends a 3D volumetric acquisition with pixel spacing less than 1 mm and slice thickness less than 2.5 mm for both inspiration and expiration scans. The images should be reconstructed with a soft tissue/smoothing algorithm without high spatial frequency enhancement. Imbio also requires 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 LDA Software are not limited to the scanners and protocols in the table, but the acquisition parameters should be similar. The Imbio CT LDA 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 and register lungs.

Scanner Make	GE	SIEMENS	PHILIPS 64
Scanner Model	VCT 64	Sensation-64	64 Slice
Scan Type	VCT Helical	Spiral	Axial Helix
Rotation Time (S)	See mA	0.5	0.5
Det. Configuration	64 x 0.625	64 x 0.6	64 x 0.625
Pitch	1.375	1.1	0.923
Speed (mm/rot)	13.75	21.1	0.5
kVp	120	120	120
mA	400 @ 0.5s (Ins) 100 @ 0.5s (Exp)	*Effective mAs*: 200 (Ins) *Effective mAs*: 50 (Exp)	200 mAs (Ins) 50 mAs (Exp)
Dose modulation	Off	CARE Dose 4D Off	Off
Reconstruction			
Algorithm	Standard	B31f	B
Thickness (mm)	0.625	0.75	0.9
Interval (mm)	0.625	0.5	0.45
DFOV(cm)	Lungs*	Lungs*	Lungs*

*Reconstruction field of view should encompass the widest diameter of the lung.

2.2.3   Imbio Recommended Protocol for Low-dose Images

Due to increased image noise, it is especially important that images from low-dose CT scans should be reconstructed using a soft tissue/smoothing kernel OR an iterative reconstruction algorithm. If available, fully iterative reconstructions should be used with the Imbio post-processing filter turned OFF. If iterative re-constructions are not available, the post-processing filter should be turned ON to reduce the effects of noise on LDA measures. For more information on Imbio's post-processing filter, see section 4.3.1. An example low-dose protocol is shown in the table below. Please note that the software operator should be familiar with the effects of x-ray dose and slice-thickness on LDA measurements.

2_INDICATIONS FOR USE AND REQUIREMENTS

Scanner Make	GE	SIEMENS	PHILIPS 64
Scanner Model	VCT 64	Sensation-64	64 Slice
Scan Type	VCT Helical	Spiral	Axial Helix
Rotation Time (S)	See mA	0.5	0.5
Det. Configuration	64 x 0.625	64 x 0.6	64 x 0.625
Pitch	1.375	1.1	0.923
Speed (mm/rot)	13.75	21.1	0.5
kVp	120	120	120
mA	80-160 @ 0.5s (Ins) 100 @ 0.5s (Exp)	*Effective mAs*: 40-80 (Ins) *Effective mAs*: 50 (Exp)	40-80 mAs (Ins) 50 mAs (Exp)
Dose modulation	On	On	On
Reconstruction			
Algorithm	Standard*	B31f*	B*
Thickness (mm)	2-3	2-3	2-3
Interval (mm)	2	2	2
DFOV(cm)	Lungs‡	Lungs‡	Lungs‡

*Fully iterative reconstructions are recommended if available. Otherwise, LDA should be run with the "Filter-ON" option to reduce the impact of quantum noise.

‡ Reconstruction field of view should encompass the widest diameter of the lung.

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. The scan protocol remains the same for expiratory scanning. The patient should be coached for full expiration holds and be capable of retaining the hold for the duration of the scan. Below is a suggested script of how to coach a patient for the inspiratory and expiratory scans.

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

Expiratory CT
For the second part of this scan, I am going to ask you to breathe out and hold it out.
First let's practice:
   Take a deep breath in
   Breath out and hold it - do not breathe
   Breathe and relax
Take a deep breath in
   Let it out
Take a deep breath in
   Let it out
Take another deep breath in
   Let it out and hold it out
   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 Density Analysis™ Software.

3.1 Scan Quality

Lung density values from a CT scan may vary due to different acquisition parameters thus causing variation in LDA results. Sources of variation include but not limited to dose, reconstruction kernel, slice thickness, scanner calibration and respiratory cycle. Users should not compare LDA 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 Density Analysis™ map and 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 2.2.1 and 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 Density 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 Density Analysis™ results should be interpreted with a knowledge of the location and extent of any comorbidities or anomalous pathologies.

Lung Density Analysis™ was designed and validated on adult lungs and has not been validated on children.

4 Components

The Imbio CT Lung Density Analysis™ Software has two components for processing data, the Functional Assessment and the Inspiration Assessment. All outputs generated by Imbio CT Lung Density Analysis™ Software are DICOM compatible.

4.1 Functional Assessment

The Functional Assessment takes two CT scans as input, an inspiration and an expiration scan. The process performs segmentation on both images and then registers the inspiration image to the expiration. Thresholding is applied to the images and then each voxel pair is classified. The process outputs an RGB image with color overlay classifying each lung voxel as either "Normal", "Functional Low Density Area" or "Persistent Low Density Area". In addition, a Functional Assessment Report is generated summarizing results, for more details see Section 5.3.

4.2 Inspiration Assessment

The Inspiration Assessment takes one CT scan as input, a full inspiration scan. The process performs segmentation on the inspiration image and then thresholding. The output image is an RGB image with color overlay classifying lung voxels below the inhalation threshold. In addition, a report is generated summarizing results.

4.3 Optional Features

Both Functional Assessment and Inspiration Assessment have the following additional features for processing; filtering, adjustable thresholding, selectable report format and personalizing report with an institution logo.

Functional Assessment has an additional feature not available for Inspiration Assessment: select registration direction. By default, the inspiration scan is registered to the expiration scan, however the user can select the option to register the expiration scan to the inspiration scan.

Inspiration Assessment has two optional features not available for Functional Assessment: adjustable percentile and an additional LungMap™ report.

Important Note: If Imbio CT LDA Software is installed with the Imbio Cloud Platform or the Imbio Enterprise Platform, user preferences for optional features are set only at installation.

4.3.1 Filtering

Before classification, a noise reducing filter is applied to the lung datasets by default. This filtering can be turned off by the user.

There are tradeoffs between the two options, unfiltered and filtered. Filtering before classification allows for robust classification of low signal-to-noise ratio (SNR) images (high specificity) at the expense of missing small areas of low attenuation (reduced sensitivity). Not filtering before classification allows for identification of small areas of low attenuation areas (high sensitivity) at the expense of small erroneous classifications of low attenuation areas in noisy images (reduced specificity).

The user is allowed to determine if filtering is appropriate for classification for the input images based on the patient of interest and the noise level of the scans.

4.3.2 Adjustable Thresholds

The inhalation threshold and exhalation threshold (if applicable) may be determined by the user and provided as inputs to the LDA Software. Values for thresholds are given in Hounsfield units (HU) and are allowed in the range of -1024 HU and -500 HU.

The default inhalation threshold is -950 HU and the default exhalation threshold is -856 HU (Nature Medicine, Volume 18, Number 11, November 2012, Pages 1711-1715.).

4.3.3 Report Format

The format of the output report can be selected by the user. The two SOPClasses currently supported for the output report are Encapsulated PDF Report and Secondary Capture Image Storage. The user may select either one of these formats to be generated or both formats to be generated as output. The default format for the report is Encapsulated PDF Report.

4.3.4 Institution Logo

The LDA summary reports display the Imbio logo in the upper left corner of the report. This logo can be replaced with an alternate logo from the user's institution. The maximum logo size is 1.4 cm height by 6.0 cm width. Minimum resolution is 300 dots per inch (dpi). Given these requirements, either square or horizontal shaped logos are recommended, vertical oriented (tall) logos will not elegantly fit in the report header. The logo format can be either PNG or JPEG.

4.3.5   Registration Direction (Func. Assessment Feature Only)

The Functional Assessment registers the inspiration scan to the expiration scan by default. If desired, the user can reverse this registration direction and have the expiration scan registered to the inspiration scan.

4.3.6   Adjustable Percentile (Insp. Assessment Feature Only)

The Inspiration Assessment calculates PercX (where "X" corresponds to the desired percentile), the HU value corresponding to the Xth percentile of lung intensity values. The percentile used to compute the percentile low attenuation area can be adjusted to be any value between 0 and 100. The default value for X is 15.

4.3.7   Additional LungMap Report (Insp. Assessment Feature Only)

The Inspiration Assessment can output an additional report, the LungMap™ Report. This report simplifies the Inspiration Assessment Report results and contains information about general benefits of smoking cessation. For more information on the contents of the LungMap™ Report, see Section 6.4.

4.3.8   Additional Patient Information

Both the Inspiration and Functional Assessment Reports can be generated with an optional second page containing a list of additional information about the patient and their CT scan. The list is customizable and can display any information that is contained within the CT DICOM image meta-data.

5   Functional Assessment

The Functional Assessment generates two main outputs; a Functional Assessment Map and a Functional Assessment Report.

5.1   Inputs

The LDA Functional Assessment takes two CT scans as input, one taken during inspiration and the other during expiration. The input datasets must have the same Patient Name and Patient ID. The user may also input an inhalation threshold, an exhalation threshold, select the registration direction and/or turn filtering off. For more information on optional inputs, see Section 4.3.

5.2   Functional Assessment Map

The Functional Assessment Map is a DICOM Secondary Capture Image with voxel data that is the original expiration image with an RGB overlay. The RGB overlay color codes each lung tissue voxel, identifying the lung tissue as one of three classification categories. The classification categories are defined by an inhalation threshold (in HU), an exhalation threshold (in HU), lower limit threshold of -1024 HU and an upper limit threshold of -500 HU. See Section 4.3.2 for more information on input thresholds. Below are the definitions of the classification categories and the corresponding color of the Functional Assessment Map voxel data.

GREEN   -   **Normal**
                       Voxels with HU higher than inspiration threshold
                       and higher than expiration threshold
YELLOW   -   **Functional Low Density Area**
                       Voxels with HU higher than inspiration threshold
                       and lower than expiration threshold
RED   -   **Persistent Low Density Area**
                       Voxels with HU lower than inspiration threshold
                       and lower than expiration threshold

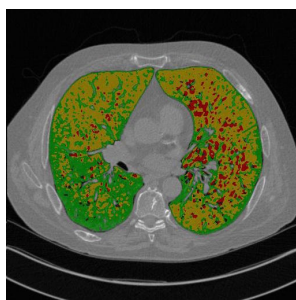An example of a slice from the Functional Assessment Map is shown below in Figure 1.

Figure 1: Slice of Functional Assessment Map

5.3 Functional Assessment Report

The Functional Assessment Report is a DICOM compatible format. It is either a Encapsulated PDF Report SOPClass or Secondary Capture Image Storage SOPClass. The report summarizes the results of the Functional Assessment Map. It contains patient information, lung slice images, and tables displaying results. An example report is shown below in Figure 2.
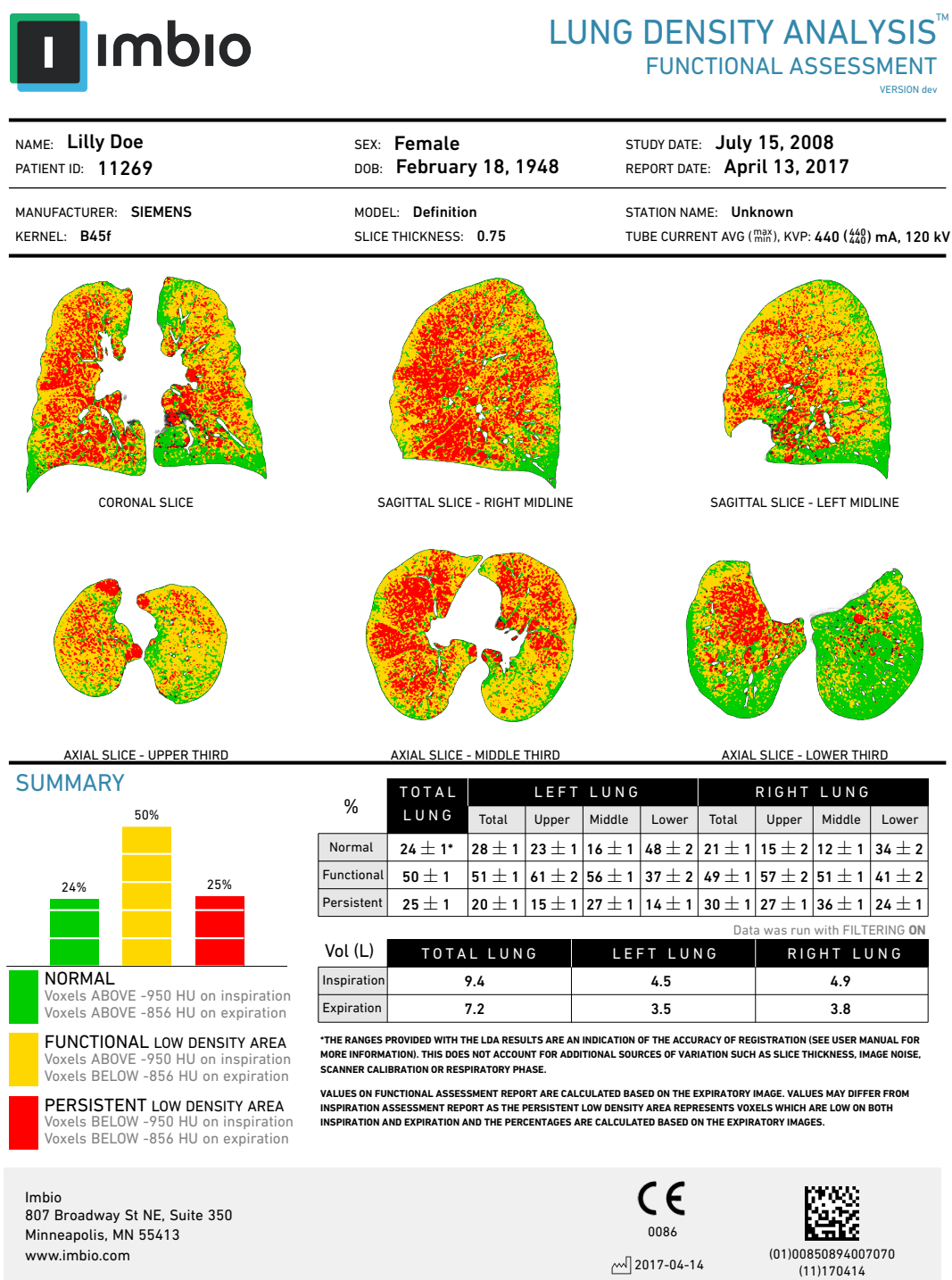
Figure 2: Example Functional Assessment Report

5_FUNCTIONAL ASSESSMENT

Report Header

Of particular importance in the report header are the reconstruction kernel, slice thickness, and x-ray tube current. These parameters affect either the effective resolution of the CT image and/or the dose, which in turn affect repeatability of lung density measurements. When comparing follow-up lung density measurements, it is important that changes in these parameters are observed and accounted for during assessment.

Report Statistics

The results summarized within the report include the percent of lung tissue identified as Normal, Functional Low Density Area and Persistent Low Density Area for right, left and total lung. Percentages are also broken down for upper, middle and lower thirds for the right and the left lung. Percentages are presented with estimated variations. The values are based off of the estimated accuracy of the registration algorithm. Large estimated variations typically reflect a nonuniform density pattern that is sensitive to registration accuracy. If the density patterns are uniform and insensitive to registration accuracy, the estimated variations will be small. Therefore, the estimated variations can be thought of as a measure of confidence in the reported values based on the expected accuracy of the registration process.

The Imbio registration algorithm will not produce a perfect transformation between the inspiration and expiration images. The effect of the registration accuracy was assessed by comparing the automated Imbio registration to a perfect registration found through manual landmark definition. LDA percentages were calculated for the automated Imbio registration and for the perfect registration for multiple subjects. It was found the LDA percentages for the automated Imbio registration all fell within the variation of the LDA percentages for the perfect registration.

Volumes of the segmented inspiration and expiration lungs are also reported. Total lung volumes are given as well as the volumes for the right and left lung.

Report Graphics

The report displays six images, displaying slices of the Functional Assessment Map in different orientations. The six images include, one coronal slice, mid sagittal slice of the right lung, mid sagittal slice of the left lung, and three axial slices, the middle of the lower, middle and upper third of the lungs. Below is an example of the images found in the report.
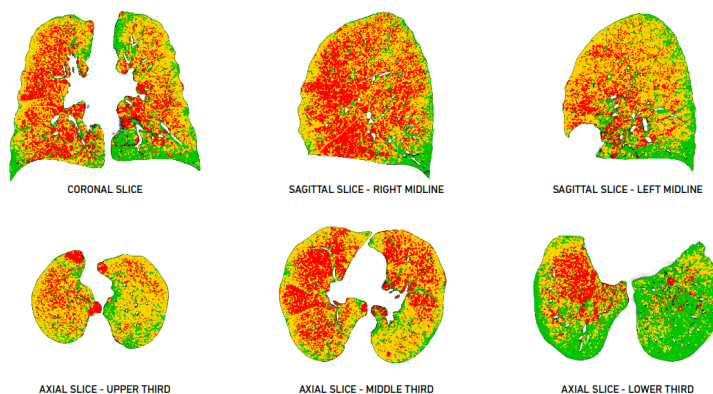

CORONAL SLICE   SAGITTAL SLICE - RIGHT MIDLINE   SAGITTAL SLICE - LEFT MIDLINE

AXIAL SLICE - UPPER THIRD   AXIAL SLICE - MIDDLE THIRD   AXIAL SLICE - LOWER THIRD

Figure 3: Example of lung images found in Functional Assessment Report

Additional Patient Information

An optional second page containing additional patient information can be added to the functional report. Any information stored within the CT DICOM image metadata can be added to the list on the second page of the report. An example showing the Institution Name, Referring Physician Name, and Product Name is shown below.

NAME: **Lilly Doe**	SEX: **Female**	STUDY DATE: **July 15, 2008**
PATIENT ID: **11269**	DOB: **February 18, 1948**	REPORT DATE: **June 29, 2017**

Institution Name:	**Unknown**
Study Time:	**15:49:34**
Performing Physicians Name:	**Unknown**
Referring Physicians Name:	**Unknown**
Accession Number:	**Unknown**
Product Name:	**Imbio LDA Inspiration Assessment 2.4.5**

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Figure 4: Example of the optional second page of the LDA report.

6 Inspiration Assessment

The Inspiration Assessment of the LDA Software generates two main outputs; the Inspiration Assessment Map and the Inspiration Assessment Report.

6.1 Inputs

The Inspiration Assessment component only takes an inspiration scan as input. In addition, the user may input an inhalation threshold, input a percentile for PercX calculation, create the additional LungMap™ Report and/or turn filtering off. For more information on optional inputs, see Section 4.3.

6.2 Inspiration Assessment Map

The Inspiration Assessment Map is a DICOM Secondary Capture Image with voxel data that is the original inspiration image with an RGB overlay. The RGB overlay identifies two classes of tissue. First, voxels that are labeled as lung tissue by the segmentation algorithm and have a HU value equal to or above the inhalation threshold are identified by a translucent blue color. The blue voxels can be used to assess the quality of the lung segmentation. Second, voxels that are labeled as lung tissue by the segmentation algorithm and have a HU value below the inhalation threshold are identified by an opaque red color. The inhalation threshold may be determined by the user and provided as inputs to the Imbio CT Lung Density Analysis™ Software. If thresholds are not defined by the user, the inhalation threshold defaults to -950 HU.

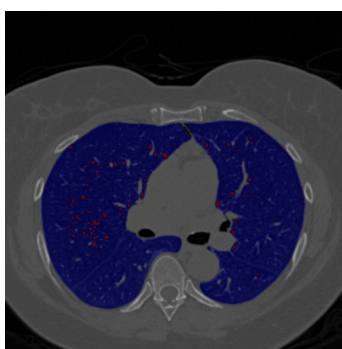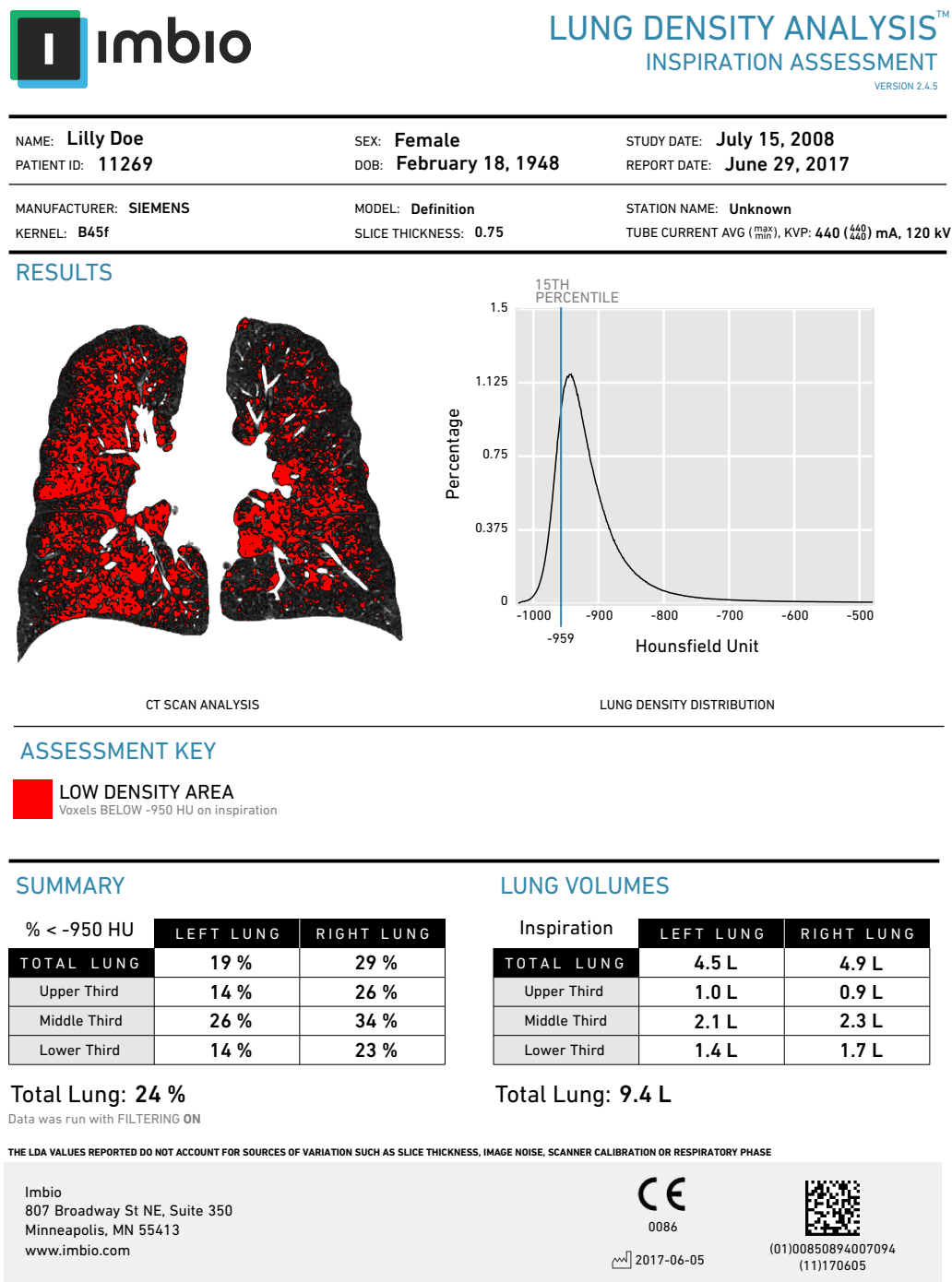An example of a slice from the Inspiration Assessment Map is shown below in Figure 4.

Figure 4: Slice of Inspiration Assessment Map

6.3 Inspiration Assessment Report

The Inspiration Assessment Report is a DICOM compatible format. It is either a Encapsulated PDF Report SOPClass or Secondary Capture Image Storage SOPClass. The report summarizes the results of the Inspiration Assessment Map. It contains patient information, lung slice images, charts and tables displaying results. An example report is shown below in Figure 5. As explained in Section 5.3, it is important to note the image acquisition parameters. Please see Section 5.3 for more details.

Figure 5: Example Inspiration Assessment Report

6_INSPIRATION ASSESSMENT

Report Statistics

The results summarized within the report include the percent of lung tissue below the inhalation threshold for right, left and both lungs. Percentages are also broken down for upper, middle and lower thirds for the right and the left lung. Volumes of the segmented inspiration lungs are also reported. Volumes are broken down between upper, middle and lower thirds for the right and left lung.

Report Graphics

The report displays an image of the mid coronal slice of the Inspiration Assessment Map. In the image shown in the report, only the voxels that are labeled as lung tissue by the segmentation algorithm and have a HU value below the inhalation threshold are shown. Since the quality of the segmentation cannot be adequately assessed by one coronal slice, the blue overlay discussed above (in Section 6.2) is not included. Below is an example of the image found in the report.
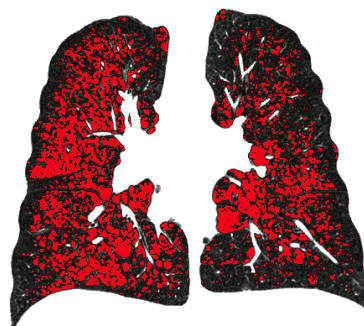
CT SCAN ANALYSIS

Figure 6: Example of lung image in Inspiration Assessment Report

The other graphic in the report is the Density Histogram. This plot visually displays the percentage of lung voxel density at each Hounsfield Unit for both lungs. In addition, a line corresponding to the PercX measurement (see Section 4.3.6 for details about PercX) is shown on the histogram. Below is an example of the image found in the report.
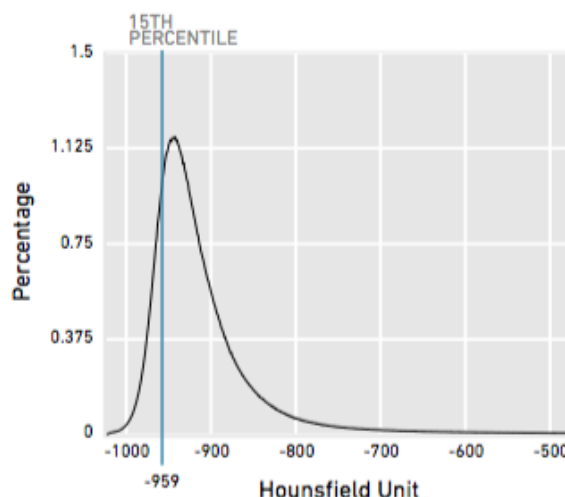

Figure 7: Example of Density Histogram in Inspiration Assessment Report

Additional Patient Information

An optional second page containing additional patient information can be added to the inspiration report. As it does not differ from the second page of the functional report, please refer to section 5.3 for more details.

6.4 LungMap™ Report

The LungMap™ Report is an optional report that is generated in addition to the Inspiration Assessment Map and the Inspiration Assessment Report. The LungMap™ Report is a DICOM compatible format. It is either a Encapsulated PDF Report SOPClass or Secondary Capture Image Storage SOPClass. The report contains the percentages of lung volume below and above the inspiration threshold. The report also contains an image of the lung and a table of benefits of smoking cessation. An example report is shown below in Figure 8.

Figure 8: Example LungMap™ Report
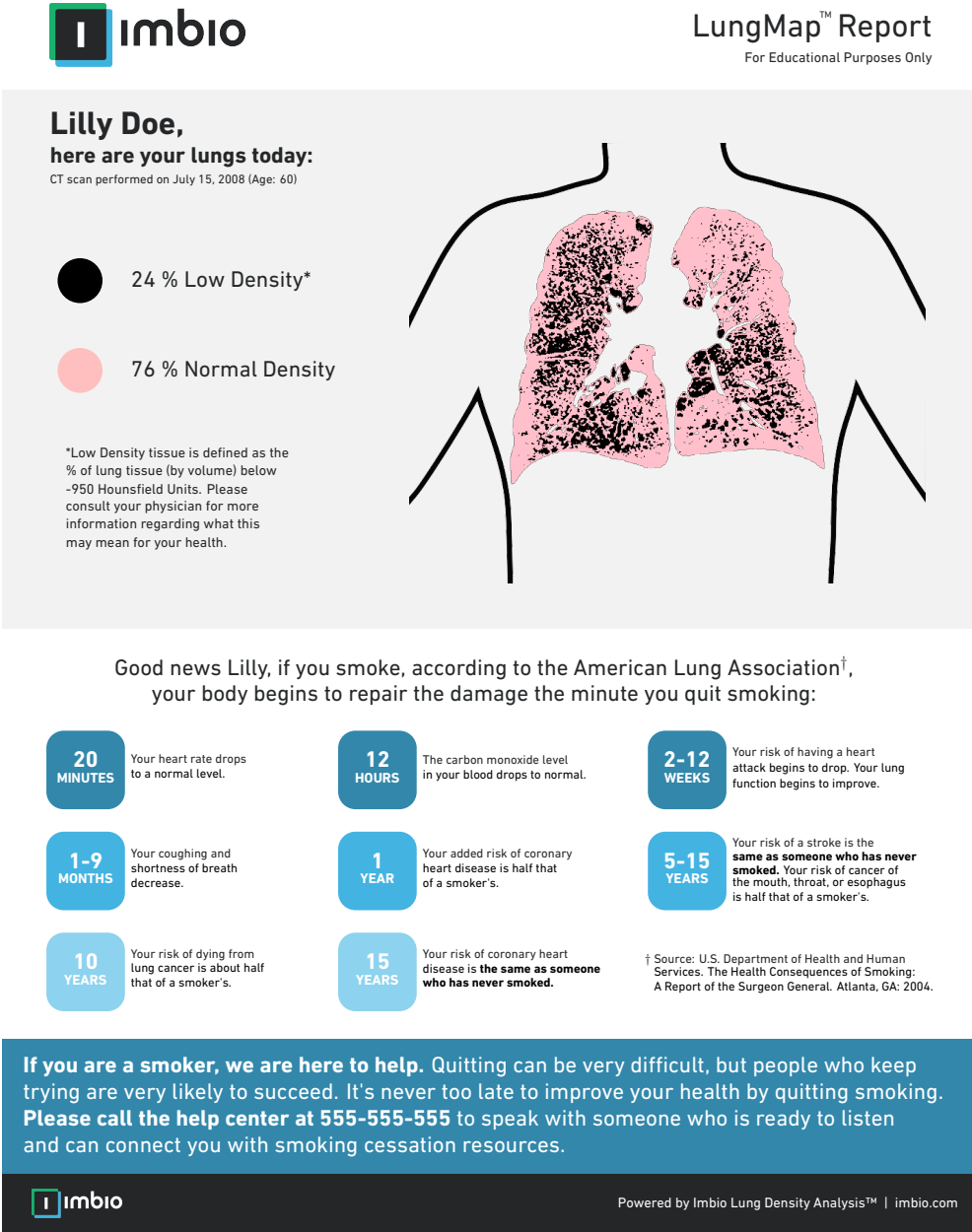
6_INSPIRATION ASSESSMENT

Report Statistics
The statistics within the report are limited to the total percentages of lung volume below and above the inspiration threshold. Unlike the Inspiration Assessment Report, the lung volumes are not included in the LungMap™ Report.

Report Graphics
The LungMap™ report displays an image of a coronal slice of the Inspiration Assessment Map towards the center of the lungs that has percentage of pixels below the threshold similar to the percentage below the threshold for the entire lung. The color of the lung pixels on this image slice imitates the colors of the physical lung; pink for normal density tissue and black for low density tissue. The image has an outline of the body outside of the lungs to give a clearer picture of the orientation and position of the lungs in the patient's body. Below is an example of the image slice found in the report.
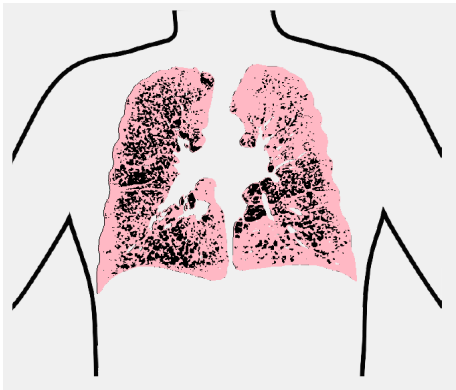

Figure 9: Example of lung image in LungMap™ Report

The other graphic in the report is a table of smoking cessation benefits (Figure 10). This table remains the same and does not change on a patient to patient basis.
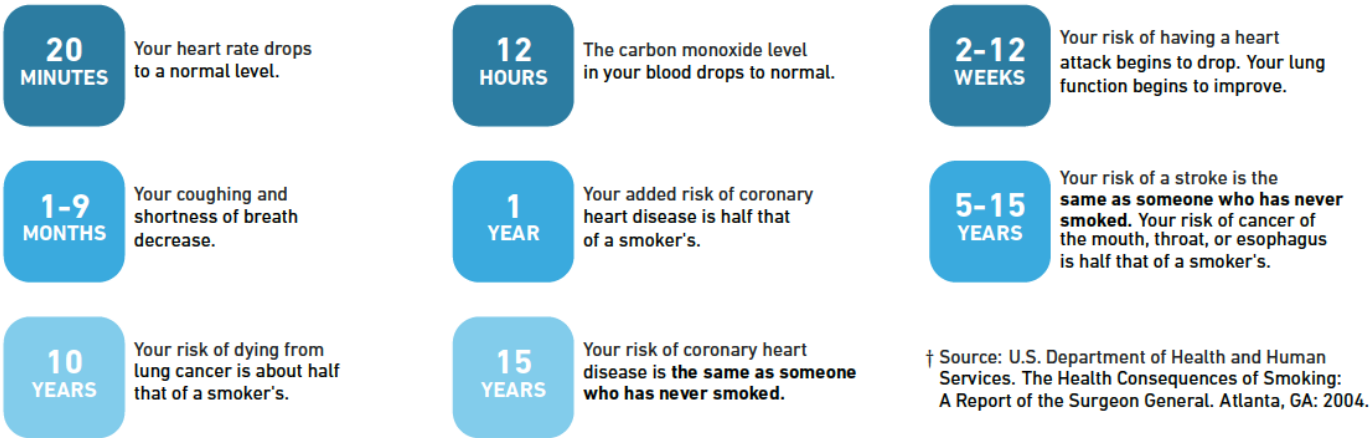

20 MINUTES	Your heart rate drops to a normal level.	**12 HOURS**	The carbon monoxide level in your blood drops to normal.	**2-12 WEEKS**	Your risk of having a heart attack begins to drop. Your lung function begins to improve.
1-9 MONTHS	Your coughing and shortness of breath decrease.	**1 YEAR**	Your added risk of coronary heart disease is half that of a smoker's.	**5-15 YEARS**	Your risk of a stroke is the **same as someone who has never smoked.** Your risk of cancer of the mouth, throat, or esophagus is half that of a smoker's.
10 YEARS	Your risk of dying from lung cancer is about half that of a smoker's.	**15 YEARS**	Your risk of coronary heart disease is **the same as someone who has never smoked.**	† Source: U.S. Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta, GA: 2004.	

Figure 10: Table of Smoking Cessation Benefits

7 Possible Encountered Exceptions

The Imbio CT Lung Density 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.

7.1 Input Errors

ERROR: Input data invalid::
This error occurs if one or more acquisition parameters do not meet Imbio's requirements. For the details on each required parameter, see Section 2.2.1.

ERROR: Input images have same Series Instance UID
This error occurs when both input images have the same Series Instance UID. The Series Instance UIDs must be unique for each input image. Check the DICOM attributes of the uploaded series.

7.2 Segmentation Errors

ERROR: Could not extract airways
ERROR: Could not separate lungs
ERROR: Could not find trachea
ERROR: No lungs found

Theses errors indicate an exception in the segmentation step of the Imbio CT Lung Density Analysis™ Software. Possible causes include the input image does not contain lungs or the input image is noisy.

ERROR: Lung larger than the expected size range
ERROR: Lung smaller than the expected size range

These errors indicate that the segmented lungs do not fall within the expected range of volumes. This could be due to a poor segmentation where non lung tissue was misidentified as lung or lung tissue was excluded from the segmentation. These errors could also be a result of a patient with anomalous anatomy.

ERROR: Airways larger than the expected size range
ERROR: Airways smaller than the expected size range

These errors indicate that the segmented airways do not fall within the expected range of volumes. This could be due to a poor segmentation where airways bled into the lung or only the trachea was able to be identified. These errors could also be a result of a patient with anomalous anatomy.

7.3   Registration Errors

```
ERROR: Borders metric indicates poor registration
ERROR: Similarity metric indicates poor registration
```

These errors indicate that the registered image does not meet the required Imbio standards. A poor registration could be due to a large difference in size between the two input images or a poor segmentation.

8 Considerations to Reduce Risk

8.1 Protocol

Users must follow CT protocol as seen in Section 2.2.

8.2 Expected Performance

The accuracy of the LDA Functional Assessment measurements is primarily determined by the quality of the image registration. An estimate of the accuracy of the measurements is given in the form of a range for each measurement on the output report (Figure 11).

%	TOTAL LUNG	LEFT LUNG				RIGHT LUNG			
		Total	Upper	Middle	Lower	Total	Upper	Middle	Lower
Normal	24 ± 2*	27 ± 2	23 ± 2	16 ± 1	48 ± 3	21 ± 2	15 ± 2	12 ± 1	34 ± 3
Functional	50 ± 1	51 ± 2	61 ± 3	56 ± 2	37 ± 4	49 ± 2	57 ± 3	51 ± 2	41 ± 4
Persistent	25 ± 1	20 ± 1	15 ± 1	27 ± 2	14 ± 2	30 ± 1	27 ± 2	36 ± 2	24 ± 1

Figure 11: Chart of LDA measurements on the Functional Assessment Report
The arrows indicate the estimated variation of the LDA measurement.

These ranges of values represent an estimate of how the measurement values would change if the images were translated in all directions within the range of the estimated accuracy of the image registration process. Note that the Imbio LDA algorithm is deterministic, meaning that the LDA measurements will be identical for repeated analyses on the same input data set. Therefore, the major determinant of measurement precision is the noise level in the input images. The noise level of the input images should be considered when comparing measurements from multiple acquisitions.

8.3   Algorithm Limitations

The Imbio CT Lung Density Analysis™ Software checks input parameters and notifies users with warning or error messages. Even so, there are a small number of cases where no warning or error is detected and the output report is generated with potentially misleading results. Below are examples. Users of the software should look for this type of output. If present, the results should not be used. The Imbio CT Lung Density Analysis™ Software should only be used by intended users as specified in Section 2.1.

1. Misidentified trachea: During segmentation, the top of the left or right lung may be misidentified as the trachea. This will lead to a small portion of the lung to be excluded from analysis. This error can be identified by viewing the output Functional Assessment Map. Figure 12 gives an example of this type of error.
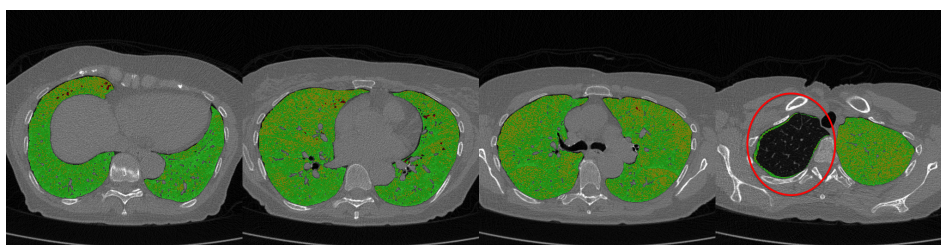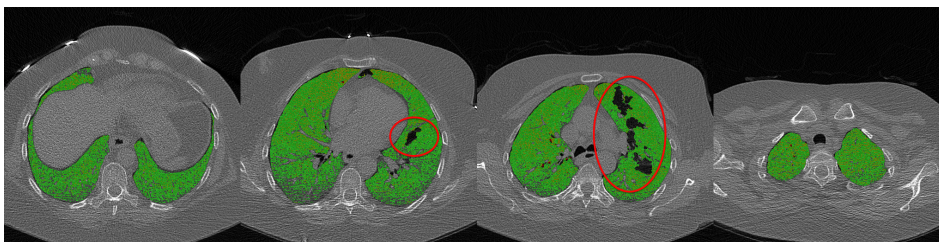

Figure 12: Slices of Functional Assessment Map showing misidentified trachea error.

2. Missing lung: During segmentation, only one lung may be identified. With this error, a warning is generated notifying the user that only one lung was identified. Figure 13 shows an example of the Functional Assessment Map when only one lung is identified.
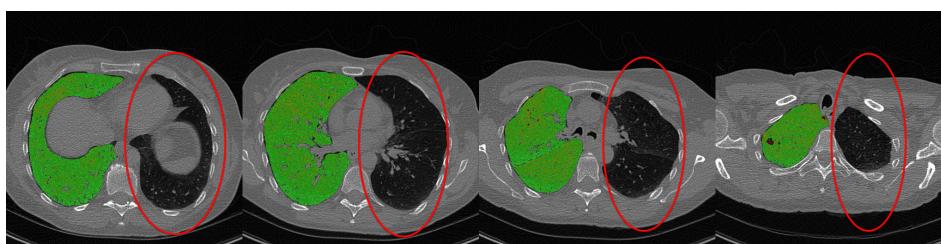
Figure 13: Slices of Functional Assessment Map showing missing lung error.

3. Airway bleeding into lungs: During segmentation, part of the lungs may be misidentified as the major airways. This will lead to a small portion of the lung to be excluded from analysis. This error can be identified by viewing the output Functional Assessment Map. Figure 14 gives an example of this type of error.

Figure 14: Slices of Functional Assessment Map showing airway bleeding into lung error.

4. Esophagus inclusion: During segmentation, the esophagus may be misidentified as part of the lungs. This will lead to an addition of tissue to the analysis. An example of this type of error is shown in Figure 15.
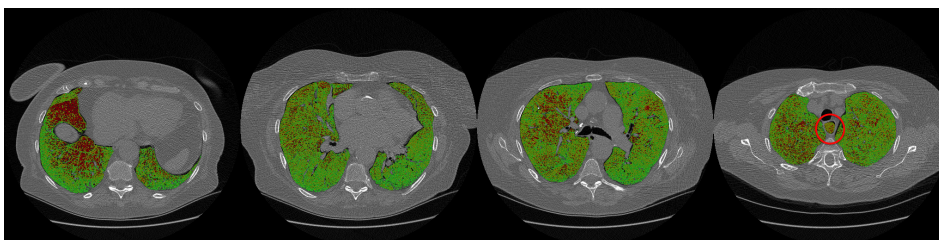
Figure 15: Slices of Functional Assessment Map showing esophagus inclusion error.

5. Gas inclusion: If gas is present below the lungs within the scan, during segmentation, the gas may be misidentified as lung tissue. This will lead to an addition of tissue to the analysis. Figure 16 gives an example of this type of error.
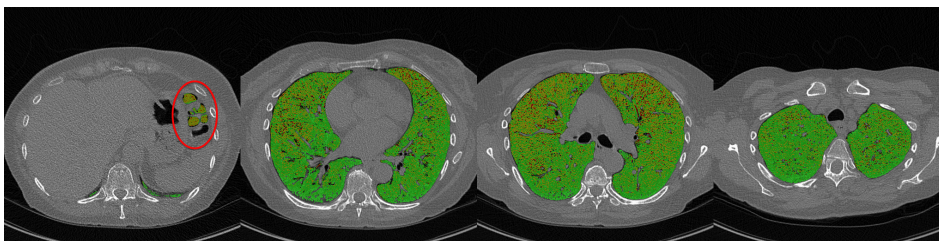
Figure 16: Slices of Functional Assessment Map showing gas inclusion error.

6. Misaligned Registration: During registration, lungs could be poorly registered but still generate a report. This will lead to a portion of the lung to be excluded from analysis as well as an inaccurate classification of misaligned voxels. Two examples of this error can be seen in Figure 17 and Figure 18.
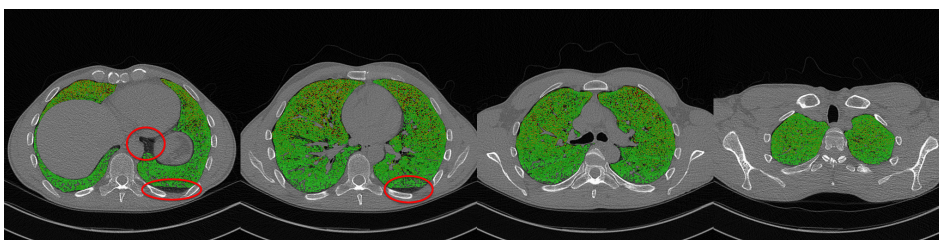

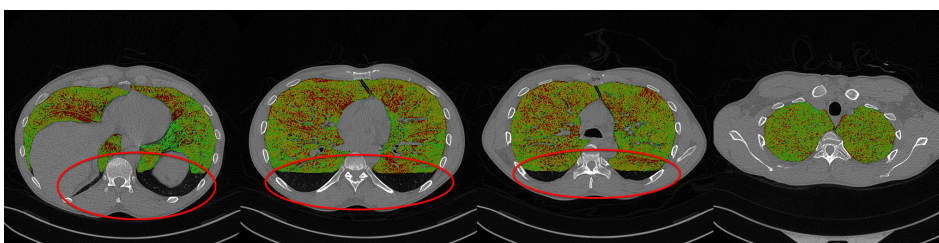Figure 17: Slices of Functional Assessment Map showing misaligned registration error.

Figure 18: Slices of Functional Assessment Map showing misaligned registration error.

7. Lung tissue exclusion due to dependent atelectasis: If a patient has dependent atelectasis, some of the lung tissue will not be correctly identified as lung tissue. This will lead to a portion of the lung to be excluded from analysis. This portion of the lung that is excluded is considered to be Normal tissue. The collapsed alveoli is due to the patient laying down for the scan. As a result of the excluded 'Normal Tissue', values may but slightly skewed. The global Normal value is expected to be at most, a few percent lower than the true value. This error can be identified by viewing the output Functional Assessment Map. Figure 19 displays an example of this type of error.
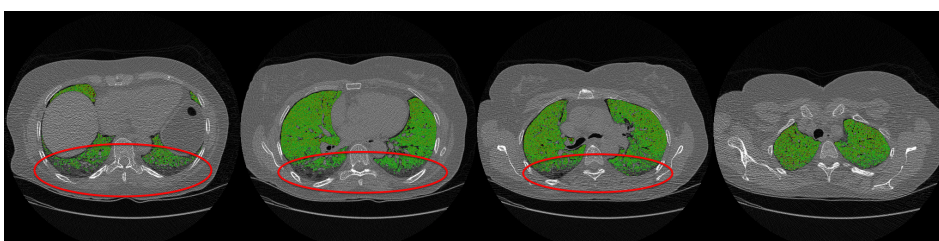

Figure 19: Slices of Functional Assessment Map showing lung tissue exclusion error.

9   Unique Device Identification

9.1   Overview

FDA is establishing a unique device identification system to adequately identify medical devices through their distribution and use. Therefore the label of Imbio's devices include a unique device identifier (UDI) in human- and machine-readable form.

9.2   Printing the Label

Printing barcode symbols is a very complex process. There are so many variables that can affect the quality and readability of your printed barcode symbols, from the quality of the ink and paper stock, to printer resolution, to something as small as lint on the imaging wire of a laser printer; therefore, we highly recommend that you engage a certified barcode print vendor to ensure the quality and readability of your barcode.

10   Command Line Commands

If Imbio CT Lung Density Analysis™ Software is installed without the Imbio Core Computing Platform (cloud or enterprise options), the LDA software is executed using the command line. The command line commands needed to run Imbio LDA are found in the Imbio LDA Installation and Quick Start Guide (Document Number: DES-7034).

11 Software Label